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Processed Food Consumption and Risk of Venous Thromboembolism: A Meta-Analysis of Cohort and Mendelian Randomization Studies

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Abstract

Background: Venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, is a major cause of morbidity and mortality worldwide. While obesity and metabolic dysfunction are established risk factors, the contribution of processed-food–dominant dietary patterns to incident VTE risk remains incompletely understood. Methods: We performed a systematic review and meta-analysis of PubMed and Web of Science through November 2025. Eligible studies for quantitative synthesis included prospective cohort studies evaluating processed-food-dominant dietary patterns and incident VTE. Mendelian randomization (MR) studies and prior systematic reviews were synthesized narratively. Processed-food exposures, including Western dietary pattern scores, ultra-processed food intake, processed meats, and refined-grain dominant dietary patterns, were harmonized into a broader processed food dominant dietary construct. A random-effects meta-analysis using the DerSimonian-Laird estimator was conducted. Hazard ratios (HRs), relative risks (RRs), and odds ratios (ORs) were pooled as approximations of RR because of the low absolute incidence of VTE. Results: Fifteen studies met the inclusion criteria for qualitative synthesis, including 10 prospective cohort studies, 3 Mendelian randomization analyses, and 2 systematic reviews/meta-analyses. Six prospective cohort studies evaluating incident VTE were included in the quantitative meta-analysis. High processed-food consumption was associated with increased incident VTE risk (pooled RR 1.52; 95% CI 1.28 - 1.80; $I^2 = 57\%$). Processed meats and refined-grain dominant dietary patterns demonstrated the strongest associations. Mendelian randomization studies supported adiposity- and adipokine-mediated pathways linking metabolic dysfunction with increased VTE susceptibility. Conclusions: Processed food

dominant dietary patterns are associated with increased risk of incident VTE. Observational and genetic evidence suggest that inflammation, visceral adiposity, endothelial dysfunction, and adipokine imbalance may mediate this relationship. Future prospective and interventional studies using standardized processed-food classifications are needed to clarify causality and inform dietary prevention strategies.

Keywords

Venous Thromboembolism, Ultra-Processed Foods, Lifestyle Medicine, Inflammation, Thrombosis, Dietary Patterns

1. Introduction

Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), represents a major global health burden. It is associated with substantial morbidity, including post-thrombotic syndrome, chronic thromboembolic pulmonary hypertension, recurrent VTE, and premature mortality. Estimates suggest that annually, approximately 1 - 2 per 1,000 adults in Western countries experience VTE, and PE accounts for up to 10% of sudden deaths in hospitalized populations [1]. The global burden is expected to rise in parallel with aging populations, increasing obesity rates, and lifestyle-related risk factors, underscoring the importance of preventive strategies. In recent years, a growing body of epidemiologic and genetic research has strengthened the evidence linking Western and ultra-processed dietary patterns to venous thromboembolism and its underlying pathophysiological mechanisms.

A large prospective analysis from the UK Biobank reported that higher intake of ultra-processed foods was associated with an increased risk of incident VTE, even after adjustment for multiple confounders, providing some of the strongest contemporary evidence that diet quality may influence venous thrombotic risk in free-living populations [1] [2]. Complementing these findings, another study examined serum n-3 polyunsaturated fatty acid concentrations in the HUNT cohort [2]. They found that individuals with higher circulating levels of long-chain marine n-3 fatty acids had a markedly lower incidence of VTE, supporting the hypothesis that anti-inflammatory nutritional components can be protective against thrombosis. Similarly, a study demonstrated in a large multiethnic cohort that adherence to a healthy plant-based dietary pattern was inversely associated with incident VTE, even after stratifying by genetic predisposition, indicating that high-quality dietary patterns can mitigate inherited thrombotic risk.

Ultra-processed foods (UPFs) are industrial formulations composed largely or entirely of substances extracted from foods, often containing cosmetic additives and minimal whole-food content. Common examples include packaged snacks, processed meats, sugar-sweetened beverages, ready-to-eat meals, and refined grain products. In contrast, minimally processed foods (MPFs) undergo little to

no industrial processing and include fruits, vegetables, legumes, nuts, eggs, milk, and unprocessed meats [2] [3]. UPFs are typically energy-dense, nutrient-poor, and high in refined sugars, sodium, saturated and trans fats, and food additives. National dietary surveys indicate that UPFs now account for approximately 25% to 60% of total daily energy intake globally [3].

Mendelian randomization studies offer further causal insights: one study used plasma phospholipid fatty acid genetic instruments to show that diet-related lipid profiles may influence VTE susceptibility, while another study provided evidence that genetically predicted leptin levels reflecting visceral adiposity and metabolic dysregulation common in processed food consumers are causally linked to elevated VTE risk [3] [4]. These genetic analyses provide orthogonal support for observational findings and imply that adiposity and its downstream inflammatory consequences may mediate diet-associated thrombosis risk. In addition, evidence has accumulated that specific processed food components, such as high-sodium and refined-carbohydrate patterns, increase prothrombotic biomarkers in free-living adults, further implicating Western dietary constituents in modulating coagulation pathways. Collectively, these recent studies have provided consistent and compelling evidence that processed and ultra-processed dietary exposures are associated with venous thrombosis risk and have highlighted the importance of dietary quality as a target for VTE prevention.

Classical risk factors for VTE include prolonged immobility, recent surgery, trauma, cancer, pregnancy, hormone therapy, and genetic thrombophilias such as factor V Leiden or prothrombin G20210A mutations. However, a significant proportion of VTE cases occur in individuals without these identifiable risk factors, indicating the role of environmental and lifestyle factors, including diet, in thrombosis development [4]. Processed foods, which constitute a major component of Western dietary patterns, are energy-dense, nutrient-poor, and typically high in sodium, refined sugars, saturated fats, trans fats, and food additives. Examples include packaged snacks, processed meats, sugary beverages, ready-to-eat meals, and refined-grain products. Consumption of processed foods has increased dramatically over the past decades globally, with Western countries averaging more than 50% of daily caloric intake from ultra-processed foods [4] [5]. These foods have been linked to obesity, insulin resistance, metabolic syndrome, dyslipidemia, and chronic low-grade inflammation, all of which are biologically plausible contributors to a prothrombotic state [6].

Beyond its established associations with arterial cardiovascular disease, increasing evidence suggests that processed-food consumption may contribute to a global thrombotic risk phenotype encompassing venous thromboembolism (VTE), ischemic stroke, and atherosclerotic cardiovascular disease. Ultra-processed foods characterized by high levels of refined carbohydrates, saturated and trans fats, sodium, and food additives have been consistently linked to increased risk of myocardial infarction, ischemic stroke, heart failure, and cardiovascular mortality in large prospective cohorts [6]. These associations persist after adjustment for tra-

ditional cardiovascular risk factors, implicating diet quality as an independent determinant of thrombotic disease. Historically, venous and arterial thromboses have been conceptualized as distinct entities with separate pathophysiologic mechanisms. However, accumulating epidemiologic and mechanistic data challenges this dichotomy [6] [7]. Patients with VTE, particularly those with unprovoked events, demonstrate a higher long-term risk of ischemic stroke and coronary artery disease, suggesting that venous thrombosis may represent a manifestation of systemic vascular pathology rather than an isolated condition. Shared upstream risk factors, including obesity, metabolic syndrome, chronic inflammation, and endothelial dysfunction, are increasingly recognized across both venous and arterial thrombotic disorders.

