Better lung function with increased handgrip strength, as well as maximum oxygen uptake, in congenital heart disease across the lifespan

Maia P Smith¹, Jan Müller²,³, Rhoia Neidenbach², Peter Ewert² and Alfred Hager²

Abstract

Background: The respiratory benefits of muscle strength are well-known in heart-healthy populations, but recommendations and research often focus instead on aerobic fitness (peak oxygen uptake) or total activity. Independent benefits of strength thus may be underestimated, especially in congenital heart disease where perceived dangers of certain types of exercise may outweigh perceived benefits. To assess whether it is plausible that pulmonary benefits of strength in heart-healthy populations also apply in congenital heart disease, we simultaneously correlated these patients' lung function with fitness, strength, and cardiac diagnosis.

Methods: Lung function (forced expiratory volume in one second percentage predicted (FEV1%pred)) was modeled as function of handgrip strength, congenital heart disease diagnosis, peak oxygen uptake and the interactions of handgrip with sex and diagnosis in 538 Germans (58% male, ages 6–82 years) in linear models corrected for age, sex, height and weight. Congenital heart disease diagnoses were: complex cyanotic; Fallot/Truncus arteriosus communis (common arterial trunk) (TAC); shunts; transposition of the great arteries (TGA); left heart; and other/none.

Results: Each kg of handgrip was associated with 0.74% higher FEV1%pred (p < 0.001) and handgrip explained almost 10% of variance in FEV1%pred. While some groups had higher FEV1%pred than others (p for global null <0.0001), all experienced similar associations with strength (p for interaction with handgrip >0.10 for both sex and diagnosis.) Correction for peak oxygen uptake eliminated the association with congenital heart disease, but not handgrip.

Conclusion: Strength was associated with better lung function in all ages even after correction for peak oxygen uptake, regardless of sex and congenital heart disease. This suggests that strength may be at least as important for lung function as aerobic fitness. Heart-safe strength training may improve pulmonary function in congenital heart disease.

Keywords

Physical activity, cohort studies, congenital heart defect, exercise, aerobic exercise, isometric activity, risk reduction behavior

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Introduction

Physical activity is commonly understood to improve lung function,¹⁶ but estimated effects and effect sizes depend on the type of activity and the population studied. Associations with total activity, while often assumed,¹ may be detectable in only one sex,⁷ or not at all,⁸ while associations with physical strength are more consistent³,⁹ but also less studied, especially in the population setting. While most evidence and recommendations¹,³,¹⁰–¹² suggest that lung function may be

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improved by physical activity and its sequelae, such as fitness, significant heterogeneity of effect remains. In addition to population characteristics such as age, this heterogeneity may be explained by heterogeneity in physical activity itself.

Physical activities have both static and dynamic components, and the two activity types have different physiological effects. Static activities, such as weightlifting, cause high intramuscular and intrathoracic pressures with relatively little movement; dynamic activities, such as distance running, involve relatively low intramuscular forces but large movements of the body or joints. Static exercises are used to build muscle strength, but have minimal effects on fitness (peak oxygen uptake (peak VO₂)) while dynamic exercises more effectively build peak VO₂ but not strength. Since much routine physical activity and many sports may be dynamic rather than static, and recommendations tend to focus on dynamic activity, it is possible for an active individual to still have low levels of static activity and strength. However, strength often has benefits independent of those of cardiovascular fitness including lung function: spirometric indices often improve following participation in sports that exercise the thorax, such as swimming and yoga; targeted respiratory-muscle training improves spirometry in populations with and without lung disease; and upper-body strength training (static exercise) is a standard part of pulmonary rehabilitation for lung disease. However, strength is not as well studied as cardiovascular fitness: studies tend to be small and/or confined to special populations such as athletes or lung-disease patients. Thus the link between aerobic fitness and spirometry requires further investigation: lung volume indices are associated with, and may be modifiable by, upper-body strength, but the evidence is less clear for an association with cardiovascular fitness.

However, it is plausible that upper-body strength drives the links between physical activity levels and lung function; thus, strength training may improve respiratory parameters. In the meantime, measures of muscle strength such as the commonly-used handgrip may prove a valuable addition to the physician’s toolkit in evaluating physical fitness. Known causal relations are outlined in Figure 1.

