# SUPPELEMENTARY DATA

## Search string

(Fontan OR Fontan-Kreutzer OR (Fontan AND procedure) OR (Fontan AND technique) OR (Fontan–Kreutzer AND procedure) OR (Fontan-Kreutzer AND technique)) **AND** ("cardiac rehabilitation" OR rehabilitation OR exercise\* OR (exercise\* AND capacity) OR (exercise\* AND training) OR (exercise\* AND intervention\*) OR (exercise\* AND therap\*) OR (exercise\* AND rehabilitation))

*Table 1. Study characteristics*. All included studies were characterised based on author, year of publication, study design, number of patients included in the study, type of exercise training, training sessions/week, time/session, training period, homebased vs supervised, and follow-up time.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Year of publication** | **Study design** | **Training group (n)** | **Control group (n)** | **Type of exercise training** | **Sessions/week** | **Time/session** | **Training period** | **Homebased vs supervised** | **Follow-up time** |
| Neidenbach | 2023 | Non blinded, RCT | 20  2 dropouts | 20  1 dropout | IMT | Daily | 3 sets 30 reps | 6 months | Homebased | 6 months |
| Minamisawa | 2001 | Cohort | 11 | 0 | AET | 2-3x | 20-30 min | 2-3 months | 3 weeks supervised  2-3 months homebased | 3 months |
| Opocher | 2005 | Cohort | 10 | 0 | AET | 2x | 30-45 min | 8 months | 3 weeks supervised  Followed by homebased | 8 months |
| Fritz | 2020 | RCT | 20 | 22  At 6 months follow-up control group started IMT till 12 months | IMT | Daily | 3 sets 10-30 reps | 6 months | Homebased, telephone supervised | 6, 12, 18 months |
| Turquetto | 2021 | RCT | AET: 10  IMT: 10 | 12 | AET or IMT | AET: 3x  IMT: daily | AET: 60 min  IMT: 3 sets 30 reps | 4 months | AET: supervised  IMT: first 2 months 1x/wk. Last 2 months 1x/2wks. | 4 months |
| Dulfer  Duppen  Duppen | 2014  2015  2015 | RCT | 26 | 17 | AET | 3x | 60 min | 12 weeks | Supervised | 12 weeks |
| Sutherland | 2018 | Randomised trial | 17 | 0 | AET + resistance training lower limb muscles | 2x | 60 min | 8 weeks | Homebased (n=11)  Supervised (n=6) | 8 weeks |
| Jacobsen  Jacobsen | 2016  2018 | Cohort | 13  11 | 0 | AET + resistance exercises | 3-4x | 45 min | 12 weeks | Homebased | 12 weeks  6 months |
| Dirks | 2020 | Cohort | 18 | 0 | AET (Cycling)+ IMT | AET: 3-6x  IMT: 6-7x | AET: 90 min total  IMT: 30 breaths | 10 months | Homebased | 4 months  10 months |
| Avitabile | 2022 | Cohort | 20 | 0 | Lower extremity focused exercise | 3x | 60 min | 24 weeks | Hybrid: 1 month Homebased | 24 weeks |
| Perrone | 2022 | Cohort | 12 | 0 | AET | 3x | 40 min | 4 weeks | Homebased | 4 weeks |
| Pyykkönen | 2022 | Cohort | 16 | 0 | AET + bodyweight exercises focused on lower limbs | 1-2x | 6-8 exercises | 6 months | Homebased | 6 months |
| Wu | 2018 | Cohort | 11 | 0 | IMT | 5x | 30 min | 12 weeks | Homebased | 12 weeks |
| Hedlund  Hedlund | 2018  2018 | Cohort with controls | 30 | 25 (healthy controls) | AET | 2x | 45 min | 12 weeks | Supervised | 12 weeks  1 year |
| Wittekind | 2018 | Cohort | 10 | 0 | AET + low resistance high repetition strength training | 2x | 60 min | 12 weeks | Supervised | 12 weeks |
| Ait ali | 2018 | Cohort with controls | 10 | 6 | CRT | 1x supervised | Supervised: 120 min  Homebased: 240±90min/wk | 3 months | Supervised + homebased | 3 months |
| Cordina | 2013 | Cohort with controls | 6 | 5 | High intensity total body resistance training focused on calf muscle | 3x | 60 min | 20 weeks | Supervised | 20 weeks, 12 month detrain |
| Longmuir | 2013 | Randomized trial | 30 | 0 | AET + resistance training (play based physical activities) | 1x | 90-120 min | 12 months | Homebased | 6, 12 and 24 months |
| Brassard | 2006 | Cohort with controls | 5 | 9 (7 healthy, 2 Fontan) | AET + resistance training | 3x | 20-30 min | 8 weeks | Supervised (n=2)  Homebased (n=3) | 8 weeks |
| Scheffers | 2023 | Randomized semi-cross-over- controlled trial | 28  Started training immediately: 14 | 14  Start 6 weeks of control period, thereafter 12 weeks of exercise period | Leg focused high weight resistance training + high protein diet | 3x | 45 min | 12 weeks | Supervised | 6 weeks  12 weeks |
| Bano | 2023 | Cohort | 5 | 0 | AET + resistance training | Start: 2x  Increasing to: 5x | 30-45 min | 3 months | Supervised | 12 weeks |
| Laohachai | 2017 | Cohort | 23  4 dropouts | 0 | IMT | Daily | 30 min | 6 weeks | Homebased | 6 weeks |

