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# Systematic Review: Effect of Lipid and Lipoprotein Profiles on Atherosclerosis and Cardiovascular Disease Risk in Premenopausal and Postmenopausal Women

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## ABSTRACT:

*Understanding the relationship between lipid profiles and cardiovascular health is crucial, particularly in the context of atherosclerosis, a major cause of cardiovascular diseases. Dyslipidemia, characterized by high LDL cholesterol and triglycerides and low HDL cholesterol, is a significant contributor to atherosclerosis. In women, menopause shifts the lipid profile from a protective to an atherogenic one due to reduced estrogen levels, increasing cardiovascular risk. Additionally, surgical procedures like hysterectomy with or without oophorectomy, which cause abrupt declines in estrogen, further disrupt lipid profiles. Among 243 initially identified publications, 15 were thoroughly reviewed, leading to the inclusion of nine studies. These studies show that surgical menopause typically results in increased total cholesterol, LDL-C, and triglycerides, and decreased HDL-C, heightening cardiovascular risk. Effective monitoring and management of lipid profiles post-surgery are essential, and ovarian conservation during hysterectomy may mitigate some adverse lipid effects. Further longitudinal studies and personalized interventions are needed to enhance cardiovascular health in women undergoing surgical menopause.*

## KEYWORDS:

*Lipid metabolism, Dyslipidemia, Hysterectomy, Oophorectomy, Cardiovascular risk.*

## 1. Introduction

The intricate relationship between lipid and lipoprotein profiles and cardiovascular health is a pivotal area of research, particularly regarding the etiology and progression of atherosclerosis[1]. Atherosclerosis, a pathological condition marked by the accumulation of lipid-laden plaques within arterial walls, stands as a preeminent cause of cardiovascular diseases (CVD) globally[2]. Among the myriad risk factors contributing to atherosclerosis, dyslipidemia—characterized by elevated levels of low-density lipoprotein cholesterol (LDL-C) and triglycerides, coupled with diminished levels of high-density lipoprotein cholesterol (HDL-C)—is notably significant[3].

The risk of atherosclerosis and subsequent CVD is modulated by various factors, including age, sex, lifestyle, and hormonal milieu. In women, the transition from premenopause to postmenopause is associated with significant hormonal shifts, particularly in estrogen levels, which profoundly affect lipid metabolism[4]. Premenopausal women typically exhibit a protective lipid profile, characterized by higher HDL-C and lower LDL-C levels compared to their male counterparts. However, postmenopausal women often experience a shift towards a more atherogenic lipid profile, with increased LDL-C levels and decreased HDL-C levels, largely attributable to the decline in estrogen levels[5].

Estrogen exerts a favorable effect on lipid metabolism by enhancing the expression of LDL receptors and promoting HDL synthesis. The reduction in estrogen levels during menopause disrupts this balance, leading to unfavorable changes in lipid profiles that heighten the risk of atherosclerosis and CVD. This shift underscores the importance of understanding the impact of menopause on lipid metabolism and

cardiovascular risk[6].

Furthermore, surgical interventions such as hysterectomy and oophorectomy, performed for various medical indications, can further perturb lipid profiles and elevate cardiovascular risk. The removal of the ovaries precipitates an abrupt decline in estrogen levels, exacerbating lipid abnormalities and increasing the propensity for atherosclerosis[7].

Given these considerations, it is imperative to investigate the effects of lipid and lipoprotein profiles on atherosclerosis and cardiovascular disease risk in premenopausal and postmenopausal women. This systematic review aims to comprehensively analyze the extant literature on this topic, addressing the following primary research questions:

1. What are the impacts of lipid and lipoprotein profiles on the development of atherosclerosis?

2. How do pre- and post-menopausal statuses affect lipid profiles and cardiovascular disease risk?

3. What are the effects of hysterectomy with or without oophorectomy on lipid metabolism and cardiovascular disease risk?

By synthesizing findings from various studies, this review endeavors to provide a nuanced understanding of the interplay between lipid metabolism, hormonal changes, and cardiovascular risk in women. The insights garnered from this review could inform targeted strategies for the prevention and management of atherosclerosis and CVD in this population, ultimately contributing to improved cardiovascular health outcomes for women across different life stages.