The benefits of strength training are particularly relevant for the care of patients with congenital heart disease (CHD). Care for these patients has historically revolved around acute survival and protection against injury but, as therapies improve, the focus is shifting towards long-term health and healthy lifestyles. These lifestyle changes may include physical activity, which is

![Figure 1. Physical activity, strength and lung function. Causal associations between static and dynamic physical activity, oxygen uptake, spirometry and strength. CPET: cardiopulmonary exercise testing.](https://academic.oup.com/eurjpc/article-26/5/492/5925630/493)
one of the most cost-effective and beneficial health interventions in healthy people and one which CHD patients often do not receive. They tend to begin with lower aerobic fitness and strength than their peers, and then further avoid activity, especially high-intensity and/or static exercise due to some combination of overprotection and legitimate fear of harm by the exercise. Indeed, at least in some forms of CHD (e.g. univentricular heart and Fontan palliation) pulmonary circulation is supported substantially by ventilation and certain activities, such as the Valsalva maneuver, are contraindicated. While these risks do not apply to all exercises or to all forms of CHD, they are higher for static exercise and for high-intensity sports which build muscle strength and cardiovascular fitness more effectively than dynamic and/or low-intensity exercise. Thus care must be taken when prescribing static exercise to CHD patients.

Furthermore, the effect of exercise on respiratory function in CHD patients may differ from that in healthy populations. Surgical and congenital modifications of the chest musculature are associated with a restrictive ventilatory pattern and also often with inability to exercise at the levels which are most beneficial. Thus patients with these defects may be limited by inadequate respiratory function and thus benefit from targeted strength training in the same way as do other populations with lung disease. Since both the potential risks and benefits of static exercise in CHD are higher than in the general population, standards of proof and standards of care may both be more exacting.

In this study we investigated the associations between handgrip, a robust and low-cost indicator of muscle strength, and both spirometric lung function and oxygen uptake in a large all-age population with and without CHD. We hoped to determine:

- Whether CHD modifies or eliminates the association between handgrip strength and spirometric lung function, which has previously been found in healthy populations;
- Whether handgrip strength is associated with peak oxygen uptake;
- Whether any association between handgrip strength and peak oxygen uptake is modified either by CHD or by sex.

**Methods**

Subjects were recruited from the outpatient section of the Department of Pediatric Cardiology and Congenital Heart Disease at the Deutsches Herzzentrum München, between January–July 2013. This is a tertiary center for all-age patients with congenital heart disease and regularly visited by patients with complex defects. Outpatients were referred to cardiopulmonary exercise testing (CPET) for routine testing, and prior to CPET they performed the handgrip test and spirometry. Other data were collected in the process of clinical examination.

Spirometry was carried out according to American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines using the spirometry device included in the CPET metabolic cart (Encore, Carefusion, currently a subsidiary of Becton, Dickinson and Company, Franklin Lakes, New Jersey, USA).

Symptom-limited CPET was carried out using the upright bicycle ergometer included in the same metabolic cart. A three-minute warm-up without load was followed by a ramp-wise increase of work load of 10 or 20 W/min according to the estimation of the attending physician/technician, to reach a cycling time of about 8–12 min after the warm-up. CPET was followed by a three-minute cool-down period with 10–20 W and a two-minute recovery period without cycling.

Oxygen uptake was measured breath by breath using the metabolic chart. Peak oxygen uptake was defined as the highest mean uptake of any 30-second time interval during exercise.

Handgrip was used to indicate muscle strength, as is common in the literature and is directly supported by at least one intervention study which found that grip improved at the same time as other measures of upper-body strength. It was measured as maximal voluntary contraction of the hand muscles with elbow in right angle position. Measurements were carried out three times on each side with a commercially available handgrip dynamometer (SAEHAN SH5001, Eschborn, Germany). The highest value was used for statistical analysis. For details, see Neidenbach et al.

