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Myocardical Infarction in Young Adults: Revisiting Risk Factors and Atherothrombotic Pathways

Petre Alexandru Cojocaru [1], Maria Loredana Țieranu [2], Mina Teodora Luminița Pioriescu [3,4], Ionuț Cezar Buciu [5], Alexandru Mugurel Belu [5], Silvana Isabella Cureraru [5,*], Eugen Nicolae Țieranu [1,5,*], Gianina Cristiana Moise [5,†] and Octavian Istratoaie [1,5,†]

[1] Department of Cardiology, University of Medicine and Pharmacy of Craiova, Craiova, Romania
[2] Department of Obstetrics and Gynaecology, Emergency County Hospital, Craiova, Romania
[3] Department of Physiology, University of Medicine and Pharmacy of Craiova, Craiova, Romania
[4] Department of Dermatology, Emergency County Hospital, Craiova, Romania
[5] Department of Cardiology, Emergency County Hospital, Craiova, Romania
* Correspondence: isabellacureraru@yahoo.ro (S.I.C.); tieranueugen@gmail.com (E.N.Ț.); Tel.: +40761827007 (S.I.C.), Tel: +40766454141 (E.N.Ț.)
† Authors with equal contribution.

Abstract

Background: Myocardial infarction (MI) in young adults, once a rarity, is increasingly recognized as a distinct clinical entity. Unlike traditional MI patients, younger individuals often present without established risk factors or advanced atherosclerosis, prompting a reevaluation of pathophysiologic paradigms and risk assessment strategies. Objective: This review aims to synthesize recent evidence on the epidemiology, traditional and emerging risk factors, pathophysiological mechanisms, and diagnostic challenges of MI in individuals under 55, with emphasis on the unique features of this population. Methods: A narrative literature review was conducted, focusing on studies from the last five years addressing MI in young adults, including data from large registries, cohort studies, and recent experimental findings.

Keywords: young adult; myocardial infarction; risk factors

1. Introduction

Traditionally considered a condition of middle-aged and older adults, MI is increasingly affecting younger individuals—often in the absence of conventional risk factors such as long-standing hypertension, diabetes, or established atherosclerosis. This emerging trend raises important questions about the adequacy of existing cardiovascular risk models and suggests the presence of alternative, underrecognized contributors to early-onset atherothrombotic disease.

In recent years, attention has turned to a range of novel risk factors that may play a disproportionately large role in the pathogenesis of MI in young adults. These include genetic variants (e.g., elevated lipoprotein(a)), inflammatory and autoimmune processes, thrombophilic states, the use of recreational substances (notably cocaine and cannabis), and persistent psychosocial stress. Lifestyle patterns unique to younger populations—such as sleep deprivation, disordered eating, and digital-era stress—also appear to exert independent cardiovascular effects.

Moreover, sex-specific aspects, especially the increasing recognition of MI in young women—often presenting without obstructive coronary disease—further complicate the clinical picture and highlight the limitations of traditional diagnostic and preventive strategies.

Given the potentially devastating socioeconomic consequences of MI of young people there is a pressing need to better characterize the spectrum of risk factors in this population. Such understanting will inform targeted prevention and long term strategy for this.

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This review explores the evolving landscape of MI in young adults, focusing on the expanding spectrum of risk factors and pathophysiological mechanisms. By reevaluating current paradigms and integrating emerging evidence, we aim to better understand, identify, and ultimately prevent premature cardiovascular events in this unique population.

2. Epidemiology of Premature Myocardic Infarctions

In recent years, the clinical landscape of MI has undergone a noteworthy demographic shift. Once considered predominantly a disease of older adults, MI is now increasingly observed in younger individuals — often in their 30s or 40s — who may lack long-standing chronic conditions traditionally associated with coronary artery disease. This evolving epidemiological profile has drawn growing attention in cardiovascular research and practice [1].

Current estimates suggest that approximately one in ten patients hospitalized for acute MI is under the age of 55. While men continue to represent the majority of these cases, recent data highlight a worrying trend: the incidence among young women appears to be rising or, at the very least, not declining at the same rate. Compounding this, women are more likely to present with atypical symptoms, experience delays in diagnosis, and suffer worse in-hospital outcomes [2].

