JOURNAL OF WOMEN'S HEALTH
Volume 00, Number 00, 2018

DOI: 10.1089/jwh.2018.6970

Breastfeeding Duration and the Risk of Coronary Artery Disease

Sheeva Rajaei, MD,[1] Joseph Rigdon, PhD,[2] Susan Crowe, MD,[3] Jennifer Tremmel, MD,[1] Sandra Tsai, MD,[4] and Themistocles L. Assimes, MD, PhD[1]

Abstract

Background: Previous studies have suggested that prolonged breastfeeding has beneficial effects on the health of the mother including the reduction of long-term risk of coronary artery disease (CAD). The mechanism of this association remains unclear.
Methods: We surveyed 643 women aged 40–65 years receiving outpatient care at Stanford University Hospital on their reproductive/lactation history, including 137 women (cases) with clinically confirmed CAD. Survey data were supplemented with traditional risk factor data for CAD obtained from the participant's medical record. We then conducted logistic regression analyses to assess the relationship between breastfeeding duration and case–control status for each of the two separate definitions of duration. The first was based on the participant's single longest duration of breastfeeding considering all live births reported and the second was based on a participant's total duration of breastfeeding summed over all live births. For each of these two definitions, we ran three sequential models each with a different reference group—(1) nulliparous women, (2) parous women that never breastfed, and (3) parous women with a short duration of breastfeeding—successively excluding women in the reference group of the previous model(s).
Results: Just over one-half (51.6%) of the women surveyed reported a history of breastfeeding. We found nominally significant associations ($p = 0.04$–0.12) for our multivariate analyses that modeled maximum duration of breastfeeding. When compared with nulliparous women, parous women who either never breastfed or always breastfed for <5 months had approximately double the risk of CAD. Among parous women, women who breastfeed for ≥5 months at least once in their lifetime had a ~30% decrease risk of CAD compared with those who did not initiate breastfeeding. Among parous women who breastfed ≥1 month, women who breastfed ≥5 months had ~50% decreased risk of CAD. We found similar point estimates of effect for analogous analyses modeling maximum breastfeeding duration but *p*-values for these analyses were not significant. Unadjusted analyses demonstrated higher valued odds ratios and lower *p*-values suggesting the presence of some confounding by traditional risk factors.
Conclusions: Parous women who breastfeed ≥5 months in at least one pregnancy seem to be at decreased risk of CAD later in their life, whereas parous women who either never breastfed or discontinued breastfeeding early seem to be at increased risk. More research is needed to more reliably quantify and determine the nature of the relationship between parity, breastfeeding duration, and risk of CAD.

Keywords: cardiovascular health, maternal cardiometabolic health, lactation

Introduction

Coronary artery disease (CAD) is a leading cause of death in women in developed nations.[1] Although traditional cardiovascular risk factors such as type 2 diabetes mellitus (T2DM), hypertension, and hyperlipidemia remain key modifiable risk factors, maternal factors are being increasingly investigated as important contributors to a woman's cardiometabolic health.[2] One modifiable maternal factor that has received substantial attention in this context is lactation. Lactation has been traditionally espoused for its diverse benefits for the child and is recommended from a variety of societies

[1]Department of Cardiovascular Medicine, Stanford University School of Medicine, Palo Alto, California.
[2]Quantitative Sciences Unit, Stanford University School of Medicine, Stanford, California.
[3]Department of Obstetrics and Gynecology, Stanford University School of Medicine, Palo Alto, California.
[4]Department of Internal Medicine, Stanford University School of Medicine, Palo Alto, California.

such as the American Academy of Pediatrics. However, evidence supporting lactation as an important factor in a woman's long-term risk of cardiometabolic disease has been building over the past decade.[3–14] In many of these reports, the benefit observed has been dose dependent with longer durations of lactation associated with further improvements in maternal cardiometabolic health.[3–14]

A uniquely altered physiologic state, lactation is associated with a diverse series of metabolic and hormonal changes in the mother.[15] Some have hypothesized that lactation initiates a resetting of the negative metabolic effects that occur during pregnancy allowing for the body to return to its prepregnancy state. Understanding how this breastfeeding impacts cardiometabolic health is of widespread interest given a woman historically could spend a substantial fraction of her fertile, premenopausal years in this altered physiologic state.

