

Trening ved hjertesvikt

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Innhold:

- Trening ved hjertesvikt: kliniske studier
- Dagens anbefalinger
- Litt treningsfysiologi
- Eksperimentelle studier ved hjertesvikt
- Egne resultater
- Planlagte studier

Kliniske studier

| First author | Year | Exercise training characteristics | | | | |
|--------------|------|-----------------------------------|-----------|-------------|-------------|---------------|
| | | Modality | Frequency | Total weeks | Home-based? | Training mode |
| Bellizzi | 1999 | 60 | 3 | 8 | no | 1 |
| Bergersen | 2004 | 60 | 2 | 13 | no | 1,2 |
| Braha | 1998 | 27 | 3 | 16 | no | 1 |
| Cher | 1997 | 65 | 2 | 22 | no | 1 |
| Cher | 2003 | 65 | 3 | 8 | no | 1,2,3 |
| Co-Rita | 2004 | 60 | 3 | 12 | no | 1,2 |
| Corcos | 2004 | 60 | 3 | 12 | no | 1 |
| Dubach | 1997 | 65 | 3 | 8 | no | 1 |
| Marx | 2002 | 65 | 3 | 8 | no | 1 |
| Grosvick | 2003 | 60 | 3-5 | 26 | no | 1,2 |
| Grosvick | 1999 | 60 | 3 | 26 | no | 1 |
| Hachinski | 2000 | 26 | 3 | 26 | both | 1,2 |
| Jain | 1992 | 60 | 3 | 4 | no | 1,2 |
| Kawada | 1994 | 30 | 3 | 3 | no | 1 |
| Kellum | 1999 | 33 | 3 | 14 | no | 1 |
| Kellum | 1996 | 30 | 3 | 13 | no | 1 |
| Kellum | 2003 | 33 | 2-3 | 13 | no | 1 |
| McAfee | 2002 | 60 | 2 | 13 | no | 1,3 |
| Kellum | 2004 | 33 | 2-4 | 26 | no | 1,3 |
| Marx | 1996 | 65 | 3-4 | 3 | no | 2,3 |
| Thibault | 2002 | 33 | 3 | 3 | no | 1 |
| Thibault | 2002 | 33 | 6 | 3 | no | 2 |
| Ohia | 2006 | 60 | 3 | 13 | no | 1,3 |
| Ohia | 2008 | 60 | 3 | 12 | no | 2,3 |
| Ohia | 2008 | 60 | 3 | 12 | no | 2,3 |
| Parodi | 2002 | 60 | 3-5 | 10 | no | 1 |
| Pa | 2002 | 60 | 3 | 10 | no | 1 |
| Ravada | 2003 | 60 | 3 | 17 | no | 1,3 |
| Schick | 2004 | 60 | 4 | 26 | both | 1,2,3 |
| Selig | 2004 | 60 | 3 | 13 | no | 3 |
| Sharma | 1999 | 60 | 3 | 12 | no | 1,2,3 |
| Tan-Lynn | 1997 | 33 | 3 | 8 | no | 1 |
| Tan-Lynn | 2000 | 60 | 3 | 8 | no | 1,3 |
| Tan-Lynn | 1996 | 33 | 3 | 8 | no | 1 |
| Whang | 1999 | 65 | 3 | 12 | no | 1,2 |
| Whang | 1998 | 65 | 3 | 10 | no | 1,2 |
| Yip | 2004 | 60 | 3 | 12 | no | 1,2 |

Training mode: 1=exercise, 2=interval, 3=exercise training of peripheral muscles.

Van Thool 2006

Kliniske studier

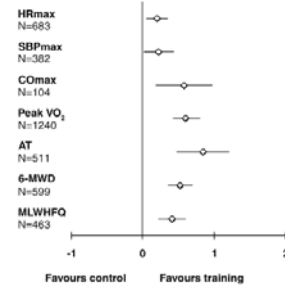


Fig. 2. SMDs of measures of outcome during exercise and quality of life that showed significant change. HR=heart rate, SBP=systolic blood pressure, CO=cardiac output, peak VO₂=peak oxygen uptake, AT=anaerobic threshold, 6-MWD=6-min walking distance, MLWHFQ=Minnesota Living with Heart Failure Questionnaire.

