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Higher oily fish consumption in late pregnancy is associated with reduced aortic stiffness in the child at age 9 years

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Abstract

Rationale—Higher pulse wave velocity (PWV) reflects increased arterial stiffness and is an established cardiovascular risk marker associated with lower long-chain n-3 polyunsaturated fatty acid intake in adults. Experimentally, maternal fatty acid intake in pregnancy has lasting effects on offspring arterial stiffness.

Objective—To examine the association between maternal consumption of oily fish, a source of long-chain n-3 polyunsaturated fatty acids, in pregnancy and child's aortic stiffness age 9 years.

Methods and Results—In a mother-offspring study (Southampton Women's Survey) the child's descending aorta PWV was measured at age 9 years using velocity-encoded phase contrast magnetic resonance imaging and related to maternal oily fish consumption assessed prospectively during pregnancy. Higher oily fish consumption in late pregnancy was associated with lower childhood aortic PWV (sex-adjusted $\beta = -0.084$ m/s/ portion/week, [95% CI -0.137 to -0.031], $p = 0.002$, $n = 226$). Mother's educational attainment was independently associated with child's PWV. PWV was not associated with the child's current oily fish consumption.

Conclusions—Level of maternal oily fish consumption in pregnancy may influence child's large artery development, with potential long-term consequences for later cardiovascular risk.

Keywords

Pregnancy; fatty acids; pulse wave velocity

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Introduction

Greater aortic stiffness increases systolic blood pressure (BP) with age¹ and predicts future cardiovascular risk and all-cause mortality². Higher pulse wave velocity (PWV) reflects increased arterial stiffness and is an established cardiovascular risk marker^{3,4}. There is now evidence that early developmental factors may partly set such risk⁵.

Long-chain *n*-3 polyunsaturated fatty acids (LC-PUFAs) are associated with reduced cardiovascular risk; consumption in adulthood reduces arterial stiffness⁶. Conversely, in rats increased saturated fatty acid intake in pregnancy increases offspring arterial stiffness⁷, suggesting that variations in maternal diet have long-term consequences for later arterial stiffness and cardiovascular risk. We examined maternal consumption of oily fish, a source of LC-PUFAs, in pregnancy in relation to the child's arterial stiffness age 9 years.

Methods

In a UK mother-offspring study (Southampton Women's Survey⁸) maternal early and late pregnancy diet and child's diet age 9 years were assessed using administered questionnaires⁹. Aortic PWV was measured in 234 children aged 9 years, with approval from the local ethics committee and informed written assent/consent.

Magnetic resonance imaging (MRI) phase-contrast velocity encoding sequences were acquired in the plane perpendicular to the aortic long axis, in the proximal descending aorta (level of the pulmonary trunk) and the distal descending aorta (above the aortic bifurcation) (Fig. 1). A phase contrast flow mapping sequence was employed with free breathing and retrospective ECG gating. A velocity encoding (VENC) gradient of 150-200 cm/s was applied in the through plane direction. Right brachial BP was recorded using a pediatric cuff immediately following the flow sequence acquisitions (Invivo MRI compatible patient monitor). Velocity flow curves were generated using open source software (Osirix). PWV (m/s) was calculated using Matlab (MathWorks, Natick, MA) and the transit time method¹⁰ from d/t (d =distance, t =transit time of the systolic wave front between the two flow acquisition sites (Fig. 1)).

Univariate linear regression analyses were performed (Stata version 13.0, Statacorp LP, TX) to relate child's PWV to maternal oily fish consumption and other maternal, infant and childhood factors shown in Table 1; multivariate analysis included variables with significant associations. β -coefficients reflect the change in outcome compared to the reference category.

Results

256 participants attended for MRI; 4 declined, 7 proved claustrophobic, 10 did not complete the protocol/had substandard images from motion artifacts. 1 extreme outlier, attributed to measurement error, was excluded. Table 1 shows characteristics of the remaining 234 children (116 boys); mean PWV was 3.5 m/s (within previously reported childhood ranges¹¹), BMI 17.3 kg/m². 26.9% of mothers smoked pre-pregnancy.

Analysed as a continuous variable, higher late pregnancy maternal oily fish consumption was associated with lower childhood aortic PWV (sex-adjusted $\beta = -0.084$ m/s /portion/week (95%CI -0.137 to -0.031), $p = 0.002$, Fig. 2), with a similar association for early pregnancy oily fish consumption ($\beta = -0.062$ (-0.124 to -0.001), $p = 0.046$). Higher mother's educational attainment (three levels, Table 1), was associated with lower childhood PWV ($\beta = -0.175$ m/s/level (-0.278 to -0.072), $p = 0.002$), as was higher social class (Table 2). The coefficients above hardly changed in multivariate analysis simultaneously including both mother's educational attainment and late pregnancy oily fish consumption; both p-values remained 0.002. Additional inclusion of maternal, neonatal and childhood characteristics significant at $p < 0.1$ (Table 2) had little influence on these associations (Table 3).

