

Hemoglobin Concentrations Predict Physical Function After A 12-Week Resistance Exercise Training and Subsequent Changes After 11 Months of Follow-Up Among Community Dwelling Older Adults

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Abstract

Background: Hemoglobin transports oxygen in blood yet its concentrations generally decrease with age. The aim of the study was to examine whether hemoglobin is connected with physical function in older age people.

Design: Intervention study.

Setting: Community.

Participants: Older adults (N=236, 73.7±5.7 years, 58.2% female).

Intervention: A 12-week resistance exercise program (3 times/week; 3 sets, 6-8 repetitions at 75-80% of the 1-repetition maximum) was conducted to increase strength and muscle mass of major muscle groups.

Measurements: Anthropometrics, muscle strength, timed up and go (TUG in sec), six-minute walking distance (6MWD in m) and blood chemical variables were measured at baseline, endpoint and after 10.7 months follow-up. The linear regression model was used to examine the association between baseline hemoglobin and physical function outcome.

Results: Only about 4% of the participants were anemic. According to calculations baseline hemoglobin was associated with TUG (0.14 to 0.36 sec improvement by 10 g/L increase of hemoglobin) at all-time points, even though this was of borderline significance for baseline (p=0.57) and endpoint (p=0.062). Hemoglobin also predicted endpoint 6 MWD (4.88m), but not at baseline (follow up 6 MWD was not available). Statistical correction for compliance did not influence results.

Conclusion: Hemoglobin is positively associated to physical function in community dwelling old aged people. Additionally, we found that baseline hemoglobin is associated to adaptations to 12-week resistance exercise training and changes in physical function during the follow-up.

Keywords: Hemoglobin; Resistance exercise intervention; Physical function

Introduction

With the increase of aging population worldwide, overall burden of chronic diseases is expected to rise. Anemia is one of the common chronic diseases among older people [1]. Hemoglobin facilitates oxygen transport in blood and hemoglobin below 12 g/dL for non-pregnant women and below 13 g/dL for men is defined as anemia by the World Health Organization (WHO) [1]. Hemoglobin concentrations decrease with age, for reasons such as chronic inflammation, chronic kidney disease, deficiencies in nutrients such as iron, vitamin B12 or folic acid [2]. Prevalence of anemia among community dwelling old adults ranges between 6-12% [3].

Anemia has been also associated with low physical function. Physical function is a critical factor in allowing older adults to maintain an independent lifestyle [4-6]. There is not much prospective data available on the association between anemia and physical function among older adults. A 4-year prospective cohort study with 1146 subjects reported that anemia was related to a decline in physical function during the study period. This relation was also seen in subjects who were free of chronic conditions associated with anemia [7]. A cross-sectional study reported the association between physical function and hemoglobin among participants within normal range of hemoglobin concentrations [8]. In accordance to their results the

authors asked whether the criteria currently used to define anemia in older adults should be reevaluated.

The current examination explored whether hemoglobin concentrations are related with physical function in the group of older adults. The original IceProQualita study was conducted as a randomized, controlled trial, which is designed to test the effects of post exercise protein ingestion on the efficacy of 12-week strength training in old adults [9]. The intention of the current analysis was to examine:

- Whether baseline hemoglobin predicts physical function,
- Whether baseline hemoglobin predicts response to 12-week resistance exercise training, and

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- Whether hemoglobin predicts changes in physical function after a period of 6 to 18 months of the follow-up.

Methods

Subjects

Subjects (N=236) were from at least ranges from of 65-92 years and were invited to participate by the advertisements announced in the Reykjavik area. The following exclusion criteria were used: low cognitive function (Mini-Mental State Examination (MMSE) <19 points) [10], major orthopedic disease, treatment with exogenous testosterone or other medication affecting lean mass, musculoskeletal disorders or other disorders that could affect their muscle mass. Additionally, the participants had to be free of any disorders related to musculoskeletal system. Registered people were evidently healthy, although few had hypertension, hyperlipidemia or type 2 diabetes. The Icelandic National Bioethics Committee approved the study protocol (VSNb2008060007/03-15) and thus performed as per the moral benchmarks set down in the 1964 Declaration of Helsinki and its later corrections. All people gave their agree consent before their consideration in the examination.

Resistance training

The resistance exercise program has been explained in (earlier) publications. In short it was intended to expand quality and mass of major muscle gatherings and the members practiced 3 days/week for twelve weeks in gatherings regulated by study staff. A training session included warm up, weight lifting and cool down including stretching. At the point when the session was done, the subjects drank a protein- and starch supplement, which was a piece of the first point of this preliminary. As this nutrition drink was not related to outcomes of the present analysis, it is not considered further in this paper.

Follow-up

All the members who finished the resistance exercise intervention program were approached to return for a subsequent investigation. Mean length of follow-up was 10.7 months (range between 6 and 18 months).

Anthropometrics

Body weight (BW) was measured in light underwear on a scale (model no. 708, Seca, Hamburg, Germany) and height was measured with a stadiometer (model no. 206; Seca, Hamburg, Germany). Body mass index (BMI) was calculated from height and weight (kg/m²). Waist circumference was measured halfway between the top of the lateral iliac crest and the lowest rib.

Muscular strength and physical function

The following tests related to strength and function were conducted:

Quadriceps strength: Quadriceps strength (maximum voluntary isometric contraction (MVIC)) was tested using an isokinetic dynamometer (Kin-Com® 500H Chattanooga).

Timed Up and Go test (TUG): This test was conducted as outlined in the publication from Podsiadlo and Richardson.

Six Minute Walk for Distance (6MWD): The 6MWD was conducted according to the guidelines from the American Thoracic Society and was performed indoors, along a flat, straight, enclosed corridor with a hard surface [11-13].

Biochemical measurements: Members were were advise to avoid vigorous exercise and liquor utilization the day before the illustration of fasting blood tests at baseline and endpoint. The blood samples were analyzed for general blood status (including hemoglobin) and high sensitivity CRP was measured with ELISA at the laboratory at the University Hospital in Reykjavik, Iceland.

Leisure-Time Physical Activity (LTPA): Information on LTPA (shown as min/week) during the last 12 months was collected using a questionnaire [14], the required information was collected accordingly, based on the compendium of physical activities and the Paffenbarger's questionnaire [15,16].

Statistical analysis

Statistical analysis was conducted using SPSS for Windows version 20.0 (SPSS, Chicago, IL, USA), and the significance level was set at $p < 0.05$. Data were checked for normality using the Kolmogorov-Smirnov test and are shown as mean \pm standard deviation (SD). Differences between baseline and endpoint values were calculated using the paired samples t-test for parametric variables and Wilcoxon matched-pair signed-rank test for non-parametric variables.

In order to know whether hemoglobin predicts physical function at baseline, the response to the 12-week resistance exercise training (endpoint) and/or changes in physical function after a period of 6 to 18 months of follow-up, linear models with fixed factors and covariates were constructed. Dependent variables were quadriceps strength, 6 MWD and TUG at baseline, endpoint, and follow-up.

Results obtained from the linear models are shown as parameter estimates. The numbers shown are the effect size B , lower confidence limits, higher confidence limits and p-values which show estimated changes in outcomes by an increase of hemoglobin by 10 g/L. For each outcome we present two models which differ in the amount of included factors and covariates used for correction.

Model 1: Baseline hemoglobin (g/L), age, gender: additionally for endpoint and follow-up models: baseline value of the relevant outcome variable.

Model 2: In addition to variables in model 1: waist, c-reactive protein; additionally for baseline and follow-up models: leisure time physical activity (minutes/week) at baseline or follow-up, respectively.

All follow-up models additionally contained length of follow-up as a covariate. The inclusion of the baseline value of the corresponding outcome variable means that the statistical models estimated the changes in physical function (rather than endpoint values) observed in the endpoint and follow-up models.

Results

Of the 236 participants that started the study, 208 (88%) finished the resistance exercise program and 154 (65%) were available at follow-up. Participants completed 91% of all prescribed strength training sessions. Anthropometrics, blood chemical variables and physical function are shown in Table 1. Only 12 participants (3 men and 7 women) were anemic.

According to the linear model's baseline hemoglobin predicted quadriceps strength at baseline, but neither at endpoint nor at follow-up. It also predicted TUG at all three time points, although this was of borderline significance for baseline and endpoint. Finally, hemoglobin predicted endpoint 6 MWD, but not at baseline (follow up 6 MWD is not available) (Table 2). Inclusion of compliance to the resistance exercise program did not affect endpoint models.

Characteristics	Total (n=236)	Men (n=98)	Women (n=138)
Age, mean ± SD	73.6 ± 5.7	74.6 ± 5.9	72.8 ± 5.5
BMI, kg/m ² , mean ± SD	28.8 ± 4.8	29.7 ± 4.6	28.1 ± 4.9
Waist, cm, mean ± SD	99.8 ± 14.4	108.5 ± 12.1	93.6 ± 12.6
C-reactive protein, mean ± SD	7.1 ± 4.6	7.4 ± 5.4	6.9 ± 4
Hemoglobin, g/L, mean ± SD	141 ± 12	147 ± 11	137 ± 11
LTPA, minutes, mean ± SD	342 ± 342	323 ± 341	356 ± 343
LTPA at follow-up, minutes, mean ± SD	285 ± 318	331 ± 374	253 ± 268
Physical function			
Quadriceps strength, N, mean ± SD			
Baseline (n=236)	464 ± 124	538 ± 124	409 ± 90
Endpoint (n=208)	521 ± 131 ^a	600 ± 131 ^a	463 ± 97 ^a
Follow-up (n=154)	494 ± 126 ^a	574 ± 117 ^a	435 ± 96 ^a
Timed-up-and-go, second, mean ± SD			
Baseline (n=236)	7.9 ± 2.2	8 ± 2.1	7.9 ± 2.3
Endpoint (n=208)	7.1 ± 1.7 ^a	7.3 ± 1.7 ^a	7 ± 1.8 ^a
Follow-up (n=154)	7.1 ± 2.6 ^a	7.7 ± 3.3 ^a	6.7 ± 1.8 ^a
6 Minutes-walk-for-distance, meters, mean ± SD			
Baseline (n=236)	453 ± 80	456 ± 86	452 ± 76
Endpoint (n=208)	496 ± 76 ^a	497 ± 86 ^a	495 ± 67 ^a

SD=Standard Deviation; BMI=Body Mass Index; LTPA=Leisure Time Physical Activity.
^aSignificant difference compared with baseline value (P≤0.5).

Table 1: Baseline characteristics and physical function.

Physical function	Model 1			Model 2				
	B ^a	95% CI	p-value	B ^a	95% CI	p-value		
Quadriceps strength, N, mean ± SD								
Baseline (n=236)	15.04	3.63	26.45	0.01	14.32	2.57	26.07	0.017
Endpoint (n=208)	-0.19	-6.91	6.53	0.957	-1.43	-8.36	5.5	0.685
Follow-up (n=154)	-5.11	-16.29	6.06	0.367	-5.28	-16.84	6.29	0.368
Timed-up-and-go, second, mean ± SD								
Baseline (n=236)	-0.14	-0.038	0.09	0.231	-0.22	-0.45	0.01	0.057
Endpoint (n=208)	-0.08	-0.22	0.07	0.294	-0.14	-0.28	0.01	0.062
Follow-up (n=154)	-0.25	-0.55	0.05	0.106	-0.36	-0.66	-0.06	0.019
6 Minutes-walk-for-distance, meters, mean ± SD								
Baseline (n=236)	2.96	-5.38	11.3	0.485	6.28	-1.42	13.97	0.109
Endpoint (n=208)	1.99	-2.44	6.42	0.377	4.88	0.52	9.25	0.028

TUG=Timed-up-and-go; 6 MWD=6 Minutes-walk-for-distance; B=Beta coefficient; CI=Confidence interval.

^aB and 95% CI show estimated changes in outcomes by an increase of haemoglobin by 10 g/L.

Model 1: Baseline haemoglobin (g/L), age, gender; additionally, for endpoint and follow up models: Baseline value of the relevant outcome variable.

Model 2: In addition to variables in model 1: waist, c-reactive protein; additionally, for baseline and follow-up models: Leisure time physical activity (minutes/week) at baseline or follow-up, respectively.

Table 2: Prediction of physical function at baseline, endpoint and follow-up by baseline haemoglobin.

Using quartiles of hemoglobin instead of hemoglobin as a continuous variable in the linear models resulted in similar but somewhat weaker results. A comparison (same correction as in models 2 in Table 2 between the first and the fourth quartile shows significantly poorer physical function in the first quartile: baseline quadriceps strength= -41.9 N; baseline TUG=+0.4 sec (however, p>0.1); endpoint 6 MWD= -16.1 m; follow-up TUG=+1.0 sec.

Discussion

This particular study had investigated associations between hemoglobin and physical function in old adults. The main finding was that hemoglobin was positively associated to physical function, although only a minority or around 4% of the participants were anemic. We found also that baseline hemoglobin predicts responses to a 12-week resistance exercise training and subsequent changes in physical function after a period of 6 to 18 months of follow-up [16].

In general, the changes in physical function observed after the

resistance exercise program were comparable to other studies [17-19]. As previous cross-sectional studies, our study also finds positive associations between hemoglobin and physical function when baseline data is used in a cross-sectional manner. Although the observed associations were not entirely consistent, it has to be considered that our sample size of 236 is rather small for that kind of analysis. In general, an important limitation of each cross-sectional analysis is that causal relationship between two variables cannot be established and the direction of association is not clear. A 4-year prospective cohort study, which included 1146 participants, reported that anemia was associated with greater mean decline in physical performance over 4 years [7]. However, there is a lack of evidence based on resistance exercise intervention studies investigating effect of baseline hemoglobin/anemia on physical performance changes over exercise intervention period among community dwelling older adults.

In the present analysis we used longitudinal data from a randomized trial which also included 6- and 18-months follow-up data

of the exercise intervention. The results are in general agreement with the abovementioned studies, which show that hemoglobin is positively associated with physical function. However, our data specifically show that low baseline hemoglobin predicts poorer improvement after a 12-week resistance exercise program. To our knowledge, this has not been shown previously. Importantly, this association does not seem to be caused by lower compliance to the exercise program, because adjusting for compliance in the statistical analysis does not change the results. Similarly, we correct for leisure time physical activity in the follow-up analysis, however the correction does not affect the results.

It is worthwhile considering whether the associations observed in the statistical analysis of continuous data translate into meaningful or clinically relevant differences when groups, e.g., hemoglobin quartiles are compared to each other. When we used quartiles of hemoglobin in the statistical analysis the results were similar but weaker. A comparison between the first and the fourth quartile shows significantly poorer physical function in the first quartile: baseline quadriceps strength=-41.9 N; endpoint 6 MWD=-16.1 m; follow-up TUG=+1.0 sec. However, the results are not entirely consistent, e.g., we did not find significant differences between quartiles in endpoint TUG or 6 MWD at follow-up.

In the current study there is a lower prevalence of anemia than commonly reported (5-12%). In general, variability in anemia prevalence possibly reflects the heterogeneity of this age group, e.g., living circumstances and health status that all influence the prevalence of anemia. Our participants were community dwelling old adults who volunteered for a resistance exercise intervention and where thus most likely not representative for this age group in Iceland.

One of the strengths of the current analysis is that we use both cross-sectional and longitudinal data for the statistical calculations. Although the results are not entirely consistent when all three time points (baseline, endpoint, follow-up) are taken into account, we still see a coherent pattern of results which is both biologically plausible and has been suggested by previous cross-sectional studies. Furthermore, our results indicate that differences between hemoglobin quartiles are relevant although most of our participants have hemoglobin concentrations within the WHO normal range. It is also a strength that in the statistical analysis we correct for many potential confounders which can affect physical function, e.g., age, body fat, habitual physical activity or inflammatory markers [20-22].

Conclusion

This particular study shows that hemoglobin is associated positively to physical function in community dwelling old adults although the prevalence of anemia was only 4%. Furthermore, we found that baseline hemoglobin predicts responses to 12-week resistance exercise training and subsequent changes in physical function after a period of 6 to 18 months of follow-up. Neither consistency to exercise training nor recreation time physical activity clarify these findings.

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The authors declare no conflict of interest. The trial is registered at the US National Library of Medicine (Nr. NCT01074879).

Author Contributions

AR: Concept and design, acquisition of subjects and/or data, analysis and interpretation of data, preparation of manuscript.

MC: Analysis and interpretation of data, preparation of manuscript.

OGG: Concept and design, acquisition of subjects and/or data, preparation of manuscript.

KB: Acquisition of subjects and/or data, preparation of manuscript.

PVJ: Concept and design, preparation of manuscript.

IT: Concept and design, preparation of manuscript.

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