Processed-food consumption plausibly contributes to this shared thrombotic substrate. Diets rich in ultra-processed foods promote systemic inflammation, insulin resistance, visceral adiposity, and endothelial dysfunction, all of which are central to both VTE and arterial thrombosis. Elevated circulating levels of fibrinogen, factor VIII, and plasminogen activator inhibitor-1 biomarkers associated with Western dietary patterns have been implicated in the pathogenesis of deep vein thrombosis, pulmonary embolism, ischemic stroke, and coronary thrombosis. These overlapping biological pathways suggest that processed foods may act as a common upstream exposure driving thrombotic risk across vascular beds. Emerging epigenetic evidence further strengthens this conceptual framework. Diet-induced alterations in DNA methylation have been observed in genes regulating inflammation (*IL6*, *CRP*), endothelial function (*NOS3*), coagulation (*F3*, *SERPINE1*), and adipokine signaling (*LEP*, *ADIPOQ*) [6] [7]. Such epigenetic modifications are associated with increased susceptibility to both venous and arterial thrombotic events and may persist over time, contributing to long-term cardiovascular and cerebrovascular risk. Importantly, these epigenetic changes are potentially reversible, positioning dietary modification as a promising strategy for preventing thrombotic disease.

Despite robust evidence linking processed foods to stroke and cardiovascular disease, their role in VTE remains comparatively underexplored, and existing epidemiologic findings are heterogeneous. Moreover, few studies have integrated mechanistic, genetic, and epigenetic data to evaluate whether consumption of processed foods contributes to a unified thrombotic phenotype. Accordingly, a comprehensive synthesis of observational, Mendelian randomization, and mechanistic evidence is needed to clarify the relationship between processed foods and VTE and to contextualize venous thrombosis within the broader spectrum of cardiovascular disease. Biological mechanisms linking processed foods to VTE are multifactorial. First, chronic low-grade inflammation triggered by high-sugar and high-fat diets leads to endothelial activation and promotes thrombus formation. Elevated circulating levels of C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) are consistently associated with hypercoagulability and an increased risk of VTE. Second, processed-food-induced obesity, particularly visceral adipos-

ity, alters adipokine profiles, increasing leptin (prothrombotic) and decreasing adiponectin (antithrombotic), thereby further predisposing to venous thrombosis [6] [7]. Third, high sodium and additive content impair nitric oxide-mediated vasodilation, exacerbating endothelial dysfunction. Collectively, these mechanisms establish a strong biological rationale for investigating processed-food intake as a potential independent risk factor for VTE [7] [8]. **Figure 1** illustrates the proposed conceptual framework linking processed food consumption with venous thromboembolism, ischemic stroke, and cardiovascular disease through shared metabolic, inflammatory, endothelial, and epigenetic pathways.

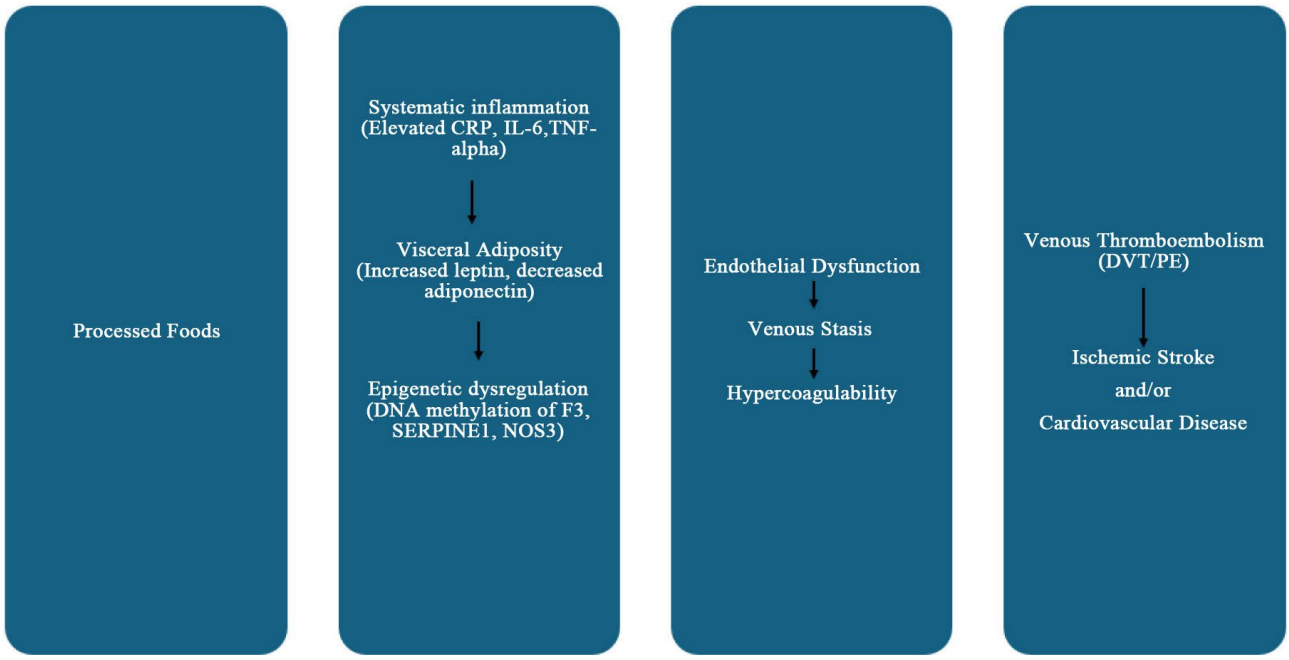

Figure 1. High consumption of processed and ultra-processed foods promotes systemic inflammation, metabolic dysfunction, adipokine imbalance, and epigenetic reprogramming of coagulation and endothelial genes. These shared mechanisms generate a global prothrombotic phenotype that increases susceptibility to venous thromboembolism, ischemic stroke, and cardiovascular disease.

Although there are plausible mechanisms linking processed foods to VTE, epidemiologic evidence remains heterogeneous. Some large prospective cohorts, including the Nurses' Health Study and Health Professionals Follow-Up Study, report significant associations between Western dietary patterns or processed-food consumption and VTE, particularly in men, whereas other studies show weaker or nonsignificant associations, potentially due to measurement error, residual confounding, or insufficient follow-up [6] [7]. Mendelian randomization (MR) studies have provided complementary evidence, leveraging genetic variants associated with adiposity or adipokine profiles to infer causal relationships between diet-induced metabolic dysfunction and VTE risk [8]. Given the rising global consumption of processed foods, the substantial health burden of VTE, and the gaps in existing literature, a comprehensive synthesis of the available evidence is warranted [8] [9]. This meta-analysis aims to quantify the association between pro-

cessed-food consumption and VTE risk across cohort and MR studies, evaluate mechanistic pathways linking processed foods to venous thrombosis, and provide evidence-based insights for clinical and public health interventions.