Van Thool 2006

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

Styrketrening

- Bedre arbeidsøkonomi uten å øke oksygenoptak
 - Bedre yteevne – orker mer
 - Bedre Livskvalitet
- Sannsynligvis sikkert

Styrketrening

TABLE 1 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 ± 5 | 161 ± 7* | 213 ± 17** |
| End-diastolic volume (mL) | 215 ± 26 | 260 ± 37 | 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 8 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 ± 0.3 | 6.0 ± 0.3* | 9.3 ± 0.7** |
| Stroke volume (mL) | 77 ± 5 | 85 ± 4 | 87 ± 5** |
| Total peripheral resistance (mm Hg ⁻¹ ·min ⁻¹) | 23 ± 2 | 30 ± 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

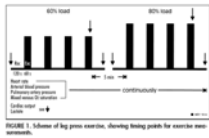
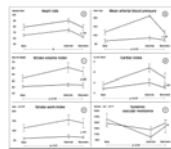


FIGURE 1. Schemes of leg press exercise, showing training paths for exercise sessions.



Meyer 1999

Studiene viser:

- Bedre oksygenopptak
- Bedre yteevne
- Bedre livskvalitet
- Sikkerhet (Meyer 1999)
- Bedre overlevelse?
- MEN
- Ikke rapportert intensitet ved intervalltrening
- Kun to studier med eldre

ESC guidelines 2008:

- Exercise training is recommended to all stable chronic HF patients. There is no evidence that exercise training should be limited to any particular HF patient subgroup (aetiology, NYHA class, LVEF or medication). Exercise training appear to have similar effects whether provided in hospital or at home.
- Class I, evidence A.
- Safety no longer an issue.
- Hvordan trene?

Working Group Report

Recommendations for exercise training in chronic heart failure patients

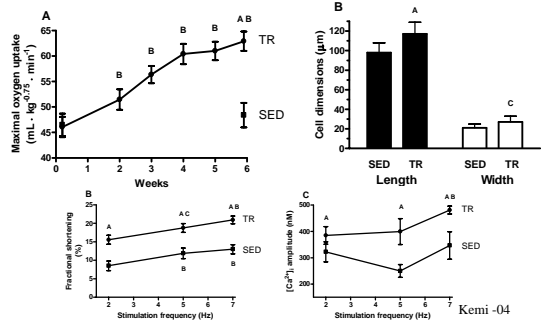
Working Group on Cardiac Rehabilitation & Exercise Physiology and Working Group on Heart Failure of the European Society of Cardiology*

EJH 2001

Anbefalinger:

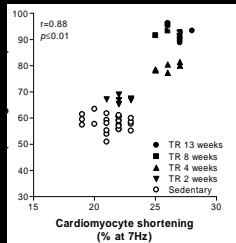
- Gå, sykle
- Intervalltrening: 30 s drag – 50% av max arbeid 40 – 80% av VO_{2max}, 60 sek hvile (10W).
- Gradvis økning i intensitet 40 til 80% forhold til symptomer og klinisk status

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

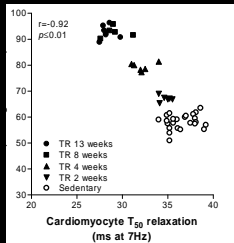


Aerobic Capacity ($\dot{V}O_{2max}$) and Contractility

Systolic Contraction

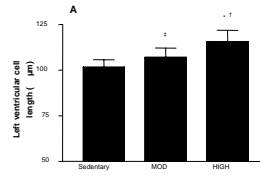
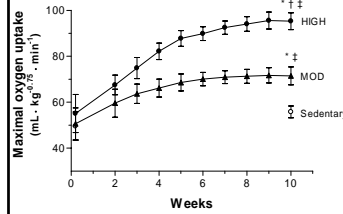


Diastolic Relaxation



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

Intensitet:



Kemi 2004

Stemmer dette hos menneske?