**Criteria for Selecting Studies.** The selection of studies for this systematic review adhered to a structured and comprehensive process designed to ensure the inclusion of high-quality and pertinent research. The methodology began with the formulation of primary research questions focusing on the impacts of lipid and lipoprotein profiles on the development of atherosclerosis, the effects of pre- and post-menopausal status on lipid profiles and cardiovascular disease (CVD) risk, and the influence of hysterectomy with or without oophorectomy on lipid metabolism and CVD risk. The search strategy encompassed multiple databases, including PubMed, Medline, the Cochrane Library, and Google Scholar, using a variety of keywords such as "Serum lipids," "Lipoproteins," "Atherosclerosis," "Hypercholesterolemia," "Menopause," "Hysterectomy," "Oophorectomy," "Cardiovascular disease," and "Lipid metabolism." The search was restricted to studies published from 1990 to 2023 and included only English-language publications.

The inclusion criteria were delineated to focus on studies involving adult human participants, encompassing both healthy individuals and those with atherosclerosis or related cardiovascular conditions. Specific attention was given to premenopausal and postmenopausal women, including those who had undergone hysterectomy or oophorectomy. The selected studies comprised various designs, such as prospective studies, longitudinal cohort studies, cross-sectional studies, case-control studies, comparative studies, and planned secondary analyses. Key outcomes included lipid and lipoprotein levels, cardiovascular disease incidence and risk factors, and changes in lipid profiles post-menopause or post-surgical intervention.

Exclusion criteria were rigorously applied to omit studies involving animal models or in vitro experiments, those lacking clear outcome measures related to lipid profiles or cardiovascular risk, and review articles, editorials, and commentaries. The study selection process involved an initial screening of titles and abstracts to exclude irrelevant studies, followed by a full-text review to confirm eligibility and perform data extraction for those meeting all criteria. Data extraction focused on study design, population characteristics, interventions, outcomes, and key findings, compiled into a standardized extraction form.

Quality assessment of the included studies employed the Newcastle-Ottawa Scale (NOS) for non-randomized studies and the Cochrane Risk of Bias Tool for randomized studies. This evaluation considered various biases, including selection, performance, detection, attrition, and reporting biases, to ensure the reliability and validity of the findings incorporated into the review.

Initially, 243 relevant publications were identified. After removing duplicates and screening titles and abstracts for relevance based on the inclusion criteria, 219 publications were excluded, leaving 24 potentially relevant articles.

Next, full-text assessments were conducted on these 24 articles to determine their suitability for inclusion. After a rigorous assessment against detailed inclusion criteria, 15 articles were found to meet the criteria and were included for further analysis.

In the final selection stage, the researchers carefully reviewed those 15 articles once more to ensure they meet all inclusion criteria. Following this review, six articles were excluded due to not meeting specific criteria, resulting in a final selection of nine studies.

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From those nine selected studies, relevant data concerning lipid metabolism changes post-surgical menopause were extracted and synthesized. This process involved analyzing trends, similarities, and differences across the studies to understand the implications for cardiovascular health resulting from alterations in lipid metabolism post-hysterectomy or oophorectomy.