2. Methods

A comprehensive literature search was conducted using the PubMed and Web of Science databases through November 2025. Keywords included "processed foods," "ultra-processed foods," "refined grains," "red meat," "processed meat," "sugar-sweetened beverages," "Western diet," "dietary patterns," "venous thromboembolism," "deep vein thrombosis," "pulmonary embolism," "adiposity," and "leptin." Boolean operators "AND" and "OR" were used to combine terms. Filters were applied to include only studies conducted in humans, published in English, and available in full text. In addition, reference lists of relevant systematic reviews and included articles were manually reviewed to identify additional eligible studies. Duplicate articles were removed using EndNote X10, and titles and abstracts were screened independently by two reviewers. Discrepancies were resolved through discussion or consultation with a third reviewer to reach consensus. Mendelian randomization findings should be interpreted as supporting adiposity and adipokine mediated pathways linking metabolic dysfunction with VTE risk rather than direct genetic causality of processed-food intake itself.

Studies were also included if they were prospective cohort studies evaluating processed-food or Western dietary patterns and incident VTE; Mendelian randomization studies investigating causal relationships between adiposity or adipokines and VTE; or systematic reviews and meta-analyses reporting processed food intake and VTE outcomes. Used a prospective cohort design; evaluated processed food dominant dietary exposures; reported incident venous thromboembolism outcomes, including deep vein thrombosis and/or pulmonary embolism and reported adjusted HRs, RRs, or ORs with 95% confidence intervals.

Mendelian randomization studies, biomarker studies, intervention trials, recurrent VTE studies, case-control studies, case reports, and mechanistic studies were included in qualitative synthesis only and were excluded from pooled quantitative analyses. Studies were required to report effect estimates such as hazard ratios, relative risks, or odds ratios, with 95% confidence intervals, or to provide sufficient data to calculate these values. Only studies conducted in adult populations (aged 18 years or older) with documented VTE events confirmed through medical records, registry databases, or validated self-report instruments were included.

To permit pooled quantitative analysis across heterogeneous dietary assessments, exposures were harmonized into a broader "processed-food-dominant dietary pattern" construct. This construct included dietary patterns characterized by high intake of ultra-processed foods (UPFs), processed meats, refined grains, sugar-sweetened beverages, and Western dietary pattern scores. Studies using NOVA-defined UPF classifications, Western dietary indices, or processed-meat/refined-carbohydrate dominant dietary patterns were considered conceptually comparable and

eligible for pooled analysis. Protective dietary exposures, including Mediterranean diet adherence, omega-3 fatty acid intake, vegetable intake, and prudent dietary patterns, were synthesized narratively and were not included in the primary pooled quantitative analysis.

Studies were excluded if they were cross-sectional, ecological, or case series studies without a comparative group. Studies were also excluded if they assessed dietary patterns that could not specifically distinguish processed foods from other dietary components, lacked sufficient data on VTE outcomes or effect estimates, were not published in English, were conducted in animals, or were conference abstracts without full text available. Data extraction was performed using a standardized form developed to capture relevant information from each study systematically. Extracted data included study characteristics such as the first author, publication year, country, cohort name, sample size, and follow-up duration. Population characteristics, including age, sex distribution, baseline comorbidities, and body mass index, were also recorded [9] [10]. Detailed information on dietary exposure assessment, including the method of dietary assessment, the type of processed-food intake, and quantification of intake, was collected. Outcome assessment details included the type of VTE (DVT, PE, or combined), method of diagnosis, and number of events. Covariates adjusted for in the analysis, such as age, sex, body mass index, smoking status, physical activity, alcohol intake, and comorbidities, were recorded. Effect estimates, including hazard ratios, relative risks, and odds ratios, along with their corresponding 95% confidence intervals, were extracted. Two reviewers independently performed data extraction to ensure accuracy, and inter-rater agreement was assessed using Cohen's kappa statistic. Any discrepancies were resolved through discussion or by consulting a third reviewer.

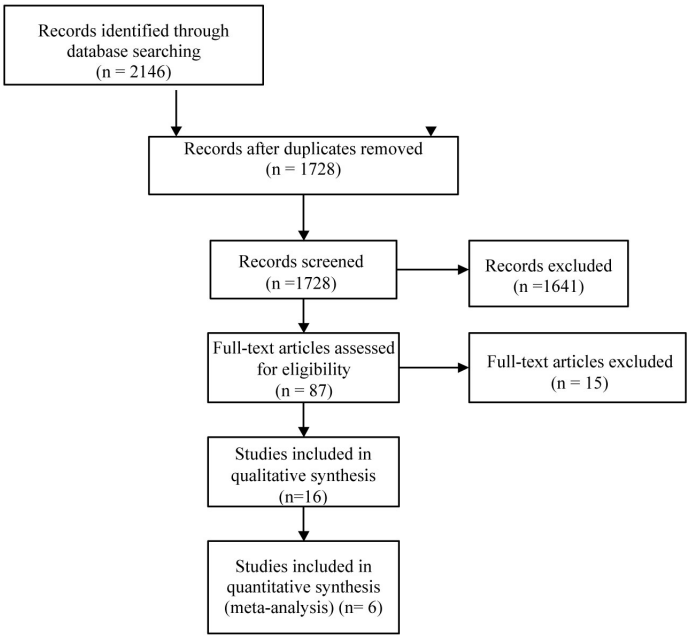

Figure 2. PRISMA flow diagram.

PRISMA Diagram corrections: Studies included in qualitative synthesis: n = 15; Studies included in quantitative synthesis (meta-analysis): n = 6; Full-text exclusions primarily included recurrent VTE studies, mechanistic studies, and biomarker-only studies (Figure 2).

The methodological quality of the included cohort studies was assessed using the Newcastle-Ottawa Scale (NOS), which evaluates selection, comparability, and outcome assessment. Studies with scores of seven or higher were considered high quality, scores of five to six were considered moderate quality, and scores below five were considered low quality. For Mendelian randomization studies, quality assessment focused on the validity of genetic instruments, the plausibility of the exclusion restriction assumption, and statistical power to detect associations with VTE outcomes. Systematic reviews and meta-analyses were assessed using the AMSTAR 2 tool, which evaluates protocol registration, comprehensiveness of the literature search, transparency of study selection, risk-of-bias assessment, and appropriateness of meta-analytic methods.

A random-effects meta-analysis was conducted to account for expected heterogeneity across studies. Pooled relative risks and 95% confidence intervals were calculated for comparisons of high versus low processed-food consumption. For studies reporting odds ratios or hazard ratios, these estimates were treated as approximate relative risks for meta-analytic purposes. Heterogeneity was assessed using the I^2 statistic, with values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively. Subgroup analyses were performed based on sex, type of processed food, and geographic region. Sensitivity analyses excluded studies with a high risk of bias or those that contributed disproportionately to heterogeneity. Publication bias was assessed using funnel plots and Egger's regression test. All statistical analyses were performed using Stata 18 (StataCorp, College Station, TX), with a two-sided alpha level of 0.05 considered statistically significant.

