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Serial Studies in Subclinical Atherosclerosis During Menopausal Transition (From the Study of Women's Health Across the Nation)

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Abstract

Cardiovascular disease (CVD) risk increases in women after the menopausal transition; why this inflection point occurs remains uncertain. We aimed to characterize the influence of menopause on vascular aging by prospective assessment of change in indices of subclinical atherosclerosis across the menopausal transition. We evaluated 411 healthy women from SWAN Heart, an ancillary study of SWAN (Study of Women's Health Across the Nation), for subclinical atherosclerosis at baseline and again after an average of 2.3 years. Carotid intima-media thickness (cIMT) and aortic pulse wave velocity (aPWV) were measured by ultrasound. Coronary artery calcium (CAC) scores were obtained by computed tomography. Women were grouped by menopausal status as premenopausal, postmenopausal or having undergone the transition during follow-up. Analyses of changes were adjusted for age at baseline and time between scans. Mean age at baseline was 51±3 years; 93 (23%) subjects transitioned to menopause (**Pre-Post**), 147 (36%) remained premenopausal (**Pre-Pre**), while 171 (41%) were postmenopausal at baseline (**Post-Post**). Blood pressure readings did not differ between groups with similar increase noted in cIMT and logCAC

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Relationships with Industry

None reported by all authors.

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+1 from baseline to follow-up. Change in aPWV from baseline to follow-up was higher in **Pre-Post** (121 ± 23 cm/s) compared to **Pre-Pre** (38 ± 250 cm/s, $p=0.029$) and **Post-Post** (41 ± 228 cm/s, $p=0.045$). In conclusion, changes in aortic stiffness were more sensitive measures of perimenopausal vascular aging than morphological indices of subclinical atherosclerosis in women undergoing the menopausal transition. Serial assessment of such changes could potentially elucidate mechanisms of disease and identify women to target for aggressive lifestyle risk factor modification.

Keywords

menopause; subclinical atherosclerosis; pulse wave velocity; coronary calcium; carotid intima-media thickness; vascular aging

INTRODUCTION

Cardiovascular disease (CVD) kills more women in the developed world than any other condition, with an estimated prevalence of 36%, and the lifetime risk of CVD death remains 1 in 2.¹ CVD rates in women, however, typically lag 10 years behind those of men up until menopause, after which there is a pronounced increase.² Although it is clear that there is a dramatic increase in CVD in women after menopause, the perimenopausal period represents an inflection point, after which the risk of CVD rises sharply. The mechanism of this inflection remains uncertain. Observational studies, most of which have been cross-sectional, have shown a higher CVD risk in postmenopausal women.^{3–5} However, menopause, aging, and the increase in CVD risk occur somewhat synchronously, and cross-sectional analyses cannot elucidate mechanisms of change. Cross-sectional analyses also look at groups, making it difficult to identify reliable markers of *individual* susceptibility to CVD, something that would be useful for targeting preventive measures to high-risk patients. SWAN Heart, an ancillary study of the Study of Women's Health Across the Nation (SWAN),⁶ examined serial morphological and physiological markers of subclinical atherosclerosis in women undergoing the menopausal transition. Earlier cross-sectional and longitudinal analysis from SWAN Heart have shown accelerated progression of morphological changes in peripheral vasculature during the late perimenopausal phase.^{7,8} In the current study, we hypothesized that longitudinal changes in the morphological and physiological markers of subclinical atherosclerosis in the SWAN Heart cohort will correlate and will be more pronounced in the women undergoing the menopausal transition.