## 2. Results

**Table 1. Review of literature for the EFFECT OF HYSTERECTOMY WITH OR WITHOUT OOPHERECTOMY ON LIPOPROTEIN METABOLISM**

| Authors & Year | Study Group | Type of Study | Aim and Objective | Result | Conclusion |
|---|---|---|---|---|---|
| Fartsh E et al. 1990 | 31premenopausal women undergoing hysterectomy and bilateral oophorectomy for non-malignant conditions | Observational Study | To study the effects of surgical menopause on lipoprotein levels and their time course | LDL cholesterol levels rose significantly from a mean of 3.57 (SD 0.66) mmol/l to 4.21 (SD 0.84) mmol/l in 6 weeks post-operation. No significant changes in other cholesterol density fractions or triglyceride levels. HDL subfractions showed no significant changes. | The increase in LDL cholesterol suggests an increased risk of coronary heart disease, but this does not wholly account for the increase in cardiovascular disease associated with oophorectomy. |
| Goldman GA et al. 1996 | Twenty-seven women, 15 premenopausal and 12 postmenopausal, undergoing surgical castration (total abdominal hysterectomy and bilateral salpingo-oophorectomy) | Prospective randomized study | To investigate the effect of endogenous estrogen on lipid and lipoprotein metabolism in premenopausal and postmenopausal women. | No significant differences were found in both groups before castration and after 6 months. A modest, but statistically significant, rise in triglycerides was observed in the premenopausal group. | The clinical significance indicates that the effect of endogenous estrogen on lipid metabolism is doubtful and should be further investigated. |
| Yoshio Suda, et al. 1998 | The study enrolled a total of 62 subjects (31 Premenopausal women undergoing oophorectomy and 31 strictly age- and body size-matched premenopausal subjects as controls) | Prospective | Investigate the influence of bilateral oophorectomy on lipid metabolism in premenopausal women. | Total cholesterol (TC) and LDL-C levels were higher in the oophorectomy group compared to the control. No significant difference was observed in HDL-C levels. | Oophorectomy induces cardiovascular diseases, requiring follow-up of changes in lipid metabolism, especially Apo-B and LDL-C. |
| Shirin Kalyan et al. 2011 | 33 Premenopausal women undergoing hysterectomy with bilateral oophorectomy were studied an average of 7 days postsurgery | Planned Secondary Analysis | Assess acute postoperative changes in lipids and inflammation following premenopausal hysterectomy with bilateral oophorectomy. | Hemoglobin, albumin, testosterone, and HDL levels decreased, while CRP levels increased post-surgery. | High levels of inflammation and abnormal lipids post-surgical menopause are important considerations for subsequent treatment and care. |
| Renymol B et al. 2017 | 70 Patients undergoing oophorectomy | Prospective Case-Control | Examine lipid profile and cardiovascular risk factors in patients undergoing oophorectomy. | Total cholesterol (TC), triglycerides (TG), and LDL-C levels were higher, while HDL-C levels were lower in the oophorectomy group. | Surgical menopause leads to significant unfavorable changes in lipid profile and diastolic blood pressure. |

| | | | | | |
|---|---|---|---|---|---|
| Duke Appiah et al. 2015 | 5,115 womens 18–30 years of age undergoing menopause | Longitudinal Cohort | Compare changes in CVD risk factors before and after natural menopause, hysterectomy with ovarian conservation, or hysterectomy with bilateral oophorectomy. | HDL levels increased, while triglyceride levels decreased postmenopause. | Hysterectomy not independently associated with CVD risk factors. Young-adult levels of CVD risk factors predict postmenopausal levels. |
| Maryam Farah-mand, et al. 2017 | 13 women with surgical menopause and 39 age-matched controls with natural menopause were selected | Longitudinal Cohort | Examine metabolic changes in surgically versus naturally menopausal women. | Total cholesterol (TC) levels were higher in surgically menopausal women, while HDL-C levels were lower compared to naturally menopausal women. | Incidence of metabolic syndrome higher in surgically menopausal women, and fasting blood glucose higher in those with hysterectomy ± unilateral salpingo-oophorectomy compared to natural menopause. |
| Sukumar Mitra and Seema Das. 2020 | 45 participants enrolled in three different categories of total abdominal hysterectomy namely control group-10, bilateral salpingectomy + TAH (16) and BSO+TAH (19) done for benign conditions. | Comparative | To analyze the changes in lipid profile between oophorectomized and non-oophorectomized women undergoing hysterectomy. | Total cholesterol, triglycerides, LDL cholesterol, and total cholesterol showed varying degrees of increase in all groups postoperatively. HDL cholesterol levels exhibited a decline across all groups over the study period. | Women with diminished ovarian reserve, especially those undergoing surgical menopause with complete removal of tubes and ovaries, may face heightened cardiovascular risk factors, such as dyslipidemia, even during their reproductive years. |
| Shahla Yazdani 2014 | Women aged 46-52 years undergoing hysterectomy and bilateral salpingo-oophorectomy for benign reasons | Prospective cohort study | To investigate glucose tolerance and lipid profile changes post-surgery | Significant increase in triglycerides (132.3 to 181.2 mg/dl, P=0.005), total cholesterol (177.4 to 206.7 mg/dl, P=0.0001), and LDL cholesterol (98.4 to 115.3 mg/dl, P=0.003) post-surgery | Adverse lipid profile changes (increased TG, total cholesterol, LDL) should be carefully considered before bilateral salpingo-oophorectomy in premenopausal women undergoing hysterectomy for benign reasons |

## 3. Discussion

This systematic review elucidated the effects of lipid and lipoprotein profiles on atherosclerosis and cardiovascular disease (CVD) risk in premenopausal and postmenopausal women, including those who underwent hysterectomy and oophorectomy. The findings underscore the critical role of lipid metabolism in cardiovascular health, particularly in the context of hormonal changes associated with menopause and surgical interventions.

### Impact of Menopause on Lipid Profiles and Cardiovascular Risk

Menopause, marked by a significant decline in estrogen levels, profoundly impacts lipid metabolism, increasing the risk of atherosclerosis and CVD. Estrogen exerts a cardioprotective effect by modulating lipid profiles, primarily through the reduction of low-density lipoprotein cholesterol (LDL-C) and the elevation of high-density lipoprotein cholesterol (HDL-C). Postmenopausal women, as observed in studies included in this review, typically exhibit increased levels of total cholesterol, LDL-C, and triglycerides, alongside decreased levels of HDL-C[8].

The transition from premenopause to postmenopause is associated with a deterioration in lipid profiles, contributing to a higher risk of cardiovascular diseases[16]. This underscores the necessity for proactive lipid monitoring and management in postmenopausal women. Hormone replacement therapy (HRT) has been considered to mitigate these adverse effects,

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although its use must be carefully weighed against potential risks[17].

## 1. Impact on Lipoprotein Levels

**Total Cholesterol (TC), LDL Cholesterol (LDL-C), and Triglycerides (TG):**

- Multiple studies consistently report that hysterectomy with bilateral oophorectomy leads to unfavorable changes in lipid profiles. For instance, Goldman et al.[9] found a significant rise in triglycerides post-surgery among premenopausal women. Similarly, studies by Yoshio Suda et al. [10], Renymol B et al.[11], and Shahla Yazdani[12] documented increases in total cholesterol, LDL cholesterol, and triglycerides after surgical menopause.

- These changes are concerning because elevated levels of LDL-C and triglycerides are well-established risk factors for cardiovascular disease (CVD), contributing to atherosclerosis and coronary artery disease[18].

**HDL Cholesterol (HDL-C):**

- Conversely, HDL-C, often considered protective against CVD due to its role in reverse cholesterol transport, tends to decrease or remain unchanged post-surgery[10,11, and 12].

- This decrease in HDL-C further exacerbates the adverse lipid profile associated with surgical menopause, potentially increasing cardiovascular risk[19].

## 2. Comparison with Natural Menopause

- Maryam Farahmand et al.[13] compared surgically menopausal women with naturally menopausal controls and found higher TC levels and lower HDL-C levels in surgically menopausal women. This suggests that the method of menopause induction (surgical vs. natural) plays a significant role in lipid metabolism alterations.

- Natural menopause, marked by the gradual decline in ovarian function and estrogen levels, may lead to more subtle changes in lipid profiles compared to the abrupt hormonal changes induced by surgical menopause[20].

## 3. Cardiovascular Risk

- The observed changes in lipid profiles post-surgery, such as elevated LDL-C and decreased HDL-C, indicate an increased cardiovascular risk among women undergoing hysterectomy with oophorectomy. Elevated LDL-C is particularly concerning as it directly contributes to the development of atherosclerosis and increases the risk of cardiovascular events like heart attacks and strokes.

- Renymol B et al.[11] highlighted that these adverse lipid profile changes may persist over the long term, underscoring the importance of ongoing monitoring and management to mitigate cardiovascular risks in these women.

## 4. Inflammation and Immediate Postoperative Effects

- Shirin Kalyan et al.[14] emphasized acute postoperative changes in lipid profiles and inflammatory markers like C-reactive protein (CRP). They noted a decrease in HDL levels and an increase in CRP levels following surgical menopause.

- These immediate changes suggest a state of heightened inflammation and altered lipid metabolism in the perioperative period, which may contribute to short-term cardiovascular risks and warrant careful monitoring and possibly early intervention[21].

## 5. Variation Based on Age and Menopausal Status

- Duke Appiah et al.[15] explored age-related variations in lipid profile trajectories post-menopause. They indicated that younger women undergoing surgical menopause may experience different lipid profile changes compared to older women, potentially due to variations in baseline hormonal levels and metabolic status.

- Understanding these age-related differences is crucial for tailoring interventions and preventive strategies to mitigate cardiovascular risks in women undergoing surgical menopause[22].

## 6. Considerations for Clinical Practice

- The findings underscore the importance of individualized risk assessment before deciding on hysterectomy with oophorectomy, particularly in premenopausal women. Alternative approaches, such as ovarian conservation during hysterectomy, may mitigate some of these adverse lipid profile changes[12].

- Clinicians should carefully weigh the benefits of surgery against the potential long-term cardiovascular risks associated with altered lipid metabolism, especially in younger women who may face decades of increased CVD risk post-surgery[23].

**Preventive Measures for Managing Lipid Profiles and Cardiovascular Risk in Menopausal Women**

The systematic review emphasizes the need for effective strategies to manage lipid profile changes and cardiovascular risks associated with menopause and surgical interventions. This discussion outlines key preventive measures:

### 1. Hormone Replacement Therapy (HRT)

- **Efficacy and Risks**: HRT can improve lipid profiles by lowering LDL cholesterol and raising HDL cholesterol, potentially mitigating cardiovascular risks. However, it carries risks such as breast cancer, stroke, and venous thromboembolism, as highlighted by the Women's Health Initiative. Individualized treatment, considering factors like age and time since menopause, is essential. Transdermal estrogen and selective estrogen receptor modulators (SERMs) may offer safer alternatives[24].

### 2. Lifestyle Modifications

- **Diet**: A heart-healthy diet rich in fruits, vegetables, whole grains, and healthy fats, such as those found in the Mediterranean diet, can improve lipid levels and reduce cardiovascular risk[25].

- **Exercise**: Regular physical activity helps lower LDL cholesterol, raise HDL cholesterol, and manage weight. Activities like walking, cycling, and resistance training are beneficial[25].

- **Weight Management**: Addressing obesity, particularly abdominal fat, through diet and exercise can normalize lipid levels and decrease cardiovascular risk[25].

### 3. Pharmacological Interventions

- **Statins**: Statins effectively lower LDL cholesterol and reduce cardiovascular events, making them a key treatment for dyslipidemia in postmenopausal women.

- **Other Medications**: Fibrates, niacin, and bile acid sequestrants may be used based on individual lipid abnormalities. Emerging therapies like PCSK9 inhibitors offer additional options for those not reaching target LDL levels with statins[26].

### 4. Comprehensive Cardiovascular Risk Management

- **Regular Monitoring**: Ongoing assessment of lipid levels and cardiovascular risk factors is crucial. This includes periodic lipid profiling and evaluating other risk factors like blood pressure and glucose levels.

- **Multidisciplinary Approach**: Effective management often requires a team approach, involving primary care physicians, cardiologists, and dietitians to address all aspects of cardiovascular health[27].

### Study Limitations and Considerations

1. **Study Design and Methodology**: Most studies reviewed are observational or prospective cohorts, limiting causality and potentially influenced by confounding factors. Sample sizes and demographic diversity are often limited, affecting the generalizability of results.

2. **Measurement and Assessment Issues**: Variability in lipid measurement techniques and the short-term focus of many studies may impact the accuracy and long-term relevance of findings.

3. **Inconsistent HRT Use**: Variability in HRT use across studies can affect results, with inconsistent reporting potentially impacting conclusions about its benefits and risks.

4. **Comparisons Between Surgical and Natural Menopause**: Differences in hormonal changes between surgical and natural menopause can complicate comparisons, and baseline health status variations may not always be well-controlled.

5. **Age and Menopausal Status Variations**: Age-related differences in lipid profiles need better explanation. The lack of tailored recommendations for different age groups limits the applicability of findings.

6. **Inflammation and Immediate Postoperative Effects**: Acute postoperative changes in inflammation and lipid profiles highlight short-term risks but may not fully capture long-term cardiovascular impacts.

7. **Overall Quality of Evidence**: The quality of evidence varies, with some studies providing robust data while others have methodological weaknesses. There is a need for well-designed longitudinal studies to better understand long-term effects and refine preventive strategies.

## 4. Conclusion

In conclusion, while hysterectomy with or without oophorectomy is often necessary for various benign conditions, it is crucial to carefully consider the potential cardiovascular risks associated with changes in lipid profiles post-surgery. The adverse lipid profile alterations, including elevated LDL-C, decreased HDL-C, and increased triglycerides, highlight the importance of ongoing monitoring and proactive management to

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reduce long-term cardiovascular risks in women undergoing surgical menopause. Individualized care and a multidisciplinary approach involving gynecologists, endocrinologists, and cardiologists are essential for optimizing cardiovascular health outcomes in those women.

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