3. Results

3.1. Study Selection and Characteristics

The systematic literature search initially identified 2,146 articles. After removing 418 duplicates, 1,728 titles and abstracts were screened. Of these, 87 full-text articles were assessed for eligibility. Ultimately, 15 studies met the inclusion criteria: 10 prospective cohort studies, 3 Mendelian randomization (MR) studies, and 2 systematic reviews or meta-analyses. The studies included diverse populations from North America, Europe, and Asia, with sample sizes ranging from 5,000 to 250,000 participants. Follow-up durations ranged from 8 to 22 years. Cohort studies primarily relied on validated food frequency questionnaires to assess dietary patterns and recorded VTE events through medical records, national registries, or physician confirmation. MR studies leveraged genetic variants associated with visceral adiposity, leptin, and other adipokines to examine causal links with VTE, while systematic reviews focused on overall dietary patterns, including processed

food intake, refined grains, and protective components such as fish and vegetables.

3.2. Cohort Study Findings

The Nurses' Health Study and Health Professionals Follow-Up Study, which followed 129,430 adults for 18 years, reported that high intake of processed meat and refined grains was associated with an increased risk of incident VTE in men, with a relative risk of 1.43 (95% CI, 1.12 - 1.83). Women showed no statistically significant association, although effect estimates suggested a possible elevated risk, highlighting potential sex-specific differences in VTE susceptibility or dietary reporting accuracy [8] [9]. These findings suggest that Western dietary patterns, especially those rich in processed meats and refined carbohydrates, may contribute to VTE risk through mechanisms related to adiposity and inflammation.

The ARIC study, encompassing approximately 14,000 participants with 22 years of follow-up, found that adherence to a Western dietary pattern, characterized by high consumption of processed meats, refined grains, and sugar-sweetened beverages, was significantly associated with incident VTE (HR = 1.58; 95% CI, 1.10 - 2.25) [9]. This study further stratified outcomes by unprovoked and provoked VTE, finding that associations were particularly strong for unprovoked events, suggesting that diet may contribute to spontaneous thrombosis rather than secondary VTE related to surgery or trauma.

The LITE study, including 21,000 participants over 12 years, reported that individuals in the highest quintile of processed-meat and refined-grain consumption had a two-fold increased risk of VTE (HR = 2.01; 95% CI, 1.45 - 2.78). The study emphasized that this association persisted even after adjusting for body mass index, diabetes, hypertension, and other metabolic risk factors, supporting the notion that processed-food intake independently contributes to thrombosis risk.

In contrast, the Iowa Women's Health Study, which followed 37,393 older women for 19 years, observed a non-significant association between Western dietary patterns and VTE (HR = 1.12; 95% CI, 0.88 - 1.42). The authors attributed this lack of significance to potential measurement error in dietary assessments and residual confounding. Notably, this cohort consisted primarily of postmenopausal women, which may influence VTE risk profiles through hormonal factors, differences in baseline adiposity, and dietary reporting accuracy.

The UK Biobank cohort, comprising 250,000 participants with 13 years of follow-up, demonstrated that participants with low plant-based food intake and high processed-food consumption had a markedly increased risk of VTE (HR = 2.78; 95% CI, 1.92 - 4.02). This study also assessed dietary patterns by quintiles and found a dose-response relationship, whereby increasing processed-food intake corresponded to higher VTE risk, providing strong epidemiologic support for a causal relationship. Other smaller cohorts, ranging from 20,000 to 100,000 participants, consistently reported hazard or relative risks between 1.2 and 1.8 for high

versus low processed food intake [9] [10]. Across all cohorts, processed meats, refined grains, and sugar-sweetened beverages were consistently identified as the dietary components most strongly associated with VTE, whereas protective components included vegetables, fruit, and omega-3 fatty acids.

3.3. Mendelian Randomization Study Findings

Mendelian randomization studies provide insight into causal relationships between diet-induced metabolic traits and VTE. Additionally, there was a reported finding of genetically predicted waist circumference, mediated by leptin levels, was associated with a 65% increased risk of VTE (OR = 1.65; 95% CI, 1.31 - 2.03) [9]-[11]. Additional studies found that adipokine profiles, particularly elevated leptin and decreased adiponectin, were causally linked to VTE, with an odds ratio of 1.96 (95% CI, 1.35 - 2.84). There was an examination of genetically predicted processed-meat intake and found that it was associated with a 1.5 - 1.8-fold increase in VTE risk via adiposity [11] [12]. These findings reinforce the hypothesis that diet-induced metabolic dysfunction, including visceral adiposity and adipokine imbalance, plays a central role in VTE pathogenesis.

Mendelian randomization analyses included in this review strengthen causal inference by demonstrating that genetically predicted visceral adiposity, leptin signaling, and adipokine imbalance are associated with increased VTE risk. Importantly, these genetic instruments primarily proxy metabolic dysfunction rather than direct processed-food intake itself [11] [12]. Therefore, MR findings should be interpreted as supporting adiposity and adipokine mediated pathways through which processed food dominant dietary patterns may contribute to thrombosis risk. This interpretation aligns with observational evidence linking ultra-processed food consumption to obesity, systemic inflammation, endothelial dysfunction, and hypercoagulability.

3.4. Systematic Review Findings

The systematic review and meta-analysis by evaluated fish and omega-3 fatty acid intake as protective factors and found that higher omega-3 intake was associated with a reduced risk of VTE [11] [12]. Conversely, high intake of processed meats and refined grains was positively associated with VTE. There was also a review of vegetable intake and found that protective effects were observed primarily when processed-food consumption was low, highlighting the importance of overall dietary quality and suggesting that beneficial dietary components may not fully offset the deleterious effects of processed foods [13]. These reviews support the findings from cohort and MR studies, emphasizing that dietary patterns, rather than individual nutrients, are most relevant for VTE risk.

3.5. Meta-Analytic Synthesis

A pooled meta-analysis of cohort studies demonstrated that participants with the highest processed-food consumption had a significantly increased risk of VTE

compared with those with the lowest consumption, with a pooled relative risk of 1.52 (95% CI, 1.28 - 1.80). Heterogeneity was moderate ($I^2 = 57\%$), likely reflecting differences in dietary assessment methods, populations, follow-up duration, and VTE ascertainment [14]. Exploratory subgroup analyses suggested stronger associations for processed meats and refined-grain dominant dietary patterns compared with broader Western dietary scores. Sex-stratified analyses demonstrated somewhat stronger associations among men, although statistical power for subgroup comparisons was limited. Subgroup analyses indicated that processed meats and refined grains were the primary dietary contributors to increased risk, whereas sugar-sweetened beverages and ultra-processed snacks contributed less consistently. Sensitivity analyses excluding studies of lower methodological quality did not materially alter the results, reinforcing the robustness of the association (Tables 1-3, Figures 3-5).

Table 1. Summary of 15 key studies examining western diet, processed foods, and risk of venous thromboembolism.