We aimed to add to the existing literature by conducting a case–control study for CAD after surveying in detail the lactation experiences of postmenopausal women receiving care at the Stanford University Medical Center. Specifically, we evaluated the relationship between lactation duration and the risk of developing overt nonfatal CAD by comparing women who were either nulliparous, parous with no breastfeeding history, or parous with varied durations of breastfeeding per live birth. We hypothesized that increased length of lactation would be associated with decreased risk of CAD independent of traditional risk factors.

Methods

We surveyed a total of 660 women between 2014 and 2015 at Stanford University Hospital who were seen in either an outpatient Internal Medicine or Cardiology clinic. Women were receiving standard preventative care and/or follow-up care for preexisting conditions such as CAD. Both nulliparous and multiparous women between the ages of 40 and 65 years were sought to complete a written or electronic survey about their reproductive and lactation history. Of the 660 women surveyed, we excluded 17 who did not respond to questions on the number of pregnancies and number of births. The remaining participants formed a control group ($n=506$) consisting of women who did not have an *International Classification of Diseases, 9th revision* (*ICD-9*) code associated with atherosclerotic cardiovascular disease (CVD) and a case group ($n=137$) consisting of women who did have an *ICD-9* code corresponding to CVD (*ICD-9* codes *I21, I22, I24, I25*).

We documented participants' reproductive history by asking a series of questions including their age of menstruation/menopause, history of hysterectomy/oophorectomy, total number of pregnancies, number of pregnancies that resulted in the birth of a live child, age of first/last pregnancy, and presence of medical conditions preventing pregnancy. We assessed participants' lactation history by asking participants the question ''Did you breastfeed any of your children?'' If they did not, they were prompted to describe why. Participants who did report breastfeeding were asked to report the duration of lactation for each live birth. For each child, participants also reported reasons for discontinuing breastfeeding. Participants were also asked if any of their pregnancies were complicated by gestational or chronic hypertension, gestational diabetes, preeclampsia, or eclampsia diagnosed during any of their pregnancies.

We defined our main exposure of duration using two different methods to account for variable breastfeeding durations per child among parous women. First, we defined exposure based on a participant's single longest duration of breastfeeding among all live births reported irrespective of the number of live births (HIGH-EVER). Using this figure, we categorized participants with a history of breastfeeding into one of the four ordinal groups of duration that resulted in approximately equal number of subjects in each group: 1–4, 5–9, 10–16 or 19+ months of breastfeeding. Second, we defined exposure based on a woman's total duration of breastfeeding summer over all live births reported (TOTAL). Using this figure, we categorized women into one of the four approximately equal-sized categories of exposures: 1–7, 8–15.5, 16–26, and 26.5+ months.

We used a participant's electronic health record (EHR) at Stanford to further extract the age, self-reported race, and smoking history. We also extracted the most recent measures for body mass index (BMI),[16] systolic and diastolic blood pressure (BP) (in mmHg), total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (all in mg/dL) from the EHR. Finally, we used *ICD* codes by treating physicians in the EHR to determine whether a participant carried a diagnosis of either hypertension (*ICD* code: I10–I16), hyperlipidemia (*ICD* code: E78.0-E78.70, E78.89, E78.9), or diabetes (*ICD* code: E08-E13). Participants were labeled as having these conditions if the *ICD* code appeared in the EHR at any time. If such codes did not appear at all, we assumed these conditions did not exist.

Statistical analysis

First, we calculated standard summary statistics including counts, proportions, means, and standard deviations for the exposure of interest and all covariates stratified by case–control status. We tested differences in these summary statistics between case–control groups using Fisher's exact test for categorical variables and Wilcoxon rank-sum test for continuous variables.