Abbreviations: N= number of patients. RCT= randomised controlled trial, AET= aerobic exercise training, IMT= inspiratory muscle training. CRT: controlled respiratory training. Wk= week. Reps= repetitions.

*Table 2. Patient characteristics.* Table 2 provides the characteristics of patients included in the studies: age, sex, ventricle type, type of Fontan and age at Fontan completion.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **Age (years),**  mean (range)/mean ± SD | **Sex,**  % female | **Ventricle type,** % left | **Fontan type (number of patients)** | **Age (years) at Fontan completion,** mean (range)/mean ±SD |
| Neidenbach, 2023 | 12,3±2,2 | 25% | 45% | Extracardiac conduit: 37  Lateral tunnel: 4 | 27,5±9,6 (months) |
| Minamisawa, 2001 | 19±4 | 55% | 82% | Direct atrial to pulmonary anastomosis without valve | 14±6 |
| Opocher, 2005 | 8,7±0,6 | 10% | 70% | Total cavopulmonary connection | 1,7±0,8 |
| Dulfer, 2014  Duppen, 2015  Duppen, 2015 | 15±3  15±3  14,8±3,7 | 60% | 69% | Extracardiac conduit: 20  Intra-atrial lateral tunnel: 21  Other: 2 | 3 (2.5-5)  3 (2.5-4)  3 (2.5-4.4) |
| Fritz, 2020 | 28.6 (24.7-36.5) | 50% | 86% | Atrioventricular connection: 8  Atriopulmonary connection: 9  Total cavopulmonary connection: 25 | 6.3 (4.0-9.9) |
| Turquetto, 2021 | 20 (15-25) | 69% | 78% | Extracardiac conduit: 24  Lateral tunnel: 8 | 8 (7-11) |
| Sutherland, 2018 | Homebased: 15±2.7  Hospital based: 16±2.5 | 41% | Not reported | Extracardiac conduit: 15  Lateral tunnel: 1  Atriopulmonary connection: 1 | Not reported,  for all patients last cardiac operation longer than 5 years before enrolment. |
| Jacobsen, 2016  Jacobsen, 2018 | 10 (8-12)  10,5 (9-12) | 55% | 43% | Extracardiac conduit: 12  Lateral tunnel: 2  Patent fenestration: 7 | Not reported,  time since Fontan: 7,4±2,3 |
| Dirks, 2022 | 16,5 (10-43) | 39% | Not reported | Not reported | Not reported |
| Avitabile, 2022 | 15.6 ±1,7 | 50% | 45% | Extracardiac conduit: 14  Lateral tunnel: 6 | Not reported,  time since Fontan: 11.7±3,4 |
| Perrone, 2022 | 24±2,5 (22-27) | 50% | 0% | Not reported | Not reported |
| Pyykkönen, 2022 | 14,5±2,6 (8-18) | 37.5% | 21% | Not reported | 2.9±0,5 |
| Wu, 2018 | 28.8 (25,7-45,5) | 45% | 73% | Extracardiac conduit: 1  Lateral tunnel: 7  Atriopulmonary connection: 3 | 7,8 (3,9-16,5) |
| Hedlund, 2018  Hedlund, 2018 | 14,2±3,2 | 47% | Not reported | Extracardiac conduit (non-fenestrated) | 2.4 (1,1-6,4) |
| Wittekind, 2018 | 12±2,8 (7-18) | 60% | 50% | Extracardiac conduit: 5  Lateral tunnel: 5 | At least 5 years prior to enrolment |
| Ait ali, 2018 | 17,5±3,8 (10,4-22,8) | 13% | 43% | Extracardiac conduit: 10  Intracardiac conduit: 1  Intracardiac tunnel: 2  Kawasahima: 1 | 3,69 (0,8-7,4) |
| Cordina, 2013 | 31±4 | 18% | 82% | *Intervention*  Extracardiac conduit: 1  Atriopulmonary connection: 2  Total cavopulmonary connection: 3  *Control*  Extracardiac conduit: 1  Atriopulmonary connection: 2  Total cavopulmonary connection: 2 | Not reported,  time since last Fontan repair  intervention: 21±1  control: 18±2 |
| Longmuir, 2013 | 9, 1(7,7-10,5) | 41% | 54% | Extracardiac conduit: 53  Lateral tunnel: 7  Bjork procedure: 1 | 2,9 (2,5-3,8) |
| Brassard, 2006 | 16±5 | 43% | 100% | Not reported | Not reported |
| Scheffers, 2023 | 12.9 (10.5-15.7) | 37% | 37% | Intra-artrial later tunnel technique for total cavo-pumonary connection | 2.8 (2,3-3,8) |
| Bano, 2023 | 19.5 (17.6–21.3) | 20% | 40% | Extracardiac conduit (fenestrated): 5 | Not reported,  time since Fontan operation: 17,4 (13,8-18,6) |
| Laohachai, 2017 | 16±2 (12-20) | 48% | 57% | Extracardiac conduit (non-fenestrated) | 5±2 (3-9) |