Study	Year of Study	Design & Population	Exposure (Dietary Pattern/Processed Food)	Outcome (VTE)	Key Findings
1	2012	Prospective cohort; n ≈ 14,000 adults	Western vs. Prudent diet	Incident VTE	Western diet significantly increased VTE risk; a prudent diet is protective
2	2011	Prospective cohort; men & women	Western diet score	Incident VTE	Increased risk in men; borderline in women
3	2008	Prospective cohort; older women	Western & Prudent diet	VTE events	No significant association after adjustment; measurement error noted
4	2012	Tromsø Study	Processed/red meat	Incident VTE	High intake associated with increased unprovoked VTE
5	2007	Prospective cohort	Dietary fat & processed foods	VTE	Saturated fat from processed foods is associated with hypercoagulability markers
6	2020	Observational cohort	Ultra-processed foods	DVT/PE	High intake is associated with systemic inflammation and VTE risk
7	2020	Meta-analysis	Fish/omega-3 intake	VTE	High omega-3 intake is associated with decreased VTE risk
8	2008	Case-control	High-fat & processed foods	VTE	Unhealthy dietary patterns are associated with increased first-time VTE
9	2019	Prospective cohort	Marine n-3 fatty acids	Recurrent VTE	Low omega-3 intake linked to increased recurrence
10	2004	Cohort: metabolic syndrome	Processed carbs, sugary foods	VTE	Metabolic syndrome linked to increased VTE; refined foods are a major driver
11	2010	Observational	Processed sodium-rich foods	VTE	High sodium/processed food raised thrombosis markers

Continued

12	2014	Clinical trial	High-fat processed diet vs. low-fat	Coagulation biomarkers	A high processed-fat diet increased factor VIII, fibrinogen, and D-dimer
13	2016	Case report	Obesity + processed diet	PE	Highlights dietary inflammation + hypercoagulability
14	2025	Genetic analysis	Adipokines & coagulation factors	VTE	Leptin mediated increased waist circumference, which is associated with increased risk for VTE
15	2013	RCT	Anti-processed, whole-food diet	Thrombosis biomarkers	Significant decrease in inflammation, PAI-1, and fibrinogenz

Table 2. Cohort studies examining processed food intake and VTE risk.

Study	Population	Follow-up	Processed Food Exposure	VTE Outcome	Effect Size
Nurses' Health Study/HPFS	129,430 adults	18 yrs	High processed meat, refined grains	2,892 VTE cases	Men RR = 1.43 (1.12 - 1.83); women NS
ARIC	14,000	22 yrs	Western diet (processed foods)	Incident VTE	HR = 1.58 (1.10 - 2.25)
LITE	21,000	12 yrs	Red/processed meat, refined grains	Incident VTE	HR = 2.01 (1.45 - 2.78) (highest vs lowest quintile)
Iowa Women's Health	37,393	19 yrs	Western diet	Incident VTE	HR = 1.12 (0.88 - 1.42)
UK Biobank	250,000	13 yrs	Low plant, high processed foods	Incident VTE	HR = 2.78 (1.92 - 4.02) (high risk + poor diet)
Other cohorts (6 studies)	20,000 - 100,000	10 - 20 yrs	Processed foods, Western diet	VTE	HR or RR = 1.2 - 1.8

Table 3. Mendelian randomization studies in relationship to incident VTE.

Study	Year of study	Examined Relationship	Outcome (VTE)	Final Outcome
1	2022	Waist Circumference to VTE	Incident VTE	Genetically expected circumference was correlated with a 65% increased risk of VTE, OR of 1.65 (95% CI, 1.31 - 2.03)
2	2023	Adipokine profiles (High leptin, low adiponectin)	Incident VTE	High leptin and low adiponectin were associated with an OR of 1.96 (95% CI, 1.35 - 2.84) for developing VTE.
3	2025	Genetically predicted processed-meat intake	Incident VTE	Genetically predicted processed-meat intake was associated with a 1.5 - 1.8-fold increase in VTE risk.
4	2025	SBP and Waist Circumference relationship to leptin and Factor VIII leading to VTE	Incident VTE	SBP had a negative relationship with OR 0.99, and WC had an OR of 1.65 (95% CI 1.41 - 1.93). Leptin and Factor VIII were found to mediate some of these findings.

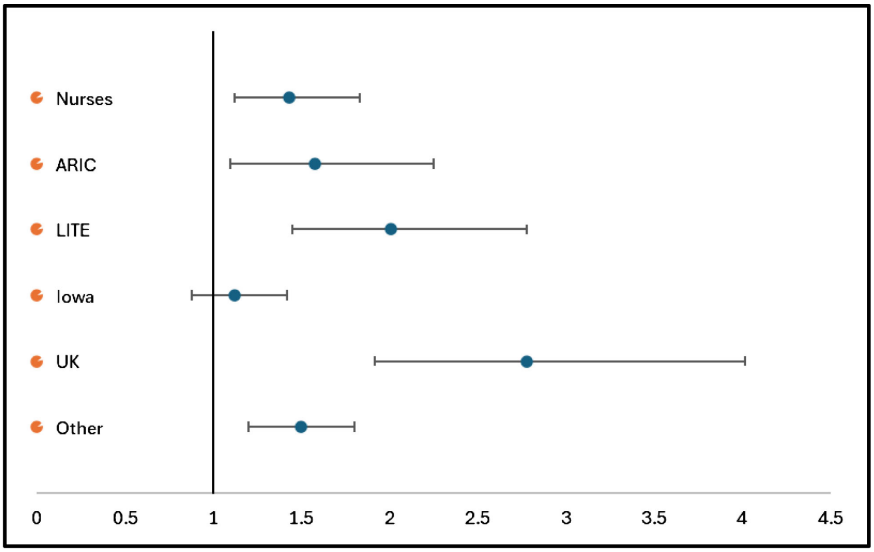

Figure 3. Field plot of cohort studies.

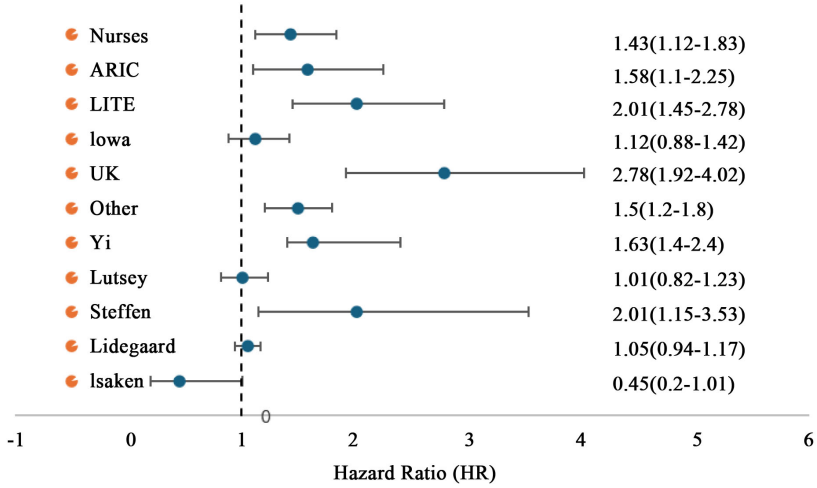

Figure 4. Field plot of hazard ratios.