Next, we used multiple imputation procedure to impute any missing covariates of interest in our multivariate models. This procedure was followed with logistic regression analyses to assess the relationship between each of our two definitions of exposure: (1) single longest duration of all live births (HIGH-EVER) and (2) total lifetime duration summed over all live births (TOTAL) and the presence of clinically significant CAD. For each of these two exposure definitions, we ran three sequential models each with a different reference group—(1) nulliparous women, (2) parous women who never breastfed, and (3) parous women with a short duration of breastfeeding—successively excluding women in the reference group of the previous model(s). Furthermore, we ran each of these three models without including covariates (unadjusted), after including nonimputed traditional risk factors as covariates (adjusted), and after including women with missing covariates who were successfully imputed. Covariates in our fully adjusted models included current age, race, BMI, tobacco use, systolic BP, cholesterol, HDL, hypertension, hyperlipidemia, or diabetes history. A p-value of <0.05 was considered to be of statistical significance. We performed a Wald chi-square test in each model to test the null hypothesis that no association between duration of breastfeeding and CAD exists across all categories/levels of

duration. We also calculated 95% confidence intervals for the odds ratio for each category of duration to test for difference in relative risk between that category and the respective reference group. All statistical analyses were carried out in R version 3.4.0 (R Core Team 2017).

Results

Table 1 summarizes the characteristics of the study population stratified by case–control status. Among controls and cases, 217 (42.9%) and 44 (32.1%), respectively, reported never being pregnant. A total of 382 (59.4%) of all subjects reported at least one live birth with 332 of these 382 women (86.9% of parous women, 51.6% of all women) reporting that they breastfed for at least 1 month. Among women who had at least one live birth, the median number of years between a participant's first pregnancy and enrollment into this study was 29.6 for controls and 34.7 for cases. A majority of participants were whites with the next largest race/ethnic group surveyed being Asians. Compared with women without

Table 1. Characteristics of Study Population Stratified by Case–Control of Coronary Artery Disease at the Time of Completion of Questionnaire

	n	*No CAD*	n	*CAD*	p
Age	506	57.0 ± 8.1	137	58.5 ± 7.6	0.069
Race/ethnicity					
White	360	71.1%	97	70.8%	0.25
Asian	77	15.2%	15	10.9%	
Black	9	1.8%	3	2.2%	
Other	37	7.3%	16	11.7%	
Unknown	23	4.5%	6	4.4%	
No. pregnancies		2.2 ± 1.7		2.6 ± 1.7	0.005
Reported maximum duration of breastfeeding					
Never pregnant/child	217	42.9%	44	32.1%	0.012
1+ child; never breastfed	34	6.7%	16	11.7%	
1–4 months	53	10.5%	27	19.7%	
5–9 months	72	14.2%	16	11.7%	
10–18 months	91	18.0%	21	15.3%	
19+ months	39	7.7%	13	9.5%	
Reported total duration of breastfeeding					
Never pregnant/child	217	42.9%	44	32.1%	0.023
1+ child; never breastfed	34	6.7%	16	11.7%	
0–7 months	68	13.4%	27	19.7%	
8–15.5 months	55	10.9%	22	16.1%	
16–26 months	67	13.2%	14	10.2%	
26.5+ months	65	12.8%	14	10.2%	
BMI (kg/m^2)	491	27.2 ± 11.1	136	28.5 ± 7.6	0.014
History of tobacco use	53	10.5%	16	11.7%	
Diagnosis of hypertension					
Yes	220	43.5%	102	74.5%	<0.0001
Diastolic BP		78.6 ± 8.1		78.1 ± 11.4	0.49
Systolic BP		131.1 ± 14.6		128.6 ± 14.2	0.12
No	286	56.5%	35	25.5%	
Diastolic BP		72.9 ± 7.6		73.5 ± 9.0	0.77
Systolic BP		116.4 ± 11.5		117.6 ± 10.9	0.64
Diagnosis of hyperlipidemia					
Yes	248	49.0%	117	85.4%	<0.0001
Total cholesterol		206.3 ± 31.6		192.9 ± 38.9	0.001
LDL		122.9 ± 26.7		112.0 ± 34.8	0.0004
HDL		62.1 ± 19.4		59.6 ± 15.0	0.54
Triglycerides		119.3 ± 70.0		121.2 ± 76.2	0.9
No	258	51.0%	20	14.6%	
Total cholesterol		185.6 ± 26.0		181.8 ± 39.1	0.73
LDL		105.1 ± 23.6		98.1 ± 27.9	0.28
HDL		67.2 ± 15.1		69.4 ± 17.8	0.89
Triglycerides		78.4 ± 35.2		78.5 ± 36.4	0.95
Diagnosis of diabetes					
Yes	69	13.6%	40	29.2%	<0.0001
Glucose		139.4 ± 40.1		141.6 ± 40.3	0.69
No	437	86.4%	97	70.8%	
Glucose		98.4 ± 11.7		101.6 ± 12.7	0.016

BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

CAD, women with CAD had a higher BMI, and carried a diagnosis of hypertension, hyperlipidemia, and T2DM. Among women with hypertension, BPs were not significantly different between cases and controls likely indirectly reflecting a high prevalence of use of antihypertensive medication. Similarly, differences in total cholesterol and LDL among hyperlipidemia participants likely reflect a higher rate of statin use among CAD cases.

We found nominally significant associations for our analyses that modeled single longest duration of breastfeeding (HIGH-EVER) (Table 2). The relative risks appeared U-shaped with the highest risk of CAD observed among women who either had children and never breastfed or breastfed for no more than 4 months. When compared with nulliparous women, parous women who either never breastfed or always breastfed for <5 months had approximately double the risk of CAD. Among parous women, women who breastfeed for ≥5 months at least once had a ~30% decreased risk of CAD compared with women who did not initiate breastfeeding. Among parous women who breastfed ≥1 month, women who breastfed ≥5 months had ~50% decreased risk of CAD. We found similar point estimates of effect for analogous analyses modeling total duration of breastfeeding summed across all pregnancies (TOTAL) but *p*-values for these analyses were not significant (Table 3).

Discussion

In this study, we investigated the associations between history of breastfeeding and risk of CAD by conducting a survey that included both parous and nulliparous predominantly middle-aged women receiving care at the Stanford University Hospital. The inclusion of both parous and nulliparous women allowed us to estimate relative risk not only within parous women but also across the continuum of parity in relation to lactation: nonchildbearing, childbearing with no breastfeeding, and childbearing with a variable degree of breastfeeding. In models fully adjusted for established risk factors of CAD, we found nominally significant associations between maximal duration of breastfeeding and the risk of CAD with an increased risk of CAD among women who had a child but either did not breastfeed at all or stopped relatively early compared with nulliparous women. Increasing duration of lactation beyond 4 months was associated with a decreased risk of CAD. Thus, women who breastfed for ≥5 months seemed to reduce their risk back to a baseline risk observed in nulliparous women. In analyses that modeled the total duration of lactation over all pregnancies, we observed similar trends in the point estimates of effect but these point estimates did not reach statistical significance.

Multiple studies have individually investigated the impact of lactation on CVD risk factors such as obesity, T2DM, hypertension, and hyperlipidemia.[5,7,9,17] Studies specifically examining the impact of lactation on diabetes risk have mostly shown that longer lactation duration results in a significant reduction in the risk of future diabetes. In fact, prospective data from the US Nurses' Health Study demonstrated that each additional year of lifetime lactation decreased diabetes risk by 14%–15% compared with nonlactating parous women.[3] Data regarding dyslipidemia has shown mostly a beneficial effect with the Norwegian Hunt2 study demonstrating a significant dose–response relationship between lactation duration and