PWV showed the expected associations with childhood systolic and diastolic BP, mean arterial pressure and heart rate (Table 2). After adjusting for mother's qualification level and child's sex, maternal oily fish consumption was not associated with childhood heart rate or BP (Table I, Online Supplement). Childhood PWV showed no associations with birthweight, or child's height, BMI and oily fish consumption at 9 years.

Discussion

Greater maternal oily fish consumption in early or late pregnancy was associated with lower child's aortic PWV and aortic stiffness at age 9 years. LC-PUFAs in oily fish and fish oils have anti-inflammatory properties, reduce BP and increase endothelial relaxation, vascular compliance and heart rate variability¹²; supplementation in adults reduces arterial stiffness⁶. LC-PUFA levels in the fetal circulation increase in late pregnancy, when fetal docosahexaenoic acid (DHA) correlates with maternal levels¹³. This may explain the stronger association between child's PWV and late *versus* early pregnancy maternal oily fish consumption.

We found no association between child's current oily fish consumption and vascular stiffness. In keeping with this, LC-PUFA supplementation during childhood offers few long-term cardiovascular benefits in terms of BP, heart rate or arterial distensibility assessed several years after the supplementation^{14–16}. Cardiovascular measures taken in infants during a period of supplementation with fish oil, and DHA or LC-PUFA supplemented infant formulae, did however show favorable heart rate and BP changes^{17–19}. These studies, together with our data showing an effect of prenatal nutrition, suggest that nutritional interventions instituted early in the lifecourse may be most effective.

PWV was linked to the child's BP, but there was no association between maternal oily fish consumption and BP. Arterial stiffening is the principal cause of increased cardiac afterload and increasing systolic BP with advancing years¹; even without an independent effect on childhood BP, structural changes in the vascular wall induced by maternal diet during development may have implications for adult cardiac function and BP. Higher childhood PWV has uncertain predictive value and does not itself cause disease, but baseline PWV does predict later aortic dilatation in children with tetralogy of Fallot²⁰.

Participants in this study are part of a prospective longitudinal cohort study covering a wide socioeconomic background. Vascular stiffness was assessed at age 9 years, before the acquisition of significant risk burden, ensuring minimal influence of other lifestyle risk factors such as smoking. Our results are thus unlikely to be confounded by the influence of other cardiovascular risk factors.

In summary, our findings suggest that normal variations in maternal oily fish consumption in pregnancy influence vascular development of the fetus, changing childhood aortic compliance, with implications for later cardiovascular disease. The findings raise the question of the major influences on maternal diet. The quality of women's diets is strongly dependent on their nutrition literacy and level of educational attainment²¹ and we found an independent and additive effect of maternal educational attainment on childhood vascular stiffness, perhaps reflecting other nutritional influences. The findings raise the possibility that interventions that improve educational attainment and nutrition literacy could reduce cardiovascular risk in the next generation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Non-standard Abbreviations and Acronyms

PWV	pulse wave velocity
MRI	Magnetic resonance imaging
VENC	velocity encoding
LC-PUFA	long-chain <i>n</i> -3 polyunsaturated fatty acid
DHA	docosahexaenoic acid

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Section on Novelty and Significance

What is known?

- Experimental studies have shown that a mother's fatty acid intake in pregnancy has lasting effects on arterial stiffness in the offspring

In human pregnancy little is known about whether a mother's diet influences arterial stiffness and cardiovascular risk in her children.

What new information does this article contribute?

- Children whose mothers had higher oily fish consumption in pregnancy had lower aortic stiffness at age 9 years, measured by magnetic resonance imaging

The findings provide further evidence that nutritional interventions instituted early in the lifecourse could be effective in reducing cardiovascular risk in the offspring.

Prenatal influences contribute to the risk of cardiovascular disease in adulthood, but the developmental exposures and underlying mechanisms are poorly understood. One possible mechanism is large artery structure and stiffness; this is partly determined in utero and greater stiffness is the principal cause of increased cardiac afterload and increasing blood pressure with age. Here, we show that higher maternal oily fish intake in pregnancy is associated with lower aortic stiffness in children aged 9-years. The findings highlight the importance of prenatal vascular development and suggest that interventions that improve a mother's nutrition could reduce cardiovascular risk in the next generation.

Figure 1. Sagittal TruFisp image showing flow positions in descending aorta, with resultant flow curves. PWV calculated as $\Delta d / \Delta t$ (distance between the flow acquisitions/time difference between the wave front arrivals).

Figure 2.

Maternal oily fish intake in late pregnancy vs PWV (means and 95% confidence intervals).

Table 1

Characteristics of the study population

	n	Median (IQR) / Mean (SD)*
<i>Maternal</i>		
BMI pre-pregnancy (kg/m ²)	233	24.1 (22.2–27.7)
Early pregnancy: oily fish portions/week	191	0.5 (0.25–1.5)
Late pregnancy: oily fish portions/week	226	0.5 (0.25–1.5)
Social class	229	
Professional/management & technical	105	45.9%
Skilled non-manual/manual	97	42.4%
Partly skilled/unskilled	27	11.8%
Educational attainment	234	
None/minimal	27	11.5%
Standard school qualifications age 16–18	131	56%
Post school qualifications	76	32.5%
Pre-pregnancy smoking status	234	
Smoker	63	26.9%
Non-smoker	171	73.1%
Parity	234	
0	122	52.1%
1+	112	47.9%
<i>Infancy</i>		
Birthweight (kg)	231	3.5 (3.1–3.8)
Breastfeeding duration	226	3 (0–7)
<i>Childhood follow-up</i>		
Age (years)	234	9.4 (9.3–9.6)
Height (cm)	234	136.4 (6.3)*
Weight (kg)	234	32.3 (29.2–37.4)
BMI (kg/m ²)	234	17.3 (15.9–19.2)
Pulse Wave Velocity (m/s)	234	3.5 (0.5)*
Systolic BP (mmHg)	232	99.4 (9.2)*
Diastolic BP (mmHg)	232	59.1 (7.5)*
Pulse pressure (mmHg)	232	40.3 (8.6)*
Mean Arterial Pressure (mmHg)	232	72.0 (68.0–76.0)
Heart rate (beats/min)	234	81.21 (74.77–88.01)
Oily fish consumption	234	0.5 (0–1)

Table 2

Univariate analyses of maternal, neonatal and childhood characteristics and child's cardiovascular measures in relation to PWV (m/s) at age 9 years (adjusted for sex).

	n	Coefficient	95%CI	p-value
<i>Maternal characteristics⁺</i>				
Early pregnancy oily fish consumption	191	-0.062	-0.124, -0.001	0.046
Late pregnancy oily fish consumption	226	-0.084	-0.138, -0.031	0.002
Social class	229	0.109	0.011, 0.207	0.03
Educational attainment	234	-0.175	-0.278, -0.072	0.001
Parity	234	-0.026	-0.158, 0.107	0.7
Smoking	234	0.057	-0.092, 0.206	0.5
<i>Infancy characteristics</i>				
Birthweight (kg)	231	0.031	-0.09, 0.152	0.6
Breastfeeding duration (months)	226	-0.015	-0.027, -0.003	0.015
<i>Child's characteristics</i>				
Height (cm)	234	0.007	-0.004, 0.017	0.2
Weight (kg)	234	0.008	-0.002, 0.018	0.1
BMI (kg/m ²)	234	0.014	-0.010, 0.039	0.3
Oily fish consumption ⁺	234	-0.037	-0.111, 0.037	0.3
<i>Child's cardiovascular measures</i>				
Systolic BP (mmHg)	232	0.011	0.004, 0.019	0.002
Diastolic BP (mmHg)	232	0.018	0.009, 0.026	<0.001
Pulse pressure (mmHg)	232	-0.0003	-0.008, 0.007	0.9
Mean arterial pressure (mmHg)	232	0.020	0.011, 0.029	<0.001
Heart rate (beats/minute)	234	0.015	0.009, 0.021	<0.001

⁺Categories shown in Table 1

Table 3

Multivariate analysis of maternal, neonatal and childhood characteristics in relation to PWV (m/s) at age 9 years (n=214).

	Coefficient	95% CI	p-value
<i>Maternal</i>			
Late pregnancy: oily fish portions/week	-0.083	-0.136, -0.030	0.002
Social class *	-0.031	-0.150, 0.088	0.611
Educational attainment *	-0.155	-0.285, -0.026	0.019
BMI (kg/m ²)	-0.009	-0.023, 0.004	0.179
<i>Infancy</i>			
Breastfeeding duration (months)	-0.008	-0.021, 0.006	0.258
<i>Child</i>			
Sex (reference category, male)	-0.066	-0.196, 0.063	0.314
<i>Intercept</i>	4.34	3.74, 4.95	<0.001

*
3 groups high-low