In accordance with previous work, CHD diagnoses were categorized into the following groups:

- Complex cardiac defects: cyanotic patients, univentricular heart after Fontan palliation, or Ebstein’s anomaly.
- Fallot/TAC: tetralogy of Fallot or common arterial trunk
- Left heart obstructions: aortic stenosis or coarctation
- Shunt: atrial septal defect, ventricular septal defect, partial or total anomalous pulmonary venous return
- TGA: congenitally corrected transposition of the great arteries, transposition of the great arteries after atrial or arterial rerouting, or other forms of repair
- Other or none: all other forms of CHD, or patients without congenital heart defect, such as referrals for patent foramen ovale (PFO) closure or arrhythmia ablation
Most of the listed defects had been treated. In particular, all patients with some conditions were treated, which includes all subjects in some of the groups. The following conditions were always treated by some combination of surgery and catheterization:

- Univentricular heart
- Tetralogy of Fallot
- Common arterial trunk
- Atrial septal defect
- Ventricular septal defect
- Partial or total anomalous pulmonary venous return
- TGA

Due to the possible heterogeneity within these groups, we also conducted a sensitivity analysis in which some of the above-mentioned groups were further subdivided. These groups are described in the Supplementary Material.

**Statistical methods**

All analyses were conducted using Statistical Analysis System (SAS). Except when noted otherwise, statistical significance was defined as \( p < 0.05 \). To avoid multiple-comparisons artifacts where many categories were compared (e.g. diagnosis group), Type 3 tests were used to obtain a \( p \)-value for the global null hypothesis that all categories were equal.

Due to the diversity of our population, initial investigations were performed graphically using scatterplots and locally-weighted curves (locally-weighted polynomial regression [LOESS]), with separate curves drawn first for each sex and then for each diagnosis within each sex. Associations which were observed in the raw data were then followed up statistically. Selected plots are shown in the Results.

**Models of forced expiratory volume in one second (FEV1)**

Because of the large and nonlinear effect of age on spirometric function, we modeled FEV1 as percentage predicted values from the Global Lung Initiative\(^{43}\) rather than as raw values. Inspection of LOESS curves showed the predicted values were not systematically confounded by age across the lifespan in either sex (not shown), but that they did increase with increasing handgrip strength (Figure 2) in all forms of CHD. These values were modeled as function of handgrip and CHD diagnosis (treated as categorical predictor with no order, and “Other” used as reference group) and additionally corrected for linear effects of confounders not of primary interest (age, sex, height, and weight). For maximum comparability of models, these confounders were not removed from the model regardless of statistical significance.

Interactions between handgrip and other predictors (male gender and diagnosis) were checked for statistical significance and removed if not significant. Previous research indicated that handgrip was more strongly associated with FEV1 in males than in females: thus we checked for this interaction. We also evaluated the interaction of diagnosis with handgrip, checking significance with type 3 tests for fixed effects, and we present \( p \)-values for the global null (that the diagnosis groups had identical associations). In a sensitivity analysis we also considered peak VO2.

Once the model had been built and all nonsignificant variables removed, linear regression was used to create the final model. We present parameter estimates, standard errors, \( p \)-values, and semipartial correlation coefficients (percentage of variance explained) for each independent effect. No correlation coefficients are given for diagnoses: these necessarily vary by the prevalence of each in the sample population.

**Models of peak VO2**

We were not able to find any all-age reference equations for peak VO2, and (like both FEV1 and handgrip) its
association with age is known to be nonlinear. We were also unable to transform the data to fit a parametric model (linear regression) due to nonlinear associations, small sample sizes within each diagnosis, and both univariate and multivariate outliers. Thus results for this association are presented only graphically.

**Results**

**Population characteristics**

Our population ranged in age from 6–82 years old and was 59% male (Table 1). Males were slightly younger than females (mean age 26 vs 30 years) but both sexes ranged from childhood to old age. Males were likelier to have left heart defects (32% vs 14% of females) and less likely to have shunts (5.4% vs 15%) but comparable in their chance of being complex cyanotic (14% vs 17%), Fallot/TAC (17% vs 23%) or TGA (17% vs 15%). In both sexes FEV1 averaged 85% of predicted (SD 18% in males, 17% in females).