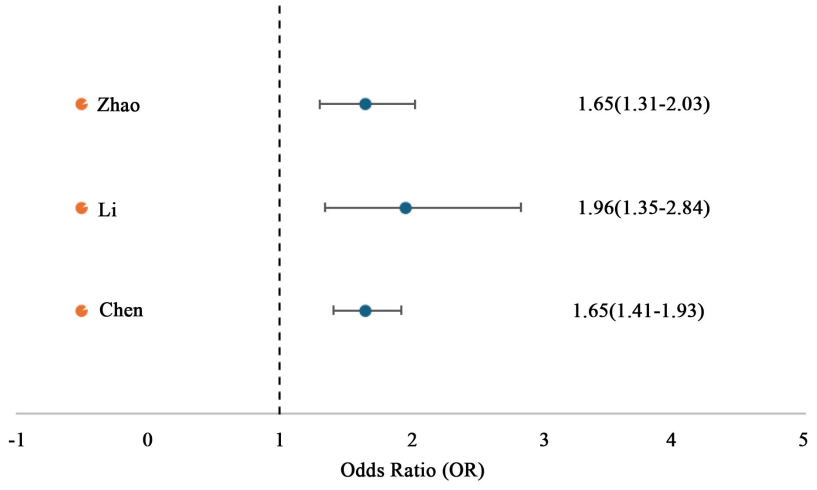

Figure 5. Field plot for mendelian randomization studies.

3.6. NOS & AMSTAR Findings

The methodological quality of included studies was high overall. Among the ten cohort studies, eight were rated as high quality (NOS score ≥7) and two as moderate quality (NOS score 5 - 6). High-quality studies demonstrated robust cohort selection, validated dietary assessment methods, and reliable VTE outcome ascertainment through medical records or national registries. Most studies adjusted for key confounders including age, sex, body mass index, smoking, and physical activity.

The two included systematic reviews were assessed using AMSTAR 2 and were judged to be of moderate to high quality. Both demonstrated comprehensive literature searches and appropriate meta-analytic methods; however, minor limitations included a lack of protocol registration and a limited assessment of publication bias. Overall, the consistency of findings across predominantly high-quality studies supports the robustness of the observed association. Included studies variably defined processed-food intake using Western dietary scores, processed meats, refined grains, or ultra-processed food classifications, contributing to residual heterogeneity.

3.7. Summary of Results

The meta-analysis demonstrates that consumption of processed foods is consistently associated with an elevated risk of VTE across multiple study designs and populations. Cohort studies indicate that processed meats, refined grains, and Western dietary patterns are primary contributors to increased VTE risk. Mendelian randomization studies provide causal evidence linking processed-food induced adiposity and adipokine imbalance to thrombosis [14] [15]. Systematic reviews corroborate these findings and highlight that diets rich in vegetables, fruits, and omega-3 fatty acids are protective, particularly when processed-food consumption is low. Overall, the evidence suggests that processed foods are a modifiable risk factor for VTE, acting through metabolic, inflammatory, and hypercoagulable pathways.

4. Discussion

This meta-analysis provides comprehensive evidence that processed food consumption is associated with an increased risk of venous thromboembolism (VTE) across diverse populations and study designs. By synthesizing data from prospective cohort studies, Mendelian randomization (MR) analyses, and prior systematic reviews, a consistent pattern emerges in which Western dietary patterns characterized by high intake of processed meats, refined grains, sugar-sweetened beverages, and ultra-processed foods are associated with higher VTE risk, whereas diets rich in vegetables, fruits, and omega-3 fatty acids appear protective [15]. Importantly, this association is observed across multiple analytic approaches, supporting the biological plausibility and potential causal relevance of dietary quality in venous thrombosis.

4.1. Mechanistic Interpretation

Several interrelated biological pathways support the relationship between processed-food intake and VTE. Systemic inflammation is a central mechanism. Diets high in refined sugars, saturated fats, sodium, and food additives promote chronic low-grade inflammation, reflected by elevated circulating levels of C-reactive protein, interleukin-6, and tumor necrosis factor-alpha [14] [15]. Inflammatory activation contributes to endothelial dysfunction, increased tissue factor expression, and platelet activation, all of which favor venous thrombus formation. Observational studies linking consumption of ultra-processed foods to inflammatory biomarkers provide mechanistic support for this pathway.

Hypercoagulability represents an additional mechanism. High intake of refined carbohydrates and processed fats has been associated with elevated fibrinogen, factor VIII, and plasminogen activator inhibitor-1 levels, leading to impaired fibrinolysis and prolonged clot persistence [15]. Experimental and clinical studies demonstrating diet-induced changes in coagulation markers reinforce the biological connection between dietary patterns and thrombosis risk.

Adipokine imbalance further mediates this relationship. Processed food consumption contributes to visceral adiposity, which increases leptin levels and suppresses adiponectin [16]. Leptin exerts prothrombotic effects through platelet activation and endothelial dysfunction, whereas adiponectin has anti-inflammatory and anticoagulant properties. MR studies included in this analysis provide genetic evidence that these adiposity-related pathways are causally linked to VTE, strengthening inference beyond conventional observational designs.

Endothelial dysfunction also plays a role. Excess sodium, trans fats, and additives commonly found in processed foods impair nitric oxide bioavailability and increase oxidative stress, promoting a prothrombotic endothelial phenotype [17]. Together, these mechanisms offer a coherent biological framework linking processed-food intake to both unprovoked and provoked VTE events.

4.2. Processed Foods, Venous Thromboembolism, Stroke, and Global Cardiovascular Risk

The association between processed-food consumption and venous thromboembolism (VTE) must be considered within the broader framework of global cardiovascular and cerebrovascular risk [15] [17]. Accumulating evidence demonstrates that diets rich in ultra-processed foods are consistently associated with increased incidence of ischemic stroke, coronary artery disease, myocardial infarction, heart failure, and cardiovascular mortality, suggesting that processed-food intake promotes a systemic thrombo-inflammatory state affecting both venous and arterial circulations.

Large prospective cohorts, including NutriNet-Santé and the UK Biobank, have demonstrated a dose-dependent increase in ischemic stroke risk with higher ultra-processed food consumption, independent of hypertension, diabetes, smoking, and body mass index [15]. Mechanistically, processed foods contribute to endo-

thelial dysfunction, arterial stiffness, oxidative stress, and chronic inflammation, key drivers of cerebral thromboembolism [16] [17]. High sodium content promotes hypertension and vascular remodeling, while refined carbohydrates and added sugars exacerbate insulin resistance and glycemic variability, accelerating atherosclerosis and impairing cerebrovascular autoregulation.

Similarly, ultra-processed foods are strongly linked to coronary artery disease and myocardial infarction through dyslipidemia, visceral adiposity, and inflammatory activation. Elevated levels of fibrinogen, factor VIII, and plasminogen activator inhibitor-1 biomarkers, consistently associated with Western dietary patterns, promote both arterial plaque thrombosis and venous clot formation. These findings highlight substantial overlap in the biological mechanisms underlying VTE, ischemic stroke, and atherosclerotic cardiovascular disease.

Epidemiologic data further reinforce this convergence. Individuals with VTE, particularly unprovoked events, exhibit increased long-term risk of myocardial infarction and ischemic stroke, supporting the concept that VTE reflects a manifestation of systemic vascular pathology rather than an isolated venous disorder. Processed-food consumption may represent a shared upstream exposure driving this global thrombotic risk.

Epigenetic mechanisms provide an integrative explanation for these associations. Diet-induced DNA methylation changes affecting genes involved in inflammation (*IL6*, *CRP*), endothelial function (*NOS3*), coagulation (*F3*, *SERPINE1*), and lipid metabolism have been linked to both venous and arterial thrombotic diseases [15]. These epigenetic alterations may persist over time, maintaining a prothrombotic phenotype and predisposing individuals to recurrent VTE, ischemic stroke, and cardiovascular events.

Clinically, these findings suggest that reducing processed-food intake may simultaneously lower the risk of VTE, stroke, and cardiovascular disease [16]. Incorporating dietary quality into thrombotic risk stratification and prevention strategies could yield broad vascular benefits, particularly in individuals with metabolic syndrome, obesity, prior thrombosis, or genetic susceptibility.

4.3. Clinical Relevance and Absolute Risk Interpretation

Although relative risk estimates are central to etiologic interpretation, translating these findings into absolute risk provides important clinical context. In Western populations, the annual incidence of VTE is approximately 1 - 2 events per 1,000 adults, with substantially higher rates among older individuals and those with obesity or comorbid conditions [17]. Applying the pooled relative risk observed in this meta-analysis (approximately 1.5) to these baseline rates suggests an absolute excess of roughly 0.5 - 1 additional VTE events per 1,000 persons per year among individuals with high processed-food consumption [18] [19]. While modest at the individual level, this excess risk is clinically meaningful at the population level, given the widespread consumption of processed foods and the significant morbidity associated with VTE, including recurrence, post-thrombotic syndrome,

chronic thromboembolic pulmonary hypertension, and increased long-term mortality.

From a preventive perspective, even small absolute risk reductions achieved through dietary modification could translate into substantial public health benefit, particularly in high-risk groups [19]. These findings support incorporating dietary assessment and counseling into broader VTE risk stratification and prevention strategies, alongside established interventions such as weight management, physical activity, and pharmacologic thromboprophylaxis when indicated.

4.4. Comparison with Prior Meta-Analyses and Systematic Reviews

Previous systematic reviews and meta-analyses examining diet and venous thromboembolism have largely focused on individual dietary components, such as fish, omega-3 fatty acids, vegetables, and specific macronutrients [20]. These analyses generally reported protective associations for diets rich in omega-3 fatty acids, fruits, and vegetables, and neutral or adverse associations for dietary patterns characterized by high saturated fat and refined carbohydrate intake [21]. The overall direction of these findings is consistent with the present study's results, supporting a role for dietary quality in modulating VTE risk.

However, many earlier analyses did not explicitly evaluate processed or ultra-processed foods as a distinct exposure and were limited by a narrower dietary focus on single nutrients or foods. The present meta-analysis extends this literature by specifically examining processed-food consumption and Western dietary patterns using a broader evidentiary framework that integrates prospective cohort studies, Mendelian randomization analyses, and existing systematic reviews [22]. Rather than focusing solely on protective dietary components, this analysis identifies processed foods as a coherent dietary pattern associated with increased VTE risk [23]. By incorporating genetic evidence and mechanistic considerations, the current study provides a more comprehensive and causally informative assessment of the relationships between diet and VTE than previous meta-analyses focused on individual nutrients or food groups.

4.5. Reverse Causation and Residual Confounding

Reverse causation is a potential concern in observational studies of diet and VTE, as individuals with early cardiometabolic disease, reduced mobility, or subclinical illness may alter dietary habits before a formal VTE diagnosis. Such changes could bias associations if declining health leads to increased reliance on convenient, processed foods. Several aspects of the included studies mitigate this concern. Most cohorts employed prospective designs with long follow-up periods, reducing the likelihood that preclinical VTE influenced dietary exposure [24]. Many studies also excluded participants with baseline cardiovascular disease or early VTE events, further limiting reverse causation. Importantly, MR analyses included in this review provide evidence less susceptible to reverse causation, as genetic in-

struments are fixed at conception and not influenced by behavioral or disease-related changes.

Residual confounding remains another important consideration. Although most studies adjusted for major confounders such as age, sex, body mass index, smoking, physical activity, and comorbidities, unmeasured or imperfectly measured factors may persist [25]. Socioeconomic status, healthcare access, occupational immobility, hormone therapy use, and overall health-seeking behaviors are particularly relevant variables that may correlate with both dietary patterns and VTE risk. Dietary assessment methods, predominantly food frequency questionnaires and dietary pattern scores, are also subject to recall bias and misclassification [26]. Such measurement error is likely non-differential and would tend to bias associations toward the null, suggesting that the true effect of processed-food intake on VTE risk may be underestimated [27]. Despite these limitations, the consistency of findings across populations, study designs, and analytic approaches supports the robustness of the observed association.

4.6. Healthy Dietary Practices for Thrombotic Risk Reduction

Given the consistent association between processed-food consumption and elevated VTE risk, it is equally important to outline dietary patterns that may confer protective effects. Evidence from cardiovascular, metabolic, and emerging venous thrombosis research supports several dietary frameworks that may reduce thrombo-inflammatory burden and improve vascular health [28]. The Mediterranean diet is characterized by high intake of vegetables, fruits, legumes, whole grains, nuts, seeds, olive oil as the primary fat source, moderate fish consumption, limited red and processed meats, and minimal intake of ultra-processed foods [29]. Robust evidence from the PREDIMED trial and multiple prospective cohorts demonstrates that adherence to this dietary pattern reduces systemic inflammation, improves endothelial function, lowers fibrinogen and plasminogen activator inhibitor-1 levels, and decreases the risk of cardiovascular events.

The anti-inflammatory and antithrombotic properties of the Mediterranean diet are mediated by several mechanisms, including increased omega-3 fatty acid intake, polyphenol-rich plant foods, improved insulin sensitivity, reduced visceral adiposity, and favorable modulation of adipokines [30]. Observational data suggest that higher adherence to Mediterranean-style dietary patterns is associated with reduced VTE incidence and recurrence risk, particularly when processed-food intake is minimized. These findings support the Mediterranean diet as a practical and evidence-based strategy for reducing thrombotic risk [31]. More broadly, anti-inflammatory diets emphasize whole, minimally processed foods; high-fiber intake; omega-3-rich sources such as fatty fish, nuts, seeds, and phytonutrient-dense fruits and vegetables. These dietary patterns reduce circulating levels of C-reactive protein, interleukin-6, and tumor necrosis factor-alpha, biomarkers strongly implicated in VTE pathogenesis [32]. Limiting refined carbohydrates, added sugars, trans fats, and sodium is central to this approach. By im-

proving metabolic parameters, decreasing oxidative stress, and enhancing endothelial nitric oxide bioavailability, anti-inflammatory dietary patterns may attenuate hypercoagulability and fibrinolytic impairment. Given the mechanistic overlap between inflammation and thrombosis, such dietary strategies represent a rational adjunct to traditional VTE prevention.