METHODS

SWAN is an ongoing multisite, multiethnic, community-based longitudinal study designed to examine physical and psychological changes in women as they transition through the menopause. Details of the study design have been previously reported.⁶ Briefly, SWAN enrolled 3302 women, aged 42–52, who were not pregnant or breastfeeding, had an intact uterus and at least 1 ovary, and had menstruated within the past 3 months. SWAN Heart is an ancillary study of SWAN that aimed to assess subclinical atherosclerosis in 608 healthy women from the Chicago and Pittsburgh sites recruited between 2001 and 2003. SWAN

Heart included two assessments, a baseline exam in SWAN study visits 4–7 (2001–2005) and a follow-up exam about two years later during SWAN study visits 6–9 (2003–2008). By design, these sites recruited non-Hispanic white women and black women only. SWAN Heart exclusion criteria included pregnancy, hysterectomy or bilateral oophorectomy, reported CVD (prior myocardial infarction, angina, stroke, transient ischemia, peripheral vascular disease, other vascular disease including fibromuscular dysplasia, collagen vascular disease), diabetes, or medications to treat these conditions. Women who used hormone therapy (HT) were also excluded from this analysis. Out of 608 participants enrolled for SWAN Heart, 149 did not participate in the SWAN Heart follow-up (75% retention rate), 39 subjects were excluded due to unknown menopausal status or premenopausal use of hormone therapy during SWAN Heart visits, and 9 subjects were excluded with a self-reported history of heart attack, stroke or angina, leaving 411 women eligible for inclusion in the present analyses. All women underwent a battery of tests of morphological (coronary calcium, carotid intima-media thickness), physiologic (aortic pulse-wave velocity) and biochemical parameters (lipid profiles) as markers of subclinical atherosclerosis. The research protocol was approved by each site's institutional review board; all women provided written informed consent.

Menopause status, use of hormone therapy and the occurrence of hysterectomy and/or oophorectomy were assessed annually in SWAN. Women were categorized as postmenopausal if they reported a complete absence of menstrual bleeding or had undergone bilateral oophorectomy in the previous 12 months. Premenopause status was defined as bleeding in the last 3 months with no cycle irregularity in the previous 12 months. Perimenopause status in SWAN was categorized as early perimenopausal (bleeding in the last 3 months with some change in cycle regularity in the last 12 months) and late perimenopausal (no bleeding in the last 3 months, but some bleeding within the last 12 months). At baseline, premenopausal women did not differ from early perimenopausal women, and late perimenopausal women did not differ from postmenopausal women on any subclinical marker. Therefore, for this analysis, to improve the sample size, early perimenopausal women were grouped with premenopausal women while late perimenopausal participants were categorized as postmenopausal. Three menopause transition groups from baseline to follow-up SWAN Heart visits were defined for analyses: premenopause to premenopause (**Pre-Pre**), premenopause to post menopause (**Pre-Post**) and postmenopause to postmenopause (**Post-Post**).

Carotid intima-media thickness (cIMT) was assessed by B-mode ultrasonography with a Hewlett Packard 5500 scanner (Hewlett-Packard, Andover, MA) at the Chicago site and a Toshiba SSA- 270A scanner (Toshiba American Medical Systems, Tustin, CA) at the Pittsburgh site with protocol described previously for the SWAN cohort.⁸ Progression was assessed as change from baseline to follow-up visits. Non-contrast-enhanced electron beam computed tomography with an Imatron C-150 Ultrafast CT scanner (Imatron, South San Francisco, CA) was performed for coronary artery calcium (CAC) scoring. Because the sample consisted of mid-life healthy women, the majority of subjects had no detectable calcium, (CAC scores of 0), resulting in extreme skewness of the distribution. Therefore, CAC was analyzed both as a continuous and as a binary variable as used in SWAN Heart

previously.⁹ For the continuous variable, the individual scores were log transformed after adding 1 to CAC ($\log[\text{CAC}+1]$). For the binary variable (absence/presence of CAC defined as Agatston score ≥ 10 AU), progression of CAC was then evaluated as presence (CAC ≥ 10 AU) or absence (CAC < 10 AU) at follow-up.