Males had stronger grip than females from puberty on; both sexes were strongest in young adulthood and declined with age. However, strength was much more variable in males than in females across the lifespan. Males averaged 41 kg grip strength (standard deviation (SD) 14) while females averaged 25 kg (SD 6.8).

**Correlates of FEV₁**

After correction for height, weight, and age, each percentage point increase in FEV₁ was associated with 0.74 kg stronger grip (\( p < 0.0001 \)) (Table 2). This association did not interact with either diagnosis or gender (\( p \) for interaction >0.10). In other words, the association between FEV₁ and handgrip was similar whether the patient was male or female, and regardless of CHD diagnosis.

FEV₁ was reduced in patients with CHD, and in no defect was FEV₁ significantly larger than that of controls. On the average, FEV₁ was reduced by 9.8 percentage points in cyanotic patients (pairwise \( p = 0.0001 \)), and 7.3 points in patients with Fallot/TAC (pairwise \( p = 0.002 \)). However, those with left heart defects, shunts, and TGA were comparable with controls (all \( p > 0.05 \)). The combined model explained 19.6% of total variance in FEV₁ percentage predicted, of which handgrip explained more than half: 9.3%. CHD diagnosis explained almost all the remainder, with very little residual confounding by anthropometric variables.

Adding peak VO₂ to the model raised the total percentage of variance explained to 29.6% (Table 3) although in this model diagnosis was no longer significant (\( p = 0.16 \)). Both the parameter estimate, and the percentage of variance explained, for handgrip decreased: the new estimates were 0.483 percentage points FEV₁ per kg, with 3.8% of total variance explained by grip (\( p < 0.0001 \)).

**Correlates of peak VO₂**

Males had higher peak VO₂ than females, and were stronger, but a scatterplot fitted with nonparametric, locally-weighted regression lines (LOESS) suggested no consistent association between peak VO₂ and handgrip strength in either sex (Figure 3). The association in females even appeared to be slightly negative. This lack of association remained in each sex after stratification by diagnosis group (not shown).

**Sensitivity analysis: further subdivision of groups**

In the sensitivity analysis where the diagnosis groups were further subdivided (Supplementary Material Tables S1–S3) many groups became very small. For example, there were 20 cyanotic patients, of which six were female. However, results were generally comparable with those given above: each kilogram of handgrip accounted for 0.67% pred FEV₁ before correction.

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**Table 1. Population characteristics mean (standard deviation (SD)) unless stated otherwise.**

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: n, %</td>
<td>315, 59%</td>
<td>223, 41%</td>
</tr>
<tr>
<td>Age, years</td>
<td>26.3 (12)</td>
<td>30.3 (15)</td>
</tr>
<tr>
<td>Mean (SD); min, max</td>
<td>7.7, 75</td>
<td>6.3, 82</td>
</tr>
<tr>
<td>Height, cm</td>
<td>173 (14)</td>
<td>162 (10)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>70 (19)</td>
<td>61 (15)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.0 (4.4)</td>
<td>23.0 (4.7)</td>
</tr>
<tr>
<td>FEV₁, l</td>
<td>3.34 (1.1)</td>
<td>2.47 (0.64)</td>
</tr>
<tr>
<td>FEV₁, percentage predicted</td>
<td>84.9 (18)</td>
<td>84.6 (17)</td>
</tr>
<tr>
<td>VO₂max, ml/min/kg</td>
<td>32.2 (10)</td>
<td>24.4 (7.1)</td>
</tr>
<tr>
<td>Mean (SD); min, max</td>
<td>8.7, 6.7</td>
<td>7.5, 4.6</td>
</tr>
<tr>
<td>Handgrip strength, kg</td>
<td>40.7 (15)</td>
<td>24.6 (6.7)</td>
</tr>
<tr>
<td>Mean (SD); 5th, 95th percentiles</td>
<td>12, 61</td>
<td>13, 36</td>
</tr>
<tr>
<td>Diagnosis group, n (%)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Complex cyanotic</td>
<td>45 (14)</td>
<td>38 (17)</td>
</tr>
<tr>
<td>Fallot/TAC</td>
<td>55 (17)</td>
<td>52 (23)</td>
</tr>
<tr>
<td>Left heart</td>
<td>100 (32)</td>
<td>31 (14)</td>
</tr>
<tr>
<td>Other or none</td>
<td>45 (14)</td>
<td>33 (15)</td>
</tr>
<tr>
<td>Shunt</td>
<td>17 (5.4)</td>
<td>35 (16)</td>
</tr>
<tr>
<td>TGA</td>
<td>53 (17)</td>
<td>34 (15)</td>
</tr>
</tbody>
</table>