1. Long slow distance running (LSD): The first group performed a continuous run at 70% HR_{max} (137 ± 7 bpm) for 45 min.
2. Lactate threshold running (LT): The second group performed a continuous run at lactate threshold (85% HR_{max} , 171 ± 10 bpm) for 24.25 min.
3. 15/15 interval running (15/15): The third group performed 47 repetitions of 15-s intervals at 90–95% HR_{max} (180 to 190 ± 6 bpm) with 15 s of active resting periods at warm-up velocity, corresponding to 70% HR_{max} (140 ± 6 bpm) between.
4. 4×4 -min interval running (4×4 min): A fourth group trained 4×4 -min interval training at 90–95% HR_{max} (180 to 190 ± 5 bpm) with 3 min of active resting periods at 70% HR_{max} (140 ± 6 bpm) between each interval.

Helgerud 2007

Stemmer dette hos menneske?

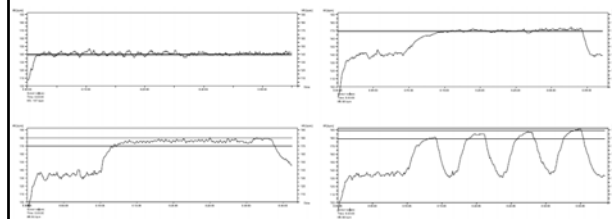


FIGURE 1—Examples of the heart rate response to the four different training regimens in a subject from each group. Subject a (HR_{max} , 200 bpm) long slow distance running (LSD) 70% HR_{max} ; Subject b (HR_{max} , 200 bpm): lactate threshold running (LT), 85% HR_{max} ; Subject c (HR_{max} , 180 bpm): 15-s interval running at 90–95% HR_{max} , with 15 s of active recovery (15/15); Subject d (HR_{max} , 199 bpm): 4×4 -min interval running

Helgerud 2007

Stemmer dette hos menneske?

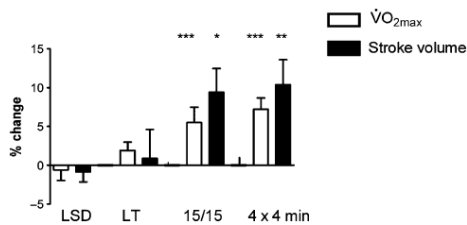
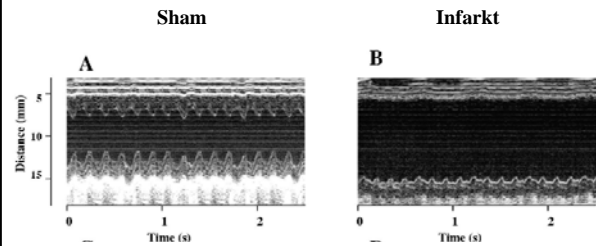


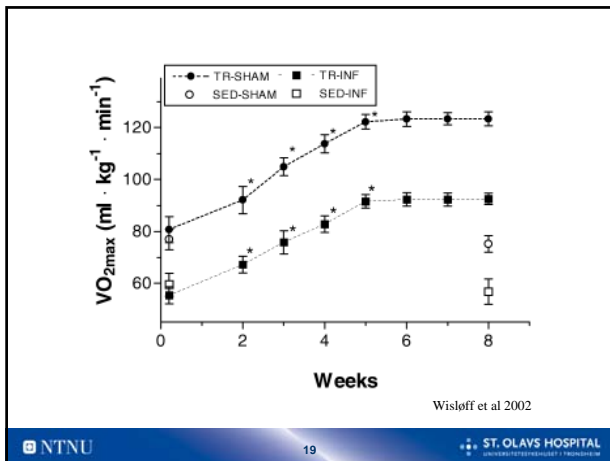
FIGURE 2—Percent change in absolute $\dot{V}O_{2max}$ ($L \cdot min^{-1}$) and absolute stroke volume of the heart ($mL \cdot beat^{-1}$) from pre- to posttraining for each of the groups, presented as mean and SE. Significantly different from pre- to posttraining: * $P < 0.05$, ** $P < 0.01$, *** = $P < 0.001$.

Helgerud 2007

Eksperimentell hjertesviktmodell (rotte med infarkt)



Wisloff et al 2002 (Ekko: Loennechen)



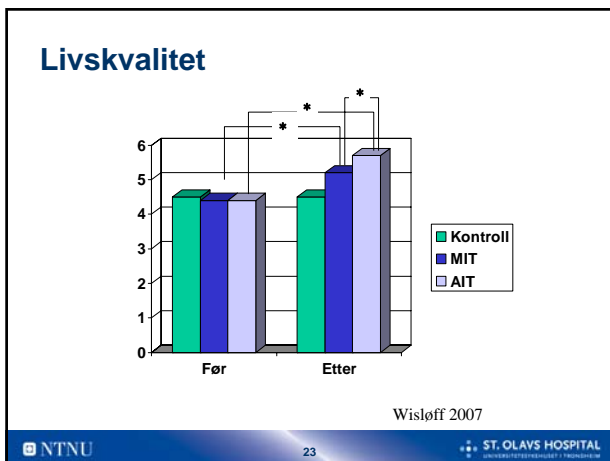
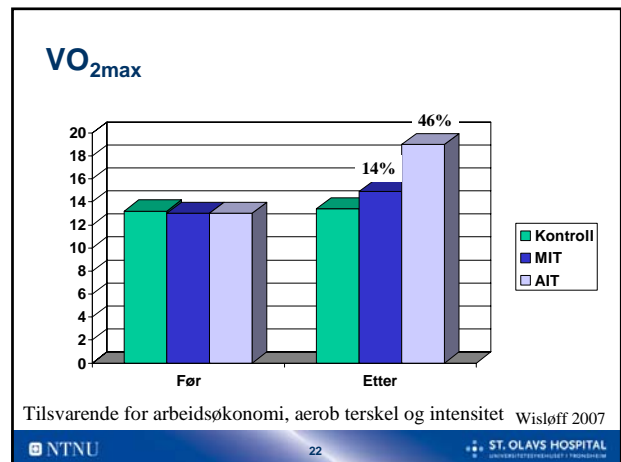
| | SED-SHAM | TR-SHAM |
|-----------------------------------|--------------|-----------------|
| Right ventricular mass (mg) | 318.8 ± 29.2 | 405.1 ± 45.3** |
| Left ventricular mass (mg) | 876.4 ± 74.1 | 1097.6 ± 84.5** |
| Left ventricular cell length (μm) | 119.3 ± 1.8 | 134.3 ± 1.8** |
| Left ventricular 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

NTNU 20 ST. OLAVS HOSPITAL

- ### 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
- NTNU 21 ST. OLAVS HOSPITAL

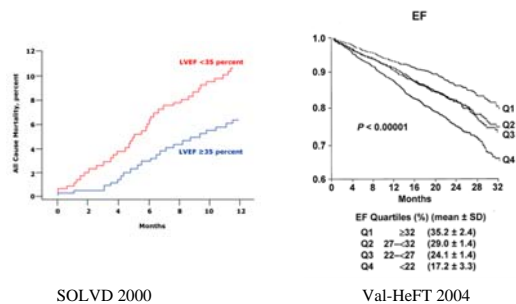


| | Kontroll | | MIT | | AIT | |
|------|--------------|--------------|--------------|--------------|--------------|--------------|
| | Pre | Post | Pre | Post | Pre | Post |
| LVDD | 67.2 ± 8.1 | 67.8 ± 12.5 | 69.1 ± 8.6 | 68.2 ± 6.5 | 66.7 ± 6.8 | 59.0 ± 6.8 |
| LVdV | 250.5 ± 64.4 | 242.1 ± 62.3 | 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