*Table 3.* Quality assessment RCTS – Cochrane risk of bias tool 2

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | *D1* | *D2* | *D3* | *D4* | *D5* | *Overall risk of bias* |
| *Dulfer*  *Duppen*  *Duppen* | Low risk | Some concerns | Low risk | Low risk | Low risk | Low risk |
| *Fritz* | Low risk | Some concerns | Low risk | Low risk | Low risk | Low risk |
| *Neidenbach* | Low risk | Some concerns | Low risk | Low risk | Low risk | Low risk |
| *Turquetto* | Low risk | Some concerns | Low risk | Low risk | Low risk | Low risk |
| *Scheffers* | Low risk | Some concerns | Low risk | Low risk | Low risk | Low risk |

Table 3 Quality assessment Cochrane risk of bias tool 2. D1: bias arising from the randomization process. D2: bias due to deviations from intended intervention. D3: bias due to missing outcome data. D4: bias in measurement of the outcome. D5: bias in selection of the reported result.

*Table 4.* Quality assessment cohort studies - STROBE checklist

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Minimasiwa | Jacobsen | Sutherland | Hedlund | Laohchai | Longmuir | Opocher | Wu | Cordina | Ait ali | brassard | wittekind | Dirks | Avitabile | perrone | Pykkönen | Bano |
| **Title and abstract** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Design in title | x | x | x | x | x | x | x |  | x | x |  | x |  | x | x | x |  |
| Abstract |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Introduction** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Background/rationales |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Objective |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Methods** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Study design |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Setting |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Participants |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Variables |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Data sources/measurement |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Bias | x | x |  | x | x | x | x | x | x | x | x | x | x | x | x |  | x |
| Study size | x | x | x | x |  |  | x |  | x | x | x |  | x | x | x | x | x |
| Quantitative variables |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Statistical methods |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Results** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Participants |  | x |  |  |  |  | x | x |  | x |  |  |  |  |  |  |  |
| Descriptive data |  |  |  |  |  |  |  |  |  |  |  |  |  |  | x |  |  |
| Outcome data |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Main results |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Other analyses |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Discussion** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Key results |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Limitations |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Interpretation |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Generalisability |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Other** **information** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| funding | x |  |  |  |  |  | x |  |  | x |  |  |  |  | x |  |  |