Arterial flow waves were simultaneously and non-invasively recorded at the carotid and femoral arteries in supine position, using unidirectional transcutaneous Doppler flow probes (model 810-a, 10 MHz, Parks Medical Electronics, Aloha, OR). The distance traveled by the pulse waveform was calculated by tape measure as the distance from the suprasternal notch to the umbilicus and the umbilicus to the femoral site minus the distance from the carotid to the suprasternal notch (to adjust for the opposite direction of the blood flow in that arterial branch). Aortic pulse wave velocity (aPWV) was then calculated by dividing the distance (d) between the two arterial sites by the difference in time of pressure wave arrival between the carotid ($t1$) and femoral artery ($t2$) referenced to the R wave of the electrocardiogram ($\text{aPWV} = d/t2 - t1$). Subjects with waveforms inadequate for assessment of aortic compliance (lower signal strength or $\text{aPWV} > 2000$ cm/sec) were considered artefactual and were excluded from analyses ($n=13$). Progression was assessed as the difference between baseline and follow-up. As reported earlier for SWAN Heart data, this measure demonstrated good reproducibility with an intra-class correlation of 0.77.¹⁰

Information on demographics, smoking, medical conditions, and family history was collected by questionnaire at the initial examination. Height and weight were also measured at each visit, along with fasting lipid profiles. The LDL-C was calculated with the Friedewald equation for subjects with triglycerides < 400 mg/dL. Medication use and new medical diagnoses were self-reported at each respective SWAN visit, and subjects were asked to bring containers for all medications used during the 2 weeks prior to each visit for verification.

All statistical analyses were performed using SAS, version 9.3. Summary statistics are presented as N (%) for categorical variables and compared among groups (**Pre-Pre**, **Pre-Post**, **Post-Post**) by logistic regression with post-hoc comparisons between the three groups. Continuous variables are presented as mean $\pm$ SD. To compare the three menopausal transition groups, analysis of variance (ANOVA) with post-hoc pairwise comparisons between the three groups was used. Significance was determined as a p-value < 0.05 . Presence of CAC at baseline (CAC ≥ 10 AU) was compared between groups by logistic regression. Similarly, for women with no CAC at baseline, incidence of CAC by follow-up was also analyzed by logistic regression. Change in continuous markers was analyzed by linear regression, adjusting for age at baseline and time between scans. For the summary figure, percent change for each woman in each subclinical marker was calculated as $100 \times ((\text{follow-up value} - \text{baseline value}) / \text{baseline value})$, putting all outcomes on the same scale.

RESULTS:

The final analysis included 411 subjects, with mean age of 51 ± 3 (range 46–59) years; mean follow-up was 2.3 years. Of these, 93 subjects transitioned from premenopause to postmenopause (**Pre-Post**), 147 remained premenopausal (**Pre-Pre**) at follow-up, while 171

subjects were postmenopausal at baseline (**Post Post**). Premenopausal women were younger at baseline; other baseline demographic, anthropomorphic, and clinical history were similar across the three menopausal transition groups and are presented in Table 1. There was no difference in baseline or follow-up BMI or blood pressure readings between the menopausal transition groups. Although the decision was made to combine pre-menopausal and early peri-menopausal groups on the basis of lack of difference in baseline values, there were no differences in any of the outcome measures (log(CAC+1), cIMT, aPWV) at follow-up (all $p>0.20$); the same was true for the late perimenopausal and postmenopausal groups (all $p>0.20$).

Detectable CAC (defined as ≥ 10 AU) was present in about 1/5 of the cohort at baseline, with no difference in incidence across the three menopausal transition groups (Table 2). Among subjects with no detectable CAC at baseline, 15% had detectable CAC at follow-up, with no difference in the progression of CAC between the three menopausal transition groups (Table 2). When analyzed as a continuous variable, **Post-Post** group had higher coronary artery calcium scores (log CAC+1) when compared to **Pre-Pre** and **Pre-Post** groups at baseline, maintaining a similar trajectory at follow-up. All women showed an increase in log CAC+1 at follow-up, but there was no difference in change from baseline between the 3 groups (Table 3).