Table 2. Association Between Single Highest Ever Duration of Breastfeeding Reported Across All Live Births (HIGH-EVER) and Coronary Artery Disease Status Using Logistic Regression, Before and After Covariate Adjustment and Multiple Imputation of Missing Covariates

	Unadjusted OR (95% CI)	p[b]	*Complete case OR (95% CI)*[a]	p[b]	*Multiple imputation OR (95% CI)*[a]	p[b]
Maximum duration of breastfeeding[c]						
Ref: never child/pregnant						
1+ child; never breastfed	2.32 (1.18–4.57)	0.01	1.79 (0.81–3.94)	0.06	1.75 (0.82–3.71)	0.04
1–4 months	2.51 (1.43–4.42)		2.78 (1.43–5.39)		2.62 (1.4–4.91)	
5–9 months	1.1 (0.58–2.06)		1.04 (0.5–2.15)		1.02 (0.51–2.02)	
10–18 months	1.14 (0.64–2.02)		1.22 (0.63–2.37)		1.3 (0.69–2.44)	
19+ months	1.64 (0.81–3.33)		1.72 (0.69–4.26)		2.04 (0.93–4.5)	
Maximum duration of breastfeeding[d]						
Ref: child +, never breastfed						
1–4 months	1.08 (0.51–2.3)	0.06	1.57 (0.63–3.92)	0.14	1.5 (0.62–3.59)	0.12
5–9 months	0.47 (0.21–1.06)		0.53 (0.2–1.39)		0.52 (0.21–1.29)	
10–18 months	0.49 (0.23–1.05)		0.71 (0.29–1.76)		0.77 (0.32–1.84)	
19+ months	0.71 (0.3–1.68)		0.89 (0.29–2.76)		1.12 (0.41–3.07)	
Maximum duration of breastfeeding[e]						
Ref: 1–4 months						
5–9 months	0.44 (0.21–0.89)	0.06	0.33 (0.14–0.8)	0.09	0.34 (0.15–0.79)	0.07
10–18 months	0.45 (0.23–0.88)		0.47 (0.21–1.06)		0.53 (0.25–1.14)	
19+ months	0.65 (0.3–1.43)		0.57 (0.2–1.65)		0.76 (0.31–1.9)	

[a]Adjusted for age, race, BMI, tobacco use, hypertension, systolic BP, hyperlipidemia, total cholesterol, HDL, triglycerides, and diabetes.
[b]Wald chi-square test for breastfeeding variable.
[c]In complete case models, 65 of 643 observations deleted because of missing data.
[d]In complete case models, 41 of 382 observations deleted because of missing data.
[e]In complete case models, 37 of 332 observations deleted because of missing data.

Table 3. Association Between Total Lifetime Duration of Breastfeeding Summed Over All Live Births (TOTAL) and Coronary Artery Disease Status Using Logistic Regression, Before and After Covariate Adjustment and Multiple Imputation of Missing Covariates

	Unadjusted OR (95% CI)	p[b]	*Complete case OR (95% CI)*[a]	p[b]	*Multiple imputation OR (95% CI)*[a]	p[b]
Total duration of breastfeeding[c]						
Ref: never child/pregnant						
1+ child; never breastfed	2.32 (1.18–4.57)	0.02	1.78 (0.81–3.9)	0.19	1.74 (0.82–3.7)	0.24
0–7 months	1.96 (1.13–3.4)		2.16 (1.14–4.09)		1.94 (1.06–3.56)	
8–15.5 months	1.97 (1.09–3.56)		1.7 (0.85–3.41)		1.82 (0.95–3.5)	
16–26 months	1.03 (0.53–2)		1.03 (0.47–2.26)		1.3 (0.63–2.68)	
26.5+ months	1.06 (0.55–2.06)		1.24 (0.57–2.7)		1.21 (0.59–2.49)	
Total duration of breastfeeding[d]						
Ref: never breastfed						
0–7 months	0.84 (0.4–1.77)	0.13	1.18 (0.48–2.86)	0.60	1.06 (0.45–2.49)	0.85
8–15.5 months	0.85 (0.39–1.84)		0.88 (0.35–2.25)		0.97 (0.4–2.37)	
16–26 months	0.44 (0.19–1.02)		0.59 (0.21–1.63)		0.76 (0.29–1.97)	
26.5+ months	0.46 (0.2–1.05)		0.71 (0.26–1.93)		0.71 (0.28–1.82)	
Total duration of breastfeeding[e]						
Ref: 0–7 months						
8–15.5 months	1.01 (0.52–1.96)	0.14	0.78 (0.34–1.76)	0.39	0.95 (0.45–2.04)	0.67
16–26 months	0.53 (0.25–1.09)		0.45 (0.17–1.16)		0.67 (0.28–1.59)	
26.5+ months	0.54 (0.26–1.13)		0.62 (0.26–1.5)		0.67 (0.29–1.51)	

[a]Adjusted for age, race, BMI, tobacco use, hypertension, systolic BP, hyperlipidemia, total cholesterol, HDL, triglycerides, and diabetes.
[b]Wald chi-square test for breastfeeding variable.
[c]In complete case models, 65 of 643 observations deleted because of missing data.
[d]In complete case models, 41 of 382 observations deleted because of missing data.
[e]In complete case models, 37 of 332 observations deleted because of missing data.

decreased total cholesterol, LDL, and triglycerides in >20,000 parous women.[18]

Several studies have shown that the benefits of prolonged breastfeeding may extend beyond those observed for individual CVD risk factors to include clinical complications of atherosclerosis such as CAD and other forms of CVD.[5,17–19] Similar to our findings, these studies also demonstrate that early discontinuation of breastfeeding substantially mitigates the benefit on risk of CVD. Of note, two of these studies found that age may modify the association between breastfeeding duration and CVD and two studies reported on an etiologically heterogeneous set of CVD outcomes combined that may have included nonischemic strokes, nonischemic congestive heart failure, valvular disease, myopericarditis, and diseases of lymphatics.[5,18] Most recently, a large prospective cohort study investigating >300,000 women in the China Kadoorie Biobank found that parous women who ever breastfed had a ~10% lower risk of future CAD and ischemic stroke and that longer breastfeeding lengths were associated with even further reduced risk.[19] This protection was not observed for hemorrhagic stroke. In contrast to our study, the Kadoorie Biobank also did not observe differences in risk of CVD between nulliparous women and parous women who never breastfed.[19] The reasons behind this discrepancy are not clear but may relate to inadequate adjustment for confounders in our study including indicators of education and socioeconomic status that were available in the Kadoorie study. Alternatively, a truly elevated risk in parous women who never breastfed or discontinued early may be reflecting long-term adverse metabolic effects of pregnancy that are not given an opportunity to be reset through prolonged breastfeeding.

What could be the mechanistic basis behind the observed associations between lactation and cardiometabolic health assuming these associations are causal in nature? The pregnant woman undergoes unique physiologic and metabolic changes that are conducive to accumulating energy stores in preparation for lactation in the postpartum state.[13,14,20,21] For one, pregnancy weight gain and increases in visceral adiposity are known to occur to support the increase in caloric expenditure postpartum that is evolutionarily designed to support a growing infant.[22,23] As a part of the normal changes that occur during pregnancy, insulin resistance and glucose intolerance considerably increase resulting in greater maternal fat reserves.[13] The lipid profile becomes atherogenic with significantly elevated levels of LDL and triglycerides allowing the greater transfer of fatty acids to the growing fetus.[20,21] Increases in BMI, specifically visceral fat, hyperlipidemia, and diabetes are all well-known risk factors for future CVD. Lactation may play a very important role in mobilizing previously accumulated fat stores in pregnancy, expending glucose and triglycerides, and overall assisting in neutralizing the negative metabolic effects of pregnancy.[20,24,25]

The strengths of this study include the detailed clinical information related to lactation and reproductive history for each live birth allowing us to define our main exposure in various ways including single maximum ever duration of breastfeeding (HIGH-EVER) and total duration summed over all pregnancies (TOTAL). Including both parous and nulliparous women also allowed us to compare parous women who breastfed and parous women who did not breastfeed with nulliparous women. Somewhat unexpectedly, the results for TOTAL duration were not significant, although the point estimates were similar to our analysis of HIGH-EVER.

This study is limited in several respects. First, the case–control design is susceptible to various biases including recall bias and selection bias. For example, the lactation data obtained through self-report many years after the exposure may have been overreported by cases in relation to controls, but such overreporting will have only served to bias findings toward the null. Our study also restricted cases to survivors of clinical CAD that could have also affected the results if protection conferred by breastfeeding is stronger among more women with more severe CAD who do not survive long after their incident event. Second, our sample size is limited and may responsible for the borderline significant associations we observed given the effect estimates observed in previous studies. Finally, the observational nature of our study cannot exclude the possibility that unmeasured confounders are responsible for the nominal associations observed despite our extensive adjustment for established risk factors of CAD. We note that our unadjusted analyses suggest that some confounding is present, and we have incomplete information on other risk factors for CAD including lifestyle measures (*e.g.*, physical activity and dietary intake) and socioeconomic status. This limitation of residual confounding applies to all studies published to date and can only be fully addressed through randomized controlled trials and/or Mendelian randomization (MR) studies. A randomized control trial of breastfeeding duration is not practically or ethically feasible given the established benefit of breastfeeding on the health of newborns and infants. However, MR studies could be feasible in the near future after genetic instrumental variables for breastfeeding duration are identified through genome-wide association studies.[26]

In summary, we found nominally significant associations between a mother's history of breastfeeding and breastfeeding duration and a women's risk of CAD later in life that was also dependent on whether the woman had any live births. In comparison with nulliparous women, women who always breastfed for relatively short durations (<5 months) or not at all have an increased risk of CAD, whereas women who breastfed for a prolonged period of time have a risk of CAD that returns to baseline. More research is needed to more reliably quantify and to determine the nature of relationship between parity, breastfeeding duration, and risk of CAD.

Acknowledgments

S.R. is supported by NIH/NHLBI grant T32 HL098049.

Author Disclosure Statement

No competing financial interests exist.

References

1. Mendis S, Puska P, Norrving B. Global atlas on cardiovascular disease prevention and control. Geneva: World Health Organization in collaboration with the World Heart Federation and the World Stroke Organization, 2011: vi, 155 p.
2. Perrine CG, Nelson JM, Corbelli J, et al. Lactation and maternal cardio-metabolic health. Annu Rev Nutr 2016;36:627–645.
3. Stuebe AM, Rich-Edwards JW, Willett WC, et al. Duration of lactation and incidence of type 2 diabetes. JAMA 2005;294:2601–2610.
4. Lee SY, Kim MT, Jee SH, Yang HP. Does long-term lactation protect premenopausal women against hypertension risk? A Korean women's cohort study. Prev Med 2005;41:433–438.
5. Schwarz EB, Ray RM, Stuebe AM, Allison MA, et al. Duration of lactation and risk factors for maternal cardiovascular disease. Obstet Gynecol 2009;113:974–982.
6. Rooney BL, Schauberger CW. Excess pregnancy weight gain and long-term obesity: One decade later. Obstet Gynecol 2002;100:245–252.
7. Yang JQ, Xu YH, Gai MY. [Breast-feeding in reducing regular insulin requirement in postpartum for insulin dependent diabetes mellitus and gestational diabetes mellitus]. Zhonghua Fu Chan Ke Za Zhi 1994;29:135–137.
8. Ram KT, Bobby P, Hailpern SM, Lo JC, et al. Duration of lactation is associated with lower prevalence of the metabolic syndrome in midlife—SWAN, the study of women's health across the nation. Am J Obstet Gynecol 2008;198:268 e1–e6.
9. Stuebe AM, Schwarz EB, Grewen K, Rich-Edwards JW, et al. Duration of lactation and incidence of maternal hypertension: A longitudinal cohort study. Am J Epidemiol 2011;174:1147–1158.
10. Gunderson EP, Lewis CE, Wei GS, Whitmer RA, et al. Lactation and changes in maternal metabolic risk factors. Obstet Gynecol 2007;109:729–738.
11. Janney CA, Zhang D, Sowers M. Lactation and weight retention. Am J Clin Nutr 1997;66:1116–1124.
12. Dewey KG, Heinig MJ, Nommsen LA. Maternal weight-loss patterns during prolonged lactation. Am J Clin Nutr 1993;58:162–166.
13. Catalano PM, Tyzbir ED, Roman NM, Amini SB, et al. Longitudinal changes in insulin release and insulin resistance in nonobese pregnant women. Am J Obstet Gynecol 1991;165(6 Pt 1):1667–1672.
14. Lippi G, Albiero A, Montagnana M, Salvagno G, et al. Lipid and lipoprotein profile in physiological pregnancy. Clin Lab 2007;53:173–177.
15. Butte NF, Wong WW, Hopkinson JM. Energy requirements of lactating women derived from doubly labeled water and milk energy output. J Nutr 2001;131:53–58.
16. Locke AE, Kahali B, Berndt SI, Justice AE, et al. Genetic studies of body mass index yield new insights for obesity biology. Nature 2015;518:197–206.
17. Stuebe AM, Michels KB, Willett WC, Manson JE, et al. Duration of lactation and incidence of myocardial infarction in middle to late adulthood. Am J Obstet Gynecol 2009;200:138. e1–e8.
18. Natland Fagerhaug T, Forsmo S, Jacobsen GW, Midthjell K, et al. A prospective population-based cohort study of lactation and cardiovascular disease mortality: The HUNT study. BMC Public Health 2013;13:1070.
19. Peters SAE, Yang L, Guo Y, Chen Y, et al. Breastfeeding and the risk of maternal cardiovascular disease: A prospective study of 300 000 Chinese women. J Am Heart Assoc 2017;6:e006081.
20. Darmady JM, Postle AD. Lipid metabolism in pregnancy. Br J Obstet Gynaecol 1982;89:211–215.
21. Knopp RH, Walden CE, Wahl PW, Bergelin R, et al. Effect of postpartum lactation on lipoprotein lipids and apoproteins. J Clin Endocrinol Metab 1985;60:542–547.

22. Kinoshita T, Itoh M. Longitudinal variance of fat mass deposition during pregnancy evaluated by ultrasonography: The ratio of visceral fat to subcutaneous fat in the abdomen. Gynecol Obstet Invest 2006;61:115–118.
23. McClure CK, Catov J, Ness R, Schwarz EB. Maternal visceral adiposity by consistency of lactation. Matern Child Health J 2012;16:316–321.
24. Stuebe AM, Rich-Edwards JW. The reset hypothesis: Lactation and maternal metabolism. Am J Perinatol 2009;26:81–88.
25. Kallio MJ, Siimes MA, Perheentupa J, Salmenpera L, et al. Serum cholesterol and lipoprotein concentrations in mothers during and after prolonged exclusive lactation. Metabolism 1992;41:1327–1330.
26. Burgess S, Thompson SG. Mendelian randomization: Methods for using genetic variants in causal estimation. Chapman & Hall/CRC interdisciplinary statistics series. Boca Raton: Chapman & Hall/CRC, 2015:xiv, 210 p.

Address correspondence to:
Sheeva Rajaei, MD
Department of Cardiovascular Medicine
Stanford University School of Medicine
1070 Arastradero Road
Palo Alto, CA 94304

E-mail: srajaei@stanford.edu