Geographical and socioeconomic differences play a significant role in the distribution of premature MI. In some high-income countries, incidence rates have plateaued or slightly decreased, largely due to better primary prevention. However, in many low- and middle-income regions, the number of young adults affected by MI remains substantial and, in some cases, continues to grow — reflecting disparities in healthcare access, education, and exposure to modifiable risk factor [3].

Although traditional cardiovascular risk factors such as tobacco use, hypertension, hypercholesterolemia, and diabetes are still prevalent among young MI patients, they often coexist with newer, underrecognized contributors. Emerging evidence implicates psychosocial stress, recreational drug use, sedentary behavior linked to modern work environments, and proinflammatory conditions in the early development of atherothrombotic events. In addition, genetic susceptibilities — such as elevated levels of lipoprotein(a) or familial hypercholesterolemia — may play a disproportionately large role in this group, especially in the absence of overt lifestyle-related risk [4].

The rising incidence of MI in younger populations, combined with their unique clinical characteristics and risk profiles, underscores the limitations of current cardiovascular risk assessment tools, which were largely developed based on older cohorts. Addressing this growing challenge requires not only earlier identification of at-risk individuals but also a broader understanding of the multifactorial nature of premature coronary disease — one that integrates biological, behavioral, environmental, and social dimensions. [5]

3. Global Incidence and Prevalence

Determining the actual prevalence of coronary artery disease (CAD) in young adults remains a significant challenge, mainly because the clinical characteristics of both atherosclerotic and non-atherosclerotic forms are still not clearly delineated. This is particularly evident in cases of myocardial infarction with non-obstructive coronary arteries (MINOCA), where the absence of standardized diagnostic protocols and limited use of intracoronary imaging often results in misdiagnosed or overlooked non-plaque mechanisms [6].

Available epidemiological data on MI in younger individuals are sparse. Findings from the Framingham Heart Study illustrate a steep age-related increase in MI incidence among men—from 12.9 per 1,000 in those aged 30–34 to 71.2 per 1,000 in the 45–54 group. Women show consistently lower rates across the same age brackets. Notably, over a quarter of the myocardial infarctions in this study were asymptomatic, with unrecognized events occurring more frequently in women.[7]

In South Asia, especially in India, early-onset CAD presents another layer of complexity [8]. Data from a cohort of 877 patients indicated that roughly a third were diagnosed before turning 45. In over

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90% of these cases, common lifestyle-related risk factors were present, including low fiber intake, smoking, hypertension, diabetes, dyslipidemia, alcohol use, sedentary habits, psychosocial stress, and central obesity. Notably, risk profiles differ by gender: young women with MI tend to have higher rates of comorbidities like hypertension, diabetes, depression, and heart failure, whereas men are more often affected by physical inactivity and elevated cholesterol levels. Evidence from the VIRGO and GENESIS-PRAXY studies also suggests that young women may experience MI via mechanisms that are less well understood, recover more slowly, and face a higher likelihood of complications, readmission, or even death compared to men their age [9,10].

Although the overall incidence of coronary heart disease (CHD) has declined in the UK, the trend does not necessarily reflect what is happening among younger adults. Data between 1992 and 2012 show very low CHD rates in the 35–44 age group—0.5% in men and 0.18% in women—but prevalence increases sharply in older age groups. Younger individuals may be underdiagnosed, likely due to less typical symptom presentation and a reduced tendency to seek medical evaluation. As a result, only 3% of all CHD diagnoses are made in people under 40, a figure that may underrepresent the true burden in this demographic [11,12].

Modifiable risk factors remain central to the rising trend in early-onset CAD. Smoking, in particular, is widespread among young adults, with rates climbing to nearly 10%. Young women in the UK have been reported to smoke more heavily and for longer durations, potentially diminishing the protective cardiovascular effects of estrogen [13]. In parallel, obesity has surged among children and young adults, with rates tripling in the last two decades. Cocaine use, another major concern, is a recognized precipitant of chest pain and myocardial infarction in younger people and continues to be frequently implