THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Medical Sciences
cite as: J Gerontol A Biol Sci Med Sci, 2017, Vol. 72, No. 4, 543–547
doi:10.1093/gerona/glw134
Advance Access publication July 20, 2016

OXFORD

Research Article

Low Birth Weight and Risk of Later-Life Physical Disability in Women

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Received December 7, 2015; Accepted June 28, 2016

Decision Editor: Stephen Kritchevsky, PhD

Abstract

Background: There is strong evidence that low and high birth weight due to in-utero programming results in elevated risk for adult diseases, though less research has been performed examining the influence of birth weight and physical disability later in life.
Methods: Baseline data from 76,055 postmenopausal women in the Women's Health Initiative, a large multi-ethnic cohort, were used to examine the association between self-reported birth weight category (<6 lbs, 6–7 lbs 15 oz, 8–9 lbs 15 oz, and ≥10 lbs) and the self-reported physical functioning score on the RAND 36-item Health Survey. Linear regression models were adjusted for age, education, race/ethnicity, body mass index, and a comorbidity score.
Results: Unadjusted models indicate that women born in the lowest and highest birth weight categories have significantly lower physical functioning scores as compared to women born in the normal weight category ($\beta = -2.22$, $p < .0001$ and $\beta = -3.56$, $p < .0001$, respectively). After adjustments, the relationship between the lowest birth weight category and physical functioning score remained significant ($\beta = -1.52$, $p < .0001$); however, the association with the highest birth weight category dissipated.
Conclusions: Preconception and prenatal interventions aimed at reducing the incidence of low birth weight infants may subsequently reduce the burden of later-life physical disability.

Keywords: Birth weight—Physical disability—Developmental Origins of Health and Disease hypothesis—Physical functioning

Disability in older adults is an important and growing public health concern. In the United States, approximately 9% of the adult population (≥18 years) has one or more disabilities in basic activities of daily living (ADLs) (1). With the projected number of people aged 65 and older to double from 35 million in 2000 to 71 million in 2030 (2), an increase in physical disability (defined as having difficulty performing daily activities such as walking, getting dressed, and taking a shower) will result in greater use of medical care, more institutionalization, and poorer physical health (3–5). Identifying contributors that increase one's risk for later-life disability is not only important to prevent physical disability, but also to understand its pathophysiology, especially among those who do not have a history of comorbidities known to result in physical disability.

There is strong evidence that low and high birth weight due to in-utero programming results in elevated risk for adult diseases (6). The Developmental Origins of Health and Disease hypothesis suggests that developmental programming from a suboptimal prenatal environment (eg, fetal malnutrition, gestational diabetes) permanently sets, or "programs" the structure and function of different organs and organ systems (6). This programming may lead to impairment of vital physiologic and metabolic systems which ultimately results in chronic conditions or disorders later in life (7). It has now been well-established that birth weight is associated with many later-in-life conditions such as hypertension, diabetes, cardiovascular disease, and cancer (8–11). Several studies have also observed significant associations between birth weight and adult grip strength (12,13), bone mass (14), senior fitness (15), physical functioning (16), and muscle strength (17–19); however, far less is known about the potential impact of birth weight on physical disability. Additionally, early life disadvantages, such as low birth weight, may contribute to health disparities observed in middle- to old-age. As physical disability rates increase with increasing age and are greater in females than in males, the objective of this study was to examine the association between birth weight and physical disability using a large cohort of women ≥50 from the Women's Health Initiative (WHI).

Methods

Study Population

This retrospective, cross-sectional study utilized data from the WHI, a large, national health study designed to advance knowledge of the causes of major chronic diseases in postmenopausal women. Detailed information regarding the study's recruitment, eligibility, and implementation can be found elsewhere (20). Briefly, from 1993 to 1998, 40 U.S. clinical centers recruited 161,608 postmenopausal women between the ages of 50–79, representing major racial/ethnic groups from the general population. Women were enrolled in one of the clinical trial arms (WHI-CT; n = 67,932) or in the long-term follow-up observational study (WHI-OS; n = 93,676). Only those enrolled in the WHI-OS reported their birth weight; thus, only these women were included in our analysis. All participating women provided written informed consent upon enrollment. Study protocols were approved by the Institutional Review Board of each clinical center (21).

Data Collection of Baseline Measures

At study entry, physical characteristics, such as weight, height, and waist and hip circumference, were measured and recorded by trained study staff. In addition, structured, self-administered questionnaires were used to collect information on demographics; dietary and lifestyle factors; and medical, reproductive, and family history. Women were asked to report their birth weight as one of the following categories: less than 6 pounds (lbs), 6–7 lbs 15 ounces (oz), 8–9 lbs 15 oz, ≥10 lbs, or unknown. They were also asked to report if they were born 4 or more weeks premature or if they were a twin or triplet.

Disability Definition

Physical disability was measured according to the physical functioning construct available in the WHI. This construct was created using responses to ten questions from the RAND 36-item Health Survey (22), which asked participants to indicate if their health limited them a little, a lot, or not at all from completing any of the following activities: vigorous activities such as running, lifting heavy objects, or strenuous sports; moderate activities such as moving a table, vacuuming, bowling, or golfing; lifting or carrying groceries; climbing several flights of stairs; climbing one flight of stairs; bending, kneeling, or stooping; walking more than one mile; walking several blocks; walking one block, or; bathing or dressing herself. Using the responses, a continuous measure ranging from 0 and 100 was constructed to represent each woman's level of physical functioning, with higher scores indicating a more favorable state.

Statistical Methods

Baseline characteristics of the study population were compared using chi-square tests for categorical variables and t tests for continuous variables. Linear regression models were used to estimate the association between birth weight and later-life disability with and without adjusting for other potential risk factors. For birth weight, the "6 lbs to 7 lbs 15 oz" category was used as the referent group as term infants born within this weight range are considered to be of normal birth weight. Covariates examined for inclusion in the models were demographic characteristics (age, education, ever smoking, and race/ethnicity), body mass index, and a comorbidity score. For the comorbidity score, a woman was given one point if she reported, at baseline, having ever had one of the following conditions: cancer, osteoporosis, type 2 diabetes, deep vein thrombosis, pulmonary edema, stroke, myocardial infarction, congestive heart failure, or liver disease. Only covariates that altered the beta-estimates by at least 10% were retained in final models. All analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC).

Results

Results from the comparison of baseline characteristics are shown in Table 1. Women born weighing less than 6 lbs tended to be younger, be of a race/ethnicity other than white, have type 2 diabetes at baseline, and to have reported having a stroke prior to study entry. Women born weighing ≥10 lbs were older, had a higher baseline body mass index, and were more likely to report a prior cancer diagnosis at study entry. Compared to women born between 6 lbs and 9 lbs 15 oz, women born weighing less than 6 lbs and ≥10 lbs were less educated and had a higher comorbidity score.

Table 2 shows the crude and adjusted estimates of the associations between birth weight and physical disability at WHI study entry. Women whose birth weight was outside the normal range (6–7 lbs 15 oz) had a significantly lower physical functioning score when compared to those born within the normal range. Importantly, those born weighing ≥10 lbs had the lowest physical functioning score compared to women in the normal weight range (β = −3.56, p < .0001). After adjusting the model for age at baseline, education, race/ethnicity, body mass index, and the comorbidity index, women born weighing less than 6 lbs still had a significantly lower physical functioning score compared to those born within the normal range (β = −1.52, p < .0001). However, the physical functioning score was no longer significantly different between women born weighing 8–9 lbs 15 oz or ≥10 lbs and those born in the normal range (p = .76 and p = .22, respectively).

Discussion

We have demonstrated that a lower birth weight is associated with increased physical disability, as measured by our physical functioning score. Adjustment for comorbidity and demographic characteristics weakened, but did not remove, this relationship. Birth weight has previously been reported to be positively associated with adult grip strength, physical functioning, and muscle strength and negatively associated with sarcopenia (12,16,17,19,23).

Identifying the mechanism(s) underlying the association between lower birth weight and physical disability is complex, as birth weight may be a marker for a variety of in utero insults (24). It has previously been proposed that changes in epigenetic processes (eg, DNA methylation and histone modifications) underlie the associations between birth weight and physical disability, as well as other study outcomes (10,11,25). There is, however, one potential direct mechanism by which birth weight could affect muscle mass. Animal studies

Table 1. Baseline Characteristics of 72,650 WHI Study Participants by Birth Weight Category

	Birth Weight Category				
	<6 lbs (*n* = 6,353)	6–7 lbs 15 oz (*n* = 51,670)	8–9 lbs 15 oz (*n* = 15,398)	≥10 lbs (*n* = 2,634)	*p*
Age at baseline (mean, *SD*)	62.9 (7.5)	63.3 (7.3)	63.4 (7.3)	65.0 (7.0)	<.0001
Race/ethnicity					<.0001
White	4,947 (7.6)	43,783 (67.6)	13,689 (21.1)	2,330 (3.6)	
Black	651 (11.6)	3,900 (69.8)	881 (15.8)	156 (2.8)	
Asian/Pacific Islander	321 (17.4)	1,335 (72.4)	166 (9.0)	21 (1.1)	
Hispanic	306 (11.8)	1,790 (69.2)	419 (16.2)	70 (2.7)	
Other/unknown	111 (10.2)	735 (67.6)	195 (17.9)	47 (4.3)	
Education					<.0001
≤High school diploma/GED	1,446 (9.5)	10,164 (66.9)	2,933 (19.3)	647 (4.3)	
School after high school	2,391 (8.6)	18,613 (67.1)	5,674 (20.4)	1,052 (3.8)	
College degree or higher	2,454 (7.6)	22,527 (69.4)	6,665 (20.5)	805 (2.5)	
Body mass index at baseline (mean, *SD*)	27.3 (6.0)	27.0 (5.7)	27.7 (6.1)	28.6 (6.6)	<.0001
Smoked ever					<.0001
<100 cigarettes ever	3,304 (8.7)	25,776 (68.3)	7,402 (19.6)	1,281 (3.4)	
≥100 cigarettes ever	2,989 (7.9)	25,487 (67.6)	7,883 (20.9)	1,333 (3.5)	
Comorbidity score (mean, *SD*)	0.29 (0.6)	0.24 (0.5)	0.24 (0.5)	0.30 (0.6)	<.0001
Breast cancer ever	286 (7.1)	2,745 (68.3)	830 (20.7)	156 (3.9)	.02
Colon cancer ever	55 (8.1)	439 (65.0)	139 (20.5)	42 (6.2)	.001
Endometrial cancer ever	135 (9.7)	901 (65.0)	291 (21.0)	59 (4.3)	.04
Other cancer in last 10 years	97 (7.8)	812 (66.0)	264 (21.4)	58 (4.7)	.06
Osteoporosis-related fracture ever	153 (10.3)	991 (66.9)	270 (18.2)	67 (4.5)	.002
Type 2 diabetes	460 (11.3)	2,687 (66.0)	770 (18.9)	150 (3.7)	<.0001
Pulmonary edema	69 (9.1)	501 (65.7)	158 (20.7)	34 (4.5)	.35
Stroke	130 (11.9)	736 (67.6)	183 (16.8)	40 (3.7)	<.0001
Myocardial infarction	177 (9.8)	1,226 (67.9)	335 (18.6)	67 (3.7)	.06
Congestive heart failure	85 (12.5)	426 (62.6)	136 (20.0)	33 (4.9)	.0001
Liver disease	170 (9.6)	1,158 (65.1)	379 (21.3)	73 (4.1)	.04

Notes: WHI = Women's Health Initiative.

p-values from chi-square tests for categorical variables and *t* tests for continuous variables. Values presented as *n* (%) unless stated as mean (*SD*).

Table 2. Results From Linear Regression Analysis of the Association Between Birth Weight to Physical Functioning Score in WHI

	Birth Weight Category			
	<6 lbs (*n* = 6,353)	6–7 lbs 15 oz (*n* = 51,670)	8–9 lbs 15 oz (*n* = 15,398)	≥10 lbs (*n* = 2,634)
Unadjusted	−2.22 (0.27) *p* < .0001	REF	−0.64 (0.19) *p* = .0006	−3.56 (0.40) *p* < .0001
Adjusted for				
Age	−2.41 (0.26) *p* < .0001	REF	−0.54 (0.18) *p* = .003	−2.54 (0.39) *p* < .0001
Education	−1.69 (0.26) *p* < .0001	REF	−0.71 (0.18) *p* < .0001	−2.94 (0.40) *p* < .0001
Race/ethnicity	−1.99 (0.27) *p* < .0001	REF	−0.80 (0.18) *p* < .0001	−3.69 (0.40) *p* < .0001
BMI	−1.95 (0.25) *p* < .0001	REF	0.21 (0.17) *p* = .23	−1.68 (0.39) *p* < .0001
Comorbidity score	−1.88 (0.26) *p* < .0001	REF	−0.64 (0.18) *p* = .0004	−3.15 (0.40) *p* < .0001
Full model*	−1.50 (0.23) *p* < .0001	REF	0.07 (0.18) *p* = .75	−0.43 (0.38) *p* = .21

Notes: BMI = body mass index, WHI = Women's Health Initiative.

Results presented as β (*SE*) and *p*-value.

*Full model adjusted for age (continuous), education level (categorical), race/ethnicity (categorical), BMI (continuous), normalized socioeconomic status (NSES) and comorbidity score (continuous).

have demonstrated that an adverse intrauterine environment, such as malnutrition, can affect muscle histology, including the quantity of muscle fibers (26,27), and any deficit in the number of fibers cannot be entirely explained by genetics or malnutrition during early development (28). As the inevitable loss of muscle fibers proceeds into older age, a person born with fewer muscle fibers would be at a considerable disadvantage later in life, which could, thus, lead to a higher risk of decreased physical functioning or increased physical disability (13). Additionally, birth weight has also been shown to be positively associated with adult bone mass (14). As bone mass decreases with increasing age, the risk for low-energy fractures due to low bone mass increases, thus increasing the risk for physical disability (14).

The association between birth weight and physical disability could also be explained through birth weight's associations with other chronic illnesses. Previous studies have identified birth weight as a risk factor for several types of adult-onset cancers (11), type 2 diabetes (10), cardiovascular disease (29,30), and other chronic illnesses (31). It is possible that the observed association between birth weight and physical disability could be explained, at least in part, through mediation by other chronic diseases. We attempted to control for the possible effects of these mediators by adjusting for the comorbidity score; however, residual association effects are possible. Strengths of our study include its large sample size of more than 72,000 participants. We were also able to evaluate a broad range of potential confounders that may account for the underlying association. Our study was limited to evaluating only self-reported categories of birth weight. While this method is less ideal compared to medical record or birth certificate abstraction, validity has been demonstrated for the correlation between medical record information and self-reported birth weight category (32,33). Additionally, any potential misclassification bias of the exposure would likely not differ across categories. Another limitation of this analysis was our inability to adjust for all possible covariates. It is also possible that some of the physical disability experienced by our subjects was due to a traumatic injury or comorbidity not captured by the WHI questionnaires. Finally, we did not have data on in utero pregnancy-related exposures and conditions (eg, in utero tobacco smoking exposure; gestational diabetes), as this information was not collected.

In conclusion, we demonstrate that increasing birth weight category appears to be significantly associated with a decreased risk for physical disability (as measured by the RAND physical function score) in postmenopausal women. Our research further supports the role of early developmental abnormalities in later-life conditions and, therefore, interventions targeted during preconception and prenatal care to reduce the incidence of low birth weight may reduce the burden of later-life physical disability.

Funding

The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through contracts HHSN268201100046C, HHSN268201100001C, HHSN268201100002C, HHSN268201100003C, HHSN268201100004C, and HHSN271201100004C.

Acknowledgments

We thank the WHI investigators and staff for their dedication and the study participants for making this program possible, including: *Program Office*: (National Heart, Lung, and Blood Institute, Bethesda, Maryland) Jacques Rossouw, Shari Ludlam, Dale Burwen, Joan McGowan, Leslie Ford, and Nancy Geller. *Clinical Coordinating Center*: (Fred Hutchinson Cancer Research Center, Seattle, Washington) Garnet Anderson, Ross Prentice, Andrea LaCroix, and Charles Kooperberg. *Investigators and Academic Centers*: (Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts) JoAnn E. Manson; (MedStar Health Research Institute/Howard University, Washington, DC) Barbara V. Howard; (Stanford Prevention Research Center, Stanford, California) Marcia L. Stefanick; (The Ohio State University, Columbus, Ohio) Rebecca Jackson; (University of Arizona, Tucson/Phoenix, Arizona) Cynthia A. Thomson; (University at Buffalo, Buffalo, New York) Jean Wactawski-Wende; (University of Florida, Gainesville/Jacksonville, Florida) Marian Limacher; (University of Iowa, Iowa City/Davenport, Iowa) Robert Wallace; (University of Pittsburgh, Pittsburgh, Pennsylvania) Lewis Kuller; (Wake Forest University School of Medicine, Winston-Salem, North Carolina) Sally Shumaker. *Women's Health Initiative Memory Study*: (Wake Forest University School of Medicine, Winston-Salem, North Carolina) Sally Shumaker.

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