| Criteria met (%) | 84% | 84% | 93% | 89% | 93% | 93% | 80% | 91% | 89% | 80% | 91% | 93% | 91% | 89% | 80% | 93% | 91% |

Table 4 Quality assessment STROBE checklist. If the items from the STROBE checklist were not or not precisely prescribed in the article the item was marked with a X. Eventually the percentage of the total items that were well prescribed in the article was calculated, demonstrated as ‘criteria met (%)’.

*Table 5. Study observations*. Table 5 provides all observations of the included studies regarding the effect of exercise training programs.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Studies** | **Peak VO2** | **VE/VCO2 slope** | **Peak workload** | **Activity levels** | **Distance walked (6mwt)** | **Cardiac output (MRI or echo)** | **Cardiac biomarkers** | **Lung function** | **Improvement Lower limb muscle** | **Quality of life** | **Adverse events** |
| Neidenbach, 2023 | = | = | = | - | - | - | - | ^ | - | - | No |
| Minamisawa, 2001 | ^ | - | ^ | - | - | - | - | - | - | - | No |
| Opocher, 2005 | ^ | - | - | - | - | - | - | - | - | - | No |
| Fritz, 2020 | = | = | - | - | - | - | - | ^ \* | - | - | Yes |
| Turquetto, 2021 | ^ | = | - | - | ^ | - | - | ^ | - | ^ | No |
| Dulfer, 2014  Duppen, 2015  Duppen, 2015 | = | = | - | -  =  - | - | = | = | - | - | ^ | - |
| Sutherland, 2018 | = | - | = | - | ^ | - | - | - | - | ^ | No |
| Jacobsen, 2016 | ^ | - | - | = | - | - | - | - | - | ^ | No |
| Jacobsen, 2018 | = | - | - | - | - | - | - | - | - | ^ | - |
| Dirks, 2022 | ^ | - | - | - | - | - | - | ^ | - | = | No |
| Avitabile, 2022 | = | - | ^ | = | - | = | - | - | = | = | No |
| Perrone, 2022 | ^ | = | - | - | - | - | ^ | - | - | - | no |
| Pyykkönen, 2022 | = | ^ | ^ | ^ | - | - | - | - | = | - | No |
| Wu, 2018 | = | = | ^ | - | - | = | - | ^ | - | = | No |
| Hedlund, 2018  Hedlund, 2018 | = | = | = | ^ | ^ | - | - | ^ | - | ^ | - |
| Wittekind, 2018 | ^ | ^ | ^ | - | - | = | - | - | - | - | No |
| Ait ali, 2018 | ^ | = | = | - | - | - | - | ^ | - | - | - |
| Cordina, 2013 | ^ | - | ^ | - | - | ^ | - | - | - | - | Yes |
| Longmuir, 2013 | = | - | - | ^ | - | - | - | - | - | - | - |
| Brassard, 2006 | = | = | = | - | - | - | - | = | = | - | - |
| Scheffers, 2023 | ^ | - | ^ | = | ^ | ^ | - | - | ^ | ^ | Yes |
| Bano, 2023 | ^ | = | - | - | - | = | - | - | - | ^ | No |
| Laohachai, 2017 | = | ^ | = | - | - | ^ | - | ^ | - | - | No |

Abbreviations. 6mwt: six minute walking test. - : not reported. =: no significant improvement or decrease, ^: significant improvement. \*: only the lung function oxygen saturation at rest improved.