BMI: body mass index; FEV₁: forced expiratory volume in one second; SD: standard deviation; TAC: Truncus arteriosus communis (common arterial trunk); TGA: transposition of the great arteries; VO₂: oxygen uptake.
for peak VO₂, and 0.46% after correction (both \( p < 0.0001 \)).

Unlike the main analyses, in this analysis diagnosis group remained statistically significant \( (p = 0.02) \) after correction for peak VO₂. However, after correction for peak VO₂ (Supplementary Material Table S3) only cyanotic patients were significantly different from controls at \( p = 0.05 \) (parameter estimate \(-13.4\)\%pred).
FEV1). At $p = 0.05$, those with Fallot ($n = 98$) and univentricular heart (UVH) ($n = 33$) were comparable with controls.

**Discussion**

**Associations with lung function**

In this population we found associations between FEV1 and handgrip that were similar in size (about 1% FEV1 per kg grip strength) to those previously found in healthy adolescents, and again males were more variable in their grip strength than females. The current sample confirms that this association persists across the lifespan and is not specific to adolescents. However, in the current population, the effect of grip strength on lung function was similar between the sexes: previously the effect had been larger for males. This may be due to age-specific effects in the previous population (e.g. puberty), residual effects of CHD in our population, or a combination of these.

In our previous research with a similar cohort to this one we presented the finding that handgrip was reduced in the entire CHD group, compared with the controls ($p < 0.001$) and decreased with defect severity. The severest reduction was present in patients with cyanosis before treatment, in right-sided cardiac anomalies, in univentricular hearts after Fontan operation, and in currently-cyanotic patients. This study adds that both handgrip and heart defect severity contribute independently to lung function, whether defect severity is quantified as categorical “diagnosis group” or continuous “peak oxygen uptake.”

Lastly, we found that the association of CHD diagnosis with FEV1 disappeared, or almost disappeared, after correction for peak VO2; that is, a subject with a given peak VO2 had similar FEV1 regardless of CHD diagnosis. This may suggest that the surgical or congenital anomalies of the chest which are associated with some types of CHD (e.g. tetralogy of Fallot, Fontan correction for UVH) did not constrain respiratory function in these patients compared with other groups with similarly limited peak VO2, such as patients with current cyanosis (regardless of cause).

**Associations with oxygen uptake**

Unlike previous researchers, we failed to find any association between handgrip strength and oxygen uptake, and nonparametric LOESS curves suggested that the uncorrected association was not even reliably increasing. However, since oxygen uptake attenuated the association between handgrip and lung function there must have been some association between handgrip and oxygen uptake, at least after correction for confounders such as age and height which varied more in our all-age population than in those studied elsewhere. Further research in a more homogeneous sample would be needed to address this.

However, this heterogeneity of effect also may be explained by the different types of physical activity common in different populations. Sports may be static (tending to build strength) and/or dynamic (tending to build aerobic capacity), thus depending on which activity is most popular, aerobic capacity and strength may covary to a greater or lesser extent. CHD patients tend to report low levels of physical activity in general, and may be counseled to avoid static activity in particular, but if they are similar to healthy adolescents then most of their total physical activity may come from daily routine (often ambulatory and thus dynamic) and thus may not be well captured by self-report. This was the case in healthy adolescents, for whom 75% of total moderate-to-vigorous physical exercise took place outside of sport. Thus it is not immediately clear whether the activity of CHD patients is more or less likely to be static than that of healthy peers, and thus whether their lower activity levels also reflect lower levels of static activity specifically.