NTNU 24 ST. OLAVS HOSPITAL

Mortalitet og EF:



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%

Konklusjon så langt:

- Høy aerob intensitets trening ved hjertesvikt gir:
 - Bedre hjertefunksjon
 - Revers remodelering
 - Burde kunne gi en vesentlig bedring i overlevelse og kliniske endepunkter
- Det mangler dokumentasjon av
 - Sikkerhet
 - Reproducerbarhet i multisenterstudie
 - Endepunkter
- Nye studier:
 - SMARTEX-HF
 - POLNOR EX

SMARTEX-HF

- Utgått fra Trondheim
- Støttes av European Association of Prevention and Rehabilitation, - Basic science nucleus
- Deltakende sentra:
 - ANTWERP – Viviane Conraads
 - BREMEN – Rainer Hambrecht
 - CARDIFF – Julian Halcox
 - COPENHAGEN – Eva Prescott
 - GLASGOW – Paul MacIntyre / Rachel Myles?
 - LEIPZIG – Axel Linke
 - MUNICH – Martin Halle
 - TRONDHEIM – Asbjørn Støylen
 - Ålesund - Torstein Hole?
 - Levanger – Olaf Kleinau?
 - UTRECHT – Nicolaas de Jonge
 - BERN – NN

SMARTEX-HF

- Design som Wisløff et al 2007
 - Tre armer: kontroll – MCT, AIT
- Reproducerbarhet av resultater. Varighet av effekt.
- Ca 200 pasienter, studien har IKKE power for endepunkter (trend- estimat)
- Ekko (kjernelab Trondheim), MR (kjernelab Zürich), VO_{2max} (kjernelab Trondheim), QoL (Minnesota), molekylærbiologiske analyser
- Finansiering:
 - Søkt Samarbeidsutvalget om et post doktor stipend
 - Søkt kontaktutvalget om 1 mill NOK / år i tre år for midt-Norge og sentral org.
- Samarbeidspartnere bærer egne utgifter

SMARTEX-HF

- Tre armer
- Inklusjon ca 200 pas i.l.a. 1 år.
- Intervensjonsperiode 12 uker
- Observasjonsperiode et år.

POLNOR EX

- Klinisk endepunktsstudie.
- Rogaland (primært senter), Trondheim (m / Ålesund og Levanger?) m/fl, flere sentra i Polen
- 750 pasienter randomisert 3:1, 450 i Polen, 150 i Norge
- To armer 450 til trening 150 til observasjon
- Clinical endpoints
 - 1. All-cause death, all-cause hospitalisations and investigator-determined heart failure hospitalisations
 - 2. Cardiovascular procedures and changes in HF therapy requirements
 - 3. Adverse events monitoring for safety

POLNOR EX

Flow chart of exercise training

| Training Phase | Location | WK | Weekly sessions | Warm-up (min) | Duration (min) | Cool-down (min) | Intensity (of peak HR) | Mode of exercise |
|----------------|-------------|--------------|-----------------|---------------|----------------|-----------------|------------------------|-----------------------------|
| Supervised | Clinic | 1-2 | 2 | 10 | 15-30 | 5 | 75% | Treadmill or cycle |
| Supervised | Clinic Home | 3-6 | 3 | 10 | 30 | 5 | Intervals to 90% | Brisk walking or equivalent |
| Maintenance | Home Clinic | 7-24 7-24 | 3 1 /month | 10 | 30 | 5 | Intervals to 90% | Brisk walking or equivalent |

Finansiering:

- Polsk norsk forskningsfond (OPI): EUR 1,6 mill.
- Budsjett: EUR 2 mill.
 - Hvert land bidrar med EUR 200 000 i tillegg:
 - Trondheim 100 000?
- Inklusjonsstart 2009. Intervensjon ut 2010.
- I Trondheim starter vi inklusjon når inklusjon til SMARTEX er ferdig.