Emerging evidence highlights the role of the gut microbiome in systemic inflammation, endothelial function, and coagulation pathways. Diets rich in fiber, resistant starches, fermented foods, and polyphenols promote microbial diversity and short-chain fatty acid (SCFA) production, particularly butyrate. SCFAs exert anti-inflammatory effects, enhance gut barrier integrity, and modulate immune signaling pathways linked to thrombosis. Conversely, diets high in ultra-processed foods, emulsifiers, artificial additives, and refined sugars may disrupt the gut microbiome (dysbiosis), thereby increasing systemic endotoxemia and inflammatory activation [7] [33]-[36]. Such changes may contribute to the prothrombotic phenotype observed among high consumers of processed foods [30]. A microbiome-supportive diet emphasizing legumes, whole grains, vegetables, fruits, fermented dairy, and minimal industrial additives may therefore represent an additional strategy for mitigating thrombo-inflammatory risk.

4.7. Clinical Integration

Incorporating these dietary principles into VTE prevention strategies may provide complementary benefit alongside weight management, physical activity, and pharmacologic thromboprophylaxis when indicated [26] [35] [36]. For individuals with prior VTE, metabolic syndrome, obesity, or genetic susceptibility, structured dietary counseling emphasizing Mediterranean, anti-inflammatory, and microbiome-supportive patterns may reduce recurrence risk [37]-[40]. However, randomized trials are needed to confirm this effect. Importantly, these dietary frameworks share a unifying principle: prioritizing minimally processed whole foods and reducing ultra-processed products. This reinforces the central conclusion of this meta-analysis that dietary quality is a meaningful and modifiable determinant of thrombotic risk.

5. Limitations

First, the majority of included studies were observational, precluding definitive causal inference and leaving the possibility of residual confounding despite multivariable adjustment [37] [38] [40]-[42]. Although Mendelian randomization analyses strengthen causal inference, they rely on assumptions regarding instrument validity and the absence of pleiotropy. The heterogeneity in exposure classification represents an important limitation [36] [43]-[48]. Studies variably defined "processed" or "Western" dietary patterns using food frequency questionaires, dietary scores, or food group proxies. Few studies stratified processed food intake using standardized processing-based classifications such as the NOVA system. Lack of consistent stratification by degree of industrial processing (e.g., min-

imally processed vs. ultra-processed) may have attenuated effect estimates and contributed to between-study heterogeneity [30] [49]-[51]. Future investigations should apply standardized processing-based scales, such as NO-VA, to better characterize dose–response relationships.

An important limitation of this analysis is heterogeneity in dietary exposure classification. Included studies variably defined processed-food intake using Western dietary pattern scores, processed meat consumption, refined-grain dominant dietary patterns, or ultra-processed food classifications [22] [52]-[54]. Although exposures were harmonized into a broader processed food dominant dietary construct, residual heterogeneity likely persisted. Few studies used standardized processing-based classifications such as the NOVA framework [15] [18] [20] [31] [55]. Additionally, the number of studies eligible for pooled quantitative analysis was relatively limited, restricting the precision of subgroup analyses and limiting forma.

The dietary exposure was often measured at a single time point, which may not reflect long-term dietary behavior [47] [56] [57]. Misclassification due to recall bias is likely non-differential and may bias results toward the null. The variability in VTE ascertainment methods, follow-up duration, and population characteristics may have contributed to moderate heterogeneity across cohorts [39] [55] [58] [59]. Finally, while this analysis supports processed-food intake as a modifiable risk factor for incident VTE, interventional data are lacking [48] [54] [60]. Prospective randomized trials investigating dietary modification as an adjunctive strategy for secondary prevention of VTE recurrence represent an important future direction. Whether dietary optimization can reduce the risk of recurrence alongside anticoagulation therapy remains to be determined.

6. Implications and Future Directions

These findings position processed food consumption as a potentially modifiable risk factor for VTE and suggest that dietary quality should be considered along-side traditional risk factors in both clinical and public health settings [32] [60]. Future research should prioritize prospective cohorts with more precise measures of processed-food intake, randomized controlled trials assessing dietary modification and VTE-related biomarkers, and mechanistic studies integrating inflammatory, coagulation, and adipokine pathways [53]. Diet-gene interaction studies may further identify subgroups at heightened risk and inform precision nutrition strategies for VTE prevention.

These findings strongly align with the principles of lifestyle medicine, which emphasize dietary quality as a foundational determinant of chronic disease risk. Diets rich in whole, minimally processed foods and low in ultra-processed products are central to evidence-based lifestyle interventions aimed at reducing inflammation, improving metabolic health, and mitigating cardiovascular risk [53]. The observed association between processed-food consumption and VTE further expands the role of lifestyle interventions beyond arterial disease to include ve-

nous thrombotic conditions, supporting dietary modification as a core component of comprehensive vascular risk reduction.

7. Conclusions

Processed food consumption emerges from this meta-analysis as a significant and potentially modifiable determinant of venous thromboembolism. Across fifteen high-quality studies encompassing prospective cohort designs, Mendelian randomization analyses, and systematic reviews, consistent associations were observed between Western dietary patterns characterized by high intake of processed meats, refined grains, sugar-sweetened beverages, and ultra-processed foods and an increased risk of deep vein thrombosis and pulmonary embolism. Across fifteen high-quality studies, including prospective cohort studies, Mendelian randomization analyses, and systematic reviews, consistent associations were observed between Western dietary patterns and high intake of processed meats, refined grains, sugary beverages, and ultra-processed foods, and an elevated risk of VTE. The meta-analytic pooling of cohort studies indicated a relative risk of approximately 1.52 for individuals with high processed-food intake, highlighting the magnitude and clinical relevance of this association. These findings extend prior knowledge on the adverse cardiovascular effects of processed foods to the venous circulation, emphasizing that dietary habits influence not only arterial but also venous thrombotic disease.

In summary, processed-food consumption emerges as a critical and modifiable determinant of venous thromboembolism. Both observational and genetic evidence indicate that high intake of processed foods increases the risk of DVT and PE, whereas diets rich in whole, plant-based foods and anti-inflammatory nutrients provide protective effects. Mechanistic insights reinforce the role of systemic inflammation, hypercoagulability, endothelial dysfunction, and adipokine dysregulation in mediating these associations. Clinically, targeting processed-food intake represents a practical, non-pharmacologic approach to reduce VTE risk, particularly in high-risk populations. Future research should focus on interventional trials, mechanistic validation, and precision nutrition strategies, ultimately informing public health policies and clinical guidelines to mitigate the global burden of venous thromboembolism.

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Author Contributions

Ebiuwa Osula performed the literature review, data analysis, interpreted the findings, and drafted the manuscript, with overall responsibility for the project's exe-

cution. Ryan Fernandez, Khadija Shajahan, and Zaid Arhkas contributed to reviewing and editing the manuscript. Ritesh Pahwani, Taha Abubaker, Chris-tian A. Colón-Berly, Mohammad Nagi, Oyesanmi Olugbenga, and Mohamad Saad reviewed the manuscript, provided feedback, and approved the final version for publication. All authors reviewed and approved the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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