**Conclusions**

In the same population, we found that muscle strength was associated with lung function, but not with aerobic fitness (peak VO2). This is consistent with a growing
body of research which finds that activities which build strength may have little effect on cardiovascular fitness (oxygen uptake)\textsuperscript{15} or vice versa.\textsuperscript{16} It is also consistent with our own previous research which found that strength, but not physical activity, was associated with lung function in adolescents,\textsuperscript{8,44} and with the findings of Greutmann et al.\textsuperscript{46} who found that handgrip, but not physical activity, was reduced in CHD patients.

We also found that type of CHD did not significantly alter the association between handgrip and lung function. Each kilogram of handgrip was associated with about an 0.74% increase in FEV\textsubscript{1}, whether lung function. Each kilogram of handgrip was associated with about an 0.74% increase in FEV\textsubscript{1}, whether the subject had severe CHD, no CHD at all, or a minor defect. The known restrictive ventilatory pattern associated with some forms of CHD was not severe enough to affect the association. Although CHD patients tended to be weaker, to have poorer lung function, and to have lower aerobic fitness the three measures intercorrelated similarly with each other, suggesting that CHD patients may benefit from activity interventions similarly to non-patients. Similar associations between strength, pulmonary function, and exercise tolerance are plausible in healthy populations\textsuperscript{22,48} and are known in those with lung diseases and dyspnea, whether this is explained\textsuperscript{22,24} or unexplained.\textsuperscript{49}

In healthy populations, handgrip is associated with upper-body strength both cross-sectionally\textsuperscript{28–32} and longitudinally,\textsuperscript{41} tending to indicate greater strength and also improving during strength-training interventions. If this association also holds in CHD patients, and the cross-sectional association we observe can be treated as causal, then upper-body strength training may improve respiratory function in CHD patients.

### Study limitations

While lung function was low in this population, this may partially represent lack of fit between Global Lung Initiative (GLI) predicted values and the German population, since a similar offset was observed in a cohort of healthy adolescents.\textsuperscript{8} However, the comparison between defects suggests that patients with more severe defects also had more pronounced limitations in FEV\textsubscript{1}. This association appeared to disappear after correction for peak VO\textsubscript{2}, but this may have been the result of insufficient statistical power rather than a true null effect. The sample size for some defects (e.g. UVH and Fallot) was relatively small, and these are the defects most reliably associated with respiratory limitations such as a restrictive ventilatory pattern.\textsuperscript{39}

While our sample was quite large, it nevertheless may have been insufficient to detect some small effects. Some CHD diagnoses were rare, especially among females, and a clinically significant effect may have been statistically undetectable. Likewise, while we found no association between handgrip and peak VO\textsubscript{2}, it is possible that some association was missed. Adding peak VO\textsubscript{2} to the model of FEV\textsubscript{1} attenuated the independent association with handgrip strength, suggesting that, after correction for the other confounders, there was some association between peak VO\textsubscript{2} and handgrip in that model which was not present in the raw data. We encourage future researchers, whose populations are more homogeneous, to address this association specifically.

### Author contribution

MPS contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted the manuscript; critically revised the manuscript; gave final approval; and agrees to be accountable for all aspects of work ensuring integrity and accuracy. JM contributed to conception and design; critically revised the manuscript; gave final approval; and agrees to be accountable for all aspects of work ensuring integrity and accuracy. PE contributed to conception and design; contributed to drafting the manuscript; critically revised the manuscript; gave final approval; and agrees to be accountable for all aspects of work ensuring integrity and accuracy. AH contributed to conception and design; contributed to acquisition, analysis, and interpretation; critically revised the manuscript; gave final approval; and agrees to be accountable for all aspects of work ensuring integrity and accuracy. RN contributed to conception and design; contributed to acquisition, analysis, and interpretation; contributed to drafting the manuscript; critically revised the manuscript; gave final approval; and agrees to be accountable for all aspects of work ensuring integrity and accuracy. JM contributed to conception and design; contributed to acquisition, analysis, and interpretation; critically revised the manuscript; gave final approval; and agrees to be accountable for all aspects of work ensuring integrity and accuracy.

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