Original research article

Effect of maternal weight during pregnancy on offspring muscle strength response to resistance training in late adulthood

Niko S. Wasenius\textsuperscript{a,b,c}, Mika Simonen\textsuperscript{e}, Liisa Penttin\textsuperscript{d}, Minna K. Salonen\textsuperscript{a,e}, Samuel Sandboge\textsuperscript{a,e}, Johan G. Eriksson\textsuperscript{a,b,e,f}

\textsuperscript{a} Folkhälslans Research Center, Helsinki, Finland
\textsuperscript{b} Department of General Practice and Primary Health Care, Helsinki, Finland
\textsuperscript{c} Department of Social Research, University of Helsinki, Helsinki, Finland
\textsuperscript{d} Institute of Biomedicine, Exercise Medicine, University of Eastern Finland, Kuopio, Finland
\textsuperscript{e} Department of Chronic Disease Prevention, National Institute of Health and Welfare, Helsinki, Finland
\textsuperscript{f} Unit of General Practice, Helsinki University Hospital, Helsinki, Finland

ABSTRACT

Purpose: Maternal obesity can unfavorably influence offspring body composition, muscle strength, and possibly muscle’s adaptability to training, but the human studies are scarce. Therefore, we aimed to investigate the effect of maternal obesity on offspring muscle strength responses to resistance training intervention in elderly frail women.

Materials/methods: Recruited participants were elderly frail women offspring of lean/normal weight mothers (n = 19, mean body mass index (BMI): 22.8 kg/m\textsuperscript{2}, range: 19.9–24.5) or overweight/obese mothers (n = 16, mean BMI: 29.7 kg/m\textsuperscript{2}, range: 28.2–34.2). Information on maternal BMI immediately prior to delivery was collected from the birth registers. All women participated in a 4-month supervised progressive resistance training intervention three times a week for 60 min. Predicted 1-RM of abdominal crunch, hip abduction, leg curl, leg press, seated row, and total strength were measured at baseline and after each month of training.

Results: According to rANOVA, strength increased significantly in both groups (p for time < 0.001), but no significant between the group difference were detected (p for time x group interaction > 0.072). On average, muscle strength of the women offspring of overweight/obese mothers tended to be lower than in women offspring of lean/normal weight mothers, but the only significant difference was found in leg curl (p = 0.006). No significant differences between the groups were found in relative strength changes from baseline to 4-months.

Conclusions: Muscle strength response to supervised resistance training is not modulated by maternal adiposity in late pregnancy in elderly frail female offspring.

1. Introduction

The Developmental Origins of Health and Disease (DOHaD) hypothesis proposes that environmental exposures during sensitive periods of development can result in phenotypic alterations affecting later health and disease susceptibility [1]. The prenatal period is associated with rapid cell division and is one of the most sensitive time periods in relation to developmental programming. In fact, recent evidence suggests that maternal adiposity during pregnancy can hamper offspring’s skeletal muscle development [2] and increase the long-term risk for obesity, cardiovascular disease, type 2 diabetes [3–5].

Key stages of skeletal muscle development occur during early embryonic stage, mid pregnancy, and postnatally [6–8]. Especially, the mid gestational period can have long-term consequences to offspring muscle strength and function [9]. During this period, the maternal obesity-induced inflammation can drive the differentiation of mesenchymal stem cells (MSCs) into adipocytes rather than myocytes [10]. Maternal obesogenic environment can also increase intramyocellular fat accumulation in offspring, decrease skeletal muscle cross-sectional area [11], and muscle strength [12]. Although the exact mechanisms that explain the effect of maternal obesity and/or obesogenic environment on offspring muscle strength are unknown, the maternal obesity-induced inflammation could play a role. According to previous evidence, maternal obesity can decrease myogenesis by up-regulating inflammatory IKK/NF-B signaling pathway and subsequently inhibiting Wnt/β-catenin signaling pathway [13]. β-catenin can have a...
critical role in the growth of adult's skeletal muscles after mechanical overload [14,15].

Interestingly, in human studies, maternal obesity has also been associated with increased concentration of inflammatory markers, e.g., interleukin-6 and C-reactive protein, in the cord blood [16]. Furthermore, in some human studies, but not in all [4], exposure to maternal adiposity has been associated with decreased fat free mass and increased fat mass in offspring [17,18]. This can lead to accumulation of intramuscular fat, which has been associated with decreased walking speed and grip strength in the elderly subjects [19]. Due to the link between the maternal obesity, inflammation and β-catenin, we hypothesized that elderly frail women offspring of overweight or obese mothers (OOM) can have compromised muscle strength response to resistance training compared to elderly frail women offspring of lean/normal weight mothers (OLM). Therefore, the purpose of this study was to compare the muscle strength changes between elderly frail women OLM and OOM after a 4-month supervised resistance training.

2. Patients and methods

2.1. Participants

Thirty-five elderly frail women (age 72.3 ± 3.2 years) from the clinical Helsinki Birth Cohort Study (HBCS) (n = 2003) were recruited for this study. Only women were recruited as the main aim of this study project was to investigate the association between risk factors of type 2 diabetes (e.g. insulin resistance) and the ageing process specifically in frail women. Recruited women were either offspring of mothers who belonged to the lowest body mass index (BMI) quartile (BMI ≤ 26.3 kg/m²; n = 19) or the highest BMI quartile (BMI ≥ 28.1 kg/m²; n = 16) at the time of the delivery. Study population specific quartiles, rather than the traditional BMI categories for normal weight (< 25.0 kg/m²), overweight (25–29.9 kg/m²), or obesity (≥ 30 kg/m²) were applied to consider for the possible role of gestational weight gain. During pregnancy, normal weight women would gain approximately 11.5–16 kg, which could change the traditional BMI category from normal to overweight. Thus, applying 25 kg/m² as a criterion for overweight in pregnancy may not be feasible. The maternal BMI thresholds were based on the data from all the mothers from the HBCS (n = 13345/2003). To retrieve information on maternal BMI, we first collected maternal body height and weight from the hospital records. The body height and weight information were then used to calculate maternal BMI at the time of the delivery as weight in kg divided by height in meters squared. Handgrip strength was used as the criterion for frailty [20]. The study participants (offspring) were considered frail if they belonged to the lower half of handgrip strength category within the HBCS study population. Data for handgrip strength measurements were obtained from the clinical examinations conducted between the years 2001 and 2004 [21]. Participants were excluded if they were currently smoking, had insulin treated diabetes, comorbidities that affected insulin sensitivity, or contraindications for participating in a resistance training intervention (e.g. chronic atrial fibrillation and pacemaker). The study was approved by the Ethics Committee of the Hospital District of Southwestern Finland (26/180/2012), and previously HBCS has been approved by the Ethics Committee of Epidemiology and Public Health of the Hospital District of Helsinki and Uusimaa (Helsinki, Finland) (344/E2/2000), and the National Public Health Institute (Helsinki, Finland). Written informed consent was obtained from all participants.

2.2. Intervention

The study participants were invited to participate in a 4-month supervised resistance training three times a week for 60 min. Training sessions consisted of 10 min of warm-up with cycle and/or elliptical ergometers and 8 different resistance exercises targeting large muscle groups of the upper and lower body (leg press, chest press, seated row, abdominal crunch, back extension, seated leg extension, seated leg curl and hip abduction). At each station, participants completed three sets of 8–15 repetitions with a load that corresponded to 50–80% of estimated 1 repetition maximum (RM). Progress in muscle strength was measured once a month and the loads for the following month were adjusted as appropriate. The training was supervised by an experienced trainer.

2.3. Muscle strength

Subjects’ estimated 1-RM for leg press, leg curl, hip abduction, seated row, abdominal crunch, and total muscle strength were measured monthly and used as a primary outcome of this study. One RM for each exercise was estimated from 8-RM tests by applying Epley’s formula [22]. Before the 8-RM tests women performed aerobic warm-up. Women were also clearly instructed that they should experience no pain and that they could stop the test at any point. Then women were introduced to the equipment and explained how to use it. With the equipment, they first performed 2–3 warm-up/practice sets with light resistance. After the women were familiarized with the machine the actual 8-RM test started. The aim was to achieve 8-RM optimally in 2–3 sets, but in maximum of 5 sets. After completing each set successfully, the load was increased if both the participant and the tester felt that she could complete 8-RM with heavier load. The training was performed with both pneumatic resistance and weight stack equipment. In pneumatic machines loads can be adjusted without steps, so small increases in predicted 1-RM were not a problem. In weight stack machines, the smallest allowed load adjustment varied between the 2.5–5 kg. If the 1-RM was close to a load that was available in the machine, then this was selected. If the 1-RM was in between of two available stack weights then the lower load was selected. Progress in muscle strength was measured once a month and the loads for the following month were adjusted as appropriate. Total muscle strength was calculated as a mean of leg press, leg curl, hip abduction, seated row, and abdominal crunch 1-RM values. In addition to absolute strength, a set of sensitivity analyses were performed, where muscle strength in relation to baseline body weight and lean body mass was investigated. Moreover, total relative change in muscle strength was also calculated (4-month muscle strength – baseline muscle strength)/ baseline muscle strength × 100).

2.4. Physical functioning

Handgrip strength and maximum isometric knee extension were measured from the dominant side in an adjustable dynamometer chair (Good Strength, Metitur Ltd., Jyväskylä, Finland). The best result out of three trials was reported in kilograms.

Gait speed and endurance were measured with the 15-foot Walk Test (4.57 m) and the 6-Minute Walk Test, respectively. In the 15-foot Walk Test the time was measured with a standard stop watch and the result was the time taken to walk 15 feet with a walking start. In the 6-Minute Walk Test, the participant was informed to walk as fast as possible yet safely. The distance covered in 6 min was measured with 5m accuracy. These tests were conducted indoors, the 6-Minute Walk Test was performed in a corridor where turning points were marked with cones, placed at 20 m distance from each other.

2.5. Body composition and anthropometrics

Body fat percentage, lean body mass, and weight were measured in light clothing before the intervention by bioelectrical impedance analysis (InBody 3.0 eight-polar tactile electrode system (Biospace Co. Ltd, Seoul, Korea). Height was measured to the nearest 0.1 cm. BMI was calculated by dividing weight (kg) with height in meters squared. Waist-to-hip ratio was calculated from the measured waist (midways between the iliac crest and lower rib margin) and hip (widest part of hip circumference) with measuring tape.
2.6. Leisure-time physical activity

During the intervention subjects were instructed to fill a diary about type, duration, and rating of perceived exertion (RPE) [23] of leisure-time physical activity (LTPA). For each reported activity a metabolic equivalent of task (MET, 1 MET = 3.5 ml O2/kg/min or 1 kcal/kg/h) value was determined [24]. Intensity of LTPA was expressed in time-weighted average intensity (TWA-MET) and volume of LTPA in MET-minutes or MET-hours. The volume of LTPA was also standardized for time by subtracting each participant’s duration of LTPA from the largest reported duration by a subject. The missing time (mean 526.2 min, standard deviation 155.0) was then multiplied with 1.5 MET and added into to the original reported volume of LTPA [25].

2.7. Statistical analyses

Data are presented as mean (standard deviation [SD] or 95% confidence intervals [CI]). Between the group comparisons of baseline age, physical functioning and physical performance were performed with Mann-Whitney test. Between the groups comparisons in body composition and anthropometrics were tested with analysis of covariance (ANCOVA). Sphericity was tested with Mauchly’s test and if significant Greenhouse-Geisser corrected p-values for F-test were reported. After a significant F-test post hoc analysis with Bonferroni correction was made. The between the groups comparison of relative change (%) from baseline to 4-months was performed with Mann-Whitney U test and expressed as median and interquartile range (IQR), due to the skewed distribution. Missing data on 1-RM strength test was imputed with last observation carried forward or next observation carried backward methods. A p-value < 0.05 was considered statistically significant. Statistical testing was conducted with IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, New York, USA).

3. Results

3.1. Baseline characteristics

Baseline characteristics are shown in Table 1. There were no statistically significant differences in anthropometrics, physical capacity or performance between the OLM or OOM. As expected maternal BMI was significantly higher in the OOM group than in the OLM group.

3.2. Adherence to training and LTPA

There were no statistically significant differences between the groups in adherence to supervised resistance training program (Table 2). Subjects participated on average in 78.6% of all training sessions. We found no statistically significant differences between the groups in the dose of LTPA during intervention (Table 2).

3.3. Change in absolute muscle strength

As described in Fig. 1, the change in muscle strength over time was similar between the groups (p for time by group interaction p ≥ 0.072). However, the strength gain over time was significant in all measured exercises (Fig. 1). This increase was observed in the first months of training. The main effect for group was only statistically significant for 1-RM leg curl (mean difference [OLM – OOM] = 4.8 kg, 95% CI, 1.4–8.1, p = 0.006). No other statistically significant main effects for group were observed (p ≥ 0.321).

3.4. Sensitivity analyses

The results remained unchanged when absolute strength was expressed relative to body weight (p for time < 0.001, p for group > 0.013, and p for time by group interaction > 0.068) or lean body mass (p for time < 0.001, p for group > 0.008, and p for time by group interaction > 0.073) (data not shown). In both analyses, the statistically significant group effect was found in leg curl strength, but not in other exercises (p > 0.314). The median relative strength change from baseline to 4-months was also similar between the groups (Table 3).

4. Discussion

We hypothesized that OOM would respond differently to 4-months of resistance training. However, the findings from the study do not support this hypothesis. It was actually discovered that muscle strength gains during the intervention were similar in the OLM and the OOM groups. In both groups, a clear increase in muscle strength was detected. Albeit, in the OOM group the average muscle strength values seemed to be lower, but they were non-significant, except for leg curl. In leg curl we detected a significant group effect, which indicated that during the intervention the OOM group had a 4.8 kg lower leg curl strength than the OLM group. However, we did not observe a difference in the slope of intervention induced strength gains. Therefore, maternal BMI does not seem to affect the offspring’s ability to improve strength with resistance training in late adulthood, albeit some differences are detected in the leg muscle strength.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (n = 35)</th>
<th>OLM (n = 19)</th>
<th>OOM (n = 16)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal body mass index (kg/m²)</td>
<td>26.0 (3.8)</td>
<td>22.8 (1.4)</td>
<td>29.7 (1.6)</td>
<td>0.000</td>
</tr>
<tr>
<td>Age (years)</td>
<td>72.3 (3.2)</td>
<td>72.6 (2.7)</td>
<td>71.9 (3.8)</td>
<td>0.289</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.5 (5.0)</td>
<td>162.7 (5.2)</td>
<td>160.0 (4.3)</td>
<td>0.106</td>
</tr>
<tr>
<td>Body composition</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.2 (11.3)</td>
<td>70.1 (10.9)</td>
<td>70.3 (12.1)</td>
<td>0.877</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.0 (4.5)</td>
<td>26.5 (4.6)</td>
<td>27.4 (4.5)</td>
<td>0.550</td>
</tr>
<tr>
<td>Fat percentage (%)</td>
<td>35.6 (6.2)</td>
<td>35.1 (6.9)</td>
<td>36.1 (5.4)</td>
<td>1.000</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>44.7 (4.2)</td>
<td>44.9 (4.0)</td>
<td>44.4 (4.4)</td>
<td>0.584</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.97 (0.07)</td>
<td>0.96 (0.07)</td>
<td>0.98 (0.07)</td>
<td>0.617</td>
</tr>
<tr>
<td>Physical capacity and Performance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-Foot Walk Test (s)</td>
<td>2.5 (0.5)</td>
<td>2.5 (0.5)</td>
<td>2.6 (0.4)</td>
<td>0.665</td>
</tr>
<tr>
<td>6-minute walk test (m)</td>
<td>521.1 (73.7)</td>
<td>527.6 (80.8)</td>
<td>513.4 (66.1)</td>
<td>0.629</td>
</tr>
<tr>
<td>Grip strength (kg)</td>
<td>26.9 (7.7)</td>
<td>25.3 (5.9)</td>
<td>25.2 (7.9)</td>
<td>0.390</td>
</tr>
</tbody>
</table>
| Knee extension strength (kg)     | 26.6 (8.5)  | 26.5 (7.9)   | 26.6 (9.4)   | 0.529   

Data are shown as mean (standard deviation). OLM - offspring of lean mothers; OOM - offspring of overweight/obese mothers.
This study does not support the lower muscle strength or reduced adaptability to resistance training in elderly female OOM. We are unaware of any previous studies that have investigated the effect of maternal overweight/obesity on muscle strength response to resistance training. Nevertheless, our findings are somewhat inconsistent with previous evidence. In previous studies, maternal obesity or obesogenic environment (e.g., high-fat diet) during pregnancy have been associated with reduced muscle mass [11,26], decreased myogenesis [13], lower protein content in muscle [27], and reduced muscle strength [12]. Moreover, maternal high-fat diet induces a 27% decrease in skeletal muscle precursor (SMP) cells [26]. SMP cells are responsible for the postnatal maintenance of muscle fibers and possibly play a pivotal role in promoting exercise induced hypertrophy, although, the exact role of SMP cells remains to be determined [28]. Furthermore, in humans, maternal obesity increases blood concentration of the IL-6 [16]. IL-6 has been associated with reduced skeletal muscle mass and strength in elderly women [29,30]. Therefore, plenty of evidence argues in favor of reduced muscle strength in offspring exposed to maternal obesity-related factors. The inconsistent findings of the present study warrant further research. It is possible that other obesogenic factors than BMI (e.g., high-fat diet or excessive gestational weight gain) could have a different kind of effect. In addition, the effect could be different in male offspring, as it is well established that developmental programming is sex dependent [31].

Albeit, no clear differences in muscle strength or muscles' adaptability were found, there was a substantial increase in the muscle strength in both groups. The increase in muscle strength was the greatest during the first two to three months of training after which it seemed to plateau in all exercises except for leg press. The greater improvement in the early months of training was probably the result of better activation of relevant motor units and their synchronization [32]. To support the role of neuronal factors for strength development, the present findings are consistent with the evidence from a recent systematic review showing that in elderly people resistance training elicits only minimal muscle hypertrophy despite the substantial increase in muscle strength [33]. This could also partly explain, why we did not observe any differences between the OOM and the OLM groups. Previous studies suggest that maternal obesity would specifically affect the muscle structure, but it may not affect activation of the motor neuron, their recruitment, or synchronization. Therefore, due to limited hypertrophy related strength gains, both groups could be equally equipped to increase strength with resistance training.

The increase in muscle strength (37–75%) was consistent with the findings of previous studies. Häkkinen et al. [32] reported that maximal isometric leg extensor force increased by 57% in elderly women within 6 months of resistance training. In another study on aging women a 58% increase in leg extensor strength was reported within 26 weeks of resistance training [34]. These findings are similar to the present ones, where leg press strength increased by 48–60%. In a study by Tracy et al. [35], however, only a 27–35% increase in maximal leg extensor strength was reported within 9 weeks of unilateral resistance training. This is most likely due to the shorter duration of the intervention compared to the present and other studies [32,36]. In contrast, Lemmer et al. [37] reported smaller increases in measured 1-RM upper body (8.5–54.1%) and lower body (26.9–34.3%) strengths in older women within 6 months of resistance training. This inconsistency with the present findings is most likely explained by the 6 familiarization sessions performed before the baseline 1-RM measurements to reduce the effect of neurological adaptations.

Subjects' compliance to training was high (78.6%) which is a strength of this study. The compliance and the dose of LTPA during the intervention were also similar between the groups, which allowed us to perform a justified comparison for the effect.

4.1. Limitations

The main limitation for this study was that groups were divided based on the maternal BMI at the time of delivery. As such, the current BMI categories are only surrogate markers of the pre-pregnancy BMI. In addition, we did not have information on maternal diet during pregnancy, which may have influenced our findings.

Additionally, the sample size was limited to only 35, which may have increased our risk for type II error (false negative). The sample size was selected based on the cost and time-consuming main outcomes (e.g., hyperinsulinemic euglycemic clamp and positron emission tomography (PET)) that were employed to investigate the main goals of the trial. The main aim of this trial was to investigate the relationships between maternal obesity, insulin resistance, and markers of ageing including telomere lengths in elderly frail women. In the future, larger studies with sufficient power, are required to confirm our findings.

Also, the lack of a control group may be viewed as a limitation for this study. However, the main purpose of this study was not to test whether resistance training affects muscle strength per se, but to investigate the effect of maternal adiposity. In this respect, a control group would have had only limited value.

Furthermore, the 1-RM was estimated based on the 8-RM test and may have resulted in some bias. The 8-RM test was selected as a safe monitoring option of muscle strength for elderly subjects with inexperience with resistance training.
5. Conclusion

Maternal overweight/obesity had no influence on the offspring muscle strength adaptability to resistance training intervention. Based on the present findings, elderly frail women offspring of either lean/normal weight mothers or overweight/obese mothers had similar strength gain during the 4-month supervised resistance training intervention. These data provide additional support that elderly frail women offspring of overweight/obese women may have lower muscle strength, but it may be muscle group specific, and needs to be confirmed with larger studies. In conclusion, elderly frail women, regardless of the maternal weight status during pregnancy, can substantially increase their muscle strength with resistance training.

Table 3
Relative change (%) in muscle strength from baseline to 4 months of resistance training.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OLM</th>
<th>OOM</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Median (IQR)</td>
<td>n</td>
</tr>
<tr>
<td>Abdominal crunch</td>
<td>19</td>
<td>37.5 (54.8)</td>
<td>15</td>
</tr>
<tr>
<td>Hip abduction</td>
<td>19</td>
<td>37.0 (44.5)</td>
<td>16</td>
</tr>
<tr>
<td>Leg curl</td>
<td>19</td>
<td>60.0 (85.0)</td>
<td>16</td>
</tr>
<tr>
<td>Leg press</td>
<td>19</td>
<td>60.3 (48.8)</td>
<td>16</td>
</tr>
<tr>
<td>Row</td>
<td>19</td>
<td>51.1 (410)</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>65.1 (31.8)</td>
<td>16</td>
</tr>
</tbody>
</table>

OLM - offspring of lean mothers; OOM - offspring of overweight/obese mothers; SD - standard deviation; IQR - interquartile range.
Author contribution

Study Design: Minna K Salonen, Samuel Sandboge, Johan Eriksson
Data Collection: Liisa Penttinen, Mika Simonen
Statistical Analysis: Niko S Wasenius
Data Interpretation: Niko S Wasenius, Mika Simonen, Minna Salonen, Johan Eriksson
Manuscript Preparation: Niko Wasenius, Mika Simonen, Minna Salonen, Liisa Penttinen, Samuel Sandboge, Johan Eriksson
Literature Search: Niko Wasenius, Mika Simonen, Minna Salonen, Liisa Penttinen
Funds Collection: Johan G Eriksson, Minna K Salonen

Financial disclosure

HBCS has been supported by grants from Finska Läkareässälkaptet, the Finnish National Governmental Subsidy for Health Sciences, Academy of Finland, Samfundet Folkhälsan, Liv och Hälsa, the Signe and Ane Gyllenberg Foundation, and EU FP7 (DORIAN) project number 278603. EU H2020-PHC-2014-DynaHealth Grant no. 633595. The funding source had no role in study design, collection or interpretation of the data, analysis, or publishing of the study.

Conflict of interests

The authors declare no conflict of interests

Acknowledgements

The authors would like to thank physiotherapist Minna Lipasti for her excellent assistance with research.

References