Baseline cIMT did not differ between the three menopause transition groups. There was an increase in cIMT from baseline to follow-up in all menopausal transition groups. However, there was no difference in change from baseline between the 3 groups (Table 3).

Baseline aPWV was highest in the **Post-Post** compared to **Pre-Post** group ($p=0.022$) with a similar trend for the **Pre-Pre** group, increasing in all three groups at follow-up compared to baseline. The change in aPWV, however, was highest in the **Pre-Post** group compared to **Pre-Pre** ($p=0.045$) and **Post-Post** (0.029) groups after adjustment for age at baseline (Table 3). When normalized to individual subject's baseline, the percentage change in aPWV in **Pre-Post** remained significant compared to **Pre-Pre** with a similar trend for **Post-Post** groups (Figure 1). Changes in aPWV correlated with change in log CAC+1 in the transitioning group but did not correlate in the non-transitioning groups (Figure 2A-C). Changes in cIMT did not correlate with the change in aPWV across the three menopause transition groups (Figure 2D-F).

At baseline, **Pre-Pre** and **Pre-Post** groups had lower total cholesterol, triglycerides, and LDL-C levels compared to the **Post-Post** group ($p<0.005$ for both groups). HDL-C levels were lower in the **Pre-Pre** compared to the **Post-Post** group ($p=0.02$) with a similar trend for the **Pre-Post** group (Table 4). Total cholesterol increased from baseline to follow-up in the **Pre-Pre** and in the **Pre-Post** groups (both $p<0.01$). Triglycerides increased in **Pre-Post** and **Pre-Pre** (both $p<0.05$). LDL-C increased in **Pre-Post** ($p<0.001$) and **Pre-Pre** ($p<0.05$). The change in total cholesterol, triglycerides and LDL-C was significantly higher in the transition group compared to the post-menopausal group with similar trends for the premenopausal group (Table 4). HDL-C levels did not change in any of the three groups during the follow-up period. Changes in lipids did not correlate with changes in aPWV, cIMT, or log (CAC+1).

DISCUSSION

SWAN takes a multidisciplinary approach and has explored the effects of racial, psychologic and socioeconomic factors on physiologic, morphologic and biochemical markers of subclinical atherosclerosis.^{7,8,11–13} Our study had three aims: to identify the influence of menopause on vascular aging, to test the hypothesis that the trajectory of change in the indices of subclinical atherosclerosis differs between the menopausal transition groups, and to potentially identify women at increased risk who could be targeted for aggressive lifestyle risk factor modification. The current data demonstrate that women undergoing a menopausal transition had a more rapid trajectory of change for aortic pulse wave velocity, a measure of vascular stiffness, than women who remained premenopausal or women who were postmenopausal throughout. To our knowledge, this is the first study to assess serial changes in markers of subclinical atherosclerosis prospectively in women undergoing the menopausal transition.

Aortic pulse wave velocity to determine arterial stiffness is a sensitive predictor of mortality and cardiovascular events.^{14,15} aPWV correlates with age and has been reported to be higher in postmenopausal women.^{16,17} In our cohort aPWV was higher in women who were postmenopausal at baseline compared to their premenopausal counterparts (Table 3), although the postmenopausal women were somewhat older as expected (Table 1). However, the difference in aPWV in the menopause transition group compared to the non-transition groups persisted despite adjustment for baseline age. While the independent effect of menopause on arterial stiffness remains controversial,^{17,18} serial measurements as in our study could allow each woman to be her own control, thus potentially generating a personalized physiologic assessment of a trajectory that might well be more predictive than data obtained in cross-sectional studies. Our results suggest an acceleration in vascular stiffness in women undergoing the menopausal transition, and this might be predictive of a subsequent trajectory.

Coronary artery calcification (CAC), has been associated with an increased risk of cardiovascular events,^{19,20} and was associated with male sex and increasing age in the CARDIA and MESA cohorts.^{21,22} In our study, while premenopausal women had lower CAC compared to postmenopausal women, all showed an increasing trajectory during the follow-up period, with no differences between the three menopausal transition groups. A potential explanation could be that in low risk cohorts such as this one, noncalcified, “soft” coronary plaques may predominate.^{23,24} Demonstration of such coronary plaques would have required contrast enhancement, which was not part of our study protocol. In our cohort, aPWV correlated with CAC only in women undergoing the transition to postmenopause.

An earlier cross-sectional analysis from SWAN Heart found an association between cIMT and risk factors but not difference between cIMT values with menopausal status or endogenous sex hormones after adjustment for age.⁷ A longitudinal analysis of 249 pre- and early perimenopausal SWAN women, however, did report an acceleration in cIMT during the late perimenopausal phase over a 9-year follow-up.⁸ While cIMT increased in the whole cohort in our analysis, the change in cIMT did not differ among the three menopausal transition groups. The contrast from the earlier SWAN report could be attributed to a shorter

follow-up duration and somewhat different menopausal status grouping. The current findings are similar to those in a cohort of 201 women aged 45–60, in which cIMT progression levels was not age-related but was accelerated over a 3 year follow-up in women undergoing the menopausal transition.²⁵ Among MESA participants, presence of CAC was a better predictor of cardiovascular events compared to a high cIMT with similar performance for cerebrovascular events over a 9.5-year follow-up.^{26,27} In our study, the trajectories for change in cIMT did not appear to distinguish between menopausal groups and did not correlate with other atherosclerosis parameters.

Serum lipid profiles are change during menopause,²⁸ and earlier SWAN analyses showed significant increases in total cholesterol, LDL-C and apolipoprotein B around menopause.²⁹ Similarly, in our analysis, total cholesterol, triglycerides and LDL-C levels were lower in premenopausal women compared to postmenopausal women at baseline and increased in **Pre-Pre** and **Pre-Post** groups from baseline to follow-up, but did not increase in the **Post-Post** group. Lipid changes were small, and did not correlate with changes in PWV, cIMT or CAC scores in any group; the degree to which they may have contributed to changes in PWV is uncertain.

Our study has several strengths, including the longitudinal design, a biracial cohort, and robust data concerning other cardiovascular risk factors. All subjects included in this analysis had serial follow-up of physiologic as well as morphologic indices of subclinical atherosclerosis. This allowed us to use each subject as her own control, as a first step in personalizing the risk assessment of a given woman for acceleration of atherosclerosis during the menopausal transition. Although SWAN Heart has several strengths, the sample size was limited because of incomplete retention. In addition, the decision to analyze serial studies further limited the sample size due to missing assessments, exclusion of subjects using hormone therapy and patients lost to follow-up. Furthermore, not all variables were available for every subject, limiting study power. Our conclusions are based on a single, fairly short (2.3 year) follow-up. With extended follow-up, correlation of perimenopausal changes with harder endpoints such as development of hypertension or clinical adverse events might be possible.

CONCLUSION

Analysis of serial studies showed a significant perimenopausal change in aortic stiffness without a change in morphological atherosclerosis assessed by either cIMT or CAC, suggesting that physiologic changes may be a particularly sensitive measure of perimenopausal changes. Changes in arterial stiffness in individual women may identify a cohort particularly prone to worsening of cardiovascular risk, potentially pointing the way for serial change to be used as a marker of trajectory in women undergoing menopausal transition. Serial studies could provide a measure of vascular aging in women at different stages of menopause irrespective of their biological age, something that might have mechanistic implications, and could conceivably help identify individual women at greater risk for progression of CVD. Such women might be expected to derive the most benefit from aggressive risk factor modification. This hypothesis could be tested further by long-term follow-up, ideally with serial studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1:

Percentage Changes in Physiologic & Morphologic Indices of Subclinical Atherosclerosis Across Menopause Transition Groups*

Abbreviations: CAC = Coronary Artery Calcium Score, cIMT = Carotid Intima-media Thickness, aPWV = Aortic Pulse Wave Velocity

*Percentage change calculated as: $100 \times (\text{follow-up value} - \text{baseline value}) / \text{baseline value}$ and adjusted for baseline age and time between scan

p-values from contrast in linear models; CAC scores of 0 at baseline excluded

Figure 2:

Correlation of change in aortic pulse wave velocity with change in morphological markers of subclinical atherosclerosis, $\log CAC+1$ (A-C), and $cIMT$ (D-F) by menopause transition groups.

Abbreviations: aPWV = Aortic pulse wave velocity, CAC = Coronary artery calcium, cIMT = carotid intima-media thickness, **Post-Post** = Postmenopause to postmenopause, **Pre-Post** = Premenopause to postmenopause, **Pre-Pre** = Premenopause to premenopause

*by Spearman rank correlation; †by Pearson correlation

TABLE 1

Baseline Characteristics of SWAN-Heart Cohort

Variable	Premenopause to Postmenopause	Premenopause to Premenopause	Postmenopause to Postmenopause	Overall
	(n = 93) (mean ± SD; n, %)	(n = 147) (mean ± SD; n, %)	(n = 171) (mean ± SD; n, %)	(N = 411) (mean ± SD; n, %)
Age (years)	50 ± 2 *	49 ± 2 *	53 ± 3 *	51 ± 3 *
Body mass Index (kg/m ²)	29.8 ± 7.1	29.2 ± 6.2	29.8 ± 6.6	29.5 ± 6.6
White	63 (67%)	94 (64%)	106 (62%)	263 (64%)
Black	30 (33%)	53 (36%)	65 (38%)	148 (36%)
Smoker	18 (19%)	20 (14%)	23 (13%)	61 (15%)
Family History of Cardiovascular disease	59 (63%)	107 (73%)	112 (65%)	278 (68%)
Hypertension	19 (20%)	32 (22%)	36 (21%)	87 (21%)
Diabetes mellitus	1 (1%)	0 (0%)	5 (3%)	6 (2%)
Hyperlipidemia	4 (4%)	6 (4%)	10 (6%)	20 (5%)

* p-value <0.001 from contrast in linear models across menopause transition groups

TABLE 2

Coronary Artery Calcium Incidence at Baseline & Progression Across Menopause Transition Groups

Variable	Premenopause to Postmenopause (n = 80 [*])	Premenopause to Premenopause (n = 120 [*])	Postmenopause to Postmenopause (n = 134 [*])	Overall (N = 334 [*])
CAC ≥ 10 AU at baseline	16 (20%)	18 (15%)	32 (24%)	66 (20%)
CAC <10 AU at baseline	64 (80%)	102 (85%)	102 (76%)	268 (80%)
Progression of CAC ^{//}	6 (9%)	16 (16%)	17 (17%)	39 (15%)

Abbreviations: AU = Agatston Units, CAC = Coronary Artery Calcium Score

^{*} with reliable baseline and follow-up CT scan data^{//} defined as CAC <10 AU at baseline and ≥ 10 AU at follow-up

Table 3.

Baseline, Follow-Up and Change in Blood Pressure Readings & Measures of Subclinical Atherosclerosis
Across Menopause Transition Groups

Variable		Premenopause to Postmenopause (n = 93)	Premenopause to Premenopause (n = 147)	Postmenopause to Postmenopause (n = 171)	Overall (N = 411) (mean ± SD)
		(mean ± SD)	(mean ± SD)	(mean ± SD)	
Systolic Blood Pressure (mmHg)	Baseline	118 ± 15	117 ± 14 [‡]	121 ± 18 [‡]	119 ± 16
	Follow-up	117 ± 16	119 ± 17	119 ± 18	119 ± 17
	§	-1 ± 12	2 ± 14 [‡]	-2 ± 15 [‡]	0 ± 14
Diastolic Blood Pressure (mmHg)	Baseline	75 ± 9	75 ± 10	77 ± 9	76 ± 10
	Follow-up	75 ± 10	74 ± 10	75 ± 9	75 ± 10
	§	0 ± 9	-1 ± 10	-2 ± 9	-1 ± 9
Log(CAC+1)					
(log+1 AU)	Baseline	0.43 ± 0.64	0.37 ± 0.54	0.51 ± 0.64	0.44 ± 0.61
	Follow-up	0.55 ± 0.72	0.55 ± 0.65	0.70 ± 0.74	0.61 ± 0.70
	§	0.12 ± 0.37	0.18 ± 0.48	0.19 ± 0.40	0.17 ± 0.42
Carotid intima-media Thickness (mm)	Baseline	0.68 ± 0.1	0.65 ± 0.08	0.68 ± 0.1	0.67 ± 0.1
	Follow-up	0.72 ± 0.1	0.69 ± 0.09 [‡]	0.72 ± 0.11 [‡]	0.71 ± 0.1
	§	0.04 ± 0.06	0.04 ± 0.06	0.04 ± 0.07	0.04 ± 0.07
Aortic Pulse Wave Velocity (cm/sec)	Baseline	757 ± 169	798 ± 196	827 ± 219	799 ± 200
	Follow-up	878 ± 208	835 ± 173	868 ± 179	859 ± 185
	§	121 ± 230 ^{*‡}	38 ± 250 [*]	41 ± 228 [‡]	60 ± 238

Abbreviations: CAC = Coronary Artery Calcium Score

* p-value <0.05 premenopause to postmenopause vs premenopause to premenopause

[‡] p-value <0.05 premenopause to postmenopause vs postmenopause to postmenopause

[‡] p-value <0.05 premenopause to premenopause vs postmenopause to postmenopause

§ mean changes () adjusted for baseline age and time between scans

Table 4.

Baseline, Follow-Up and Change in Lipid Profiles Across Menopause Transition Groups

Variable		Premenopause to Postmenopause	Premenopause to Premenopause	Postmenopause to Postmenopause	Overall
		(n = 93)	(n = 147)	(n = 171)	(N = 411)
		(mean ± SD)	(mean ± SD)	(mean ± SD)	(mean ± SD)
Total Cholesterol (mg/dL)	Baseline	194 ± 32 [†]	192 ± 32 [‡]	214 ± 40 ^{†‡}	201 ± 37
	Follow-up	209 ± 36	200 ± 32	211 ± 38	206 ± 36
	§	15 ± 27 [†]	8 ± 31 [‡]	-3 ± 35 ^{†‡}	5 ± 32
Triglycerides	Baseline	102 ± 45 [†]	107 ± 54 [‡]	137 ± 82 ^{†‡}	118 ± 67
(mg/dL)	Follow-up	115 ± 57	118 ± 66	133 ± 82	123 ± 72
	§	13 ± 44 [†]	11 ± 51 [‡]	-4 ± 66 ^{†‡}	5 ± 56
HDL-C (mg/dL)	Baseline	58 ± 14	55 ± 12 [‡]	59 ± 14 [‡]	57 ± 14
	Follow-up	59 ± 15	55 ± 14	58 ± 15	57 ± 15
	§	1 ± 9	1 ± 9	-1 ± 9	0 ± 9
LDL-C (mg/dL) ^{//}	Baseline	115 ± 30 [†]	116 ± 28 [‡]	128 ± 37 ^{†‡}	121 ± 33
	Follow-up	126 ± 34	121 ± 29	128 ± 33	125 ± 32
	§	11 ± 27 [†]	5 ± 27	0 ± 32 [‡]	4 ± 29

Abbreviations: HDL – High-density cholesterol, LDL-C = Calculated Low-density cholesterol

* p-value <0.05 premenopause to postmenopause vs premenopause to premenopause

† p-value <0.05 premenopause to postmenopause vs postmenopause to postmenopause

‡ p-value <0.05 premenopause to premenopause vs postmenopause to postmenopause

// unable to calculate LDL-c levels on 3 subjects with triglycerides >400 mg/dl

§ mean changes () adjusted for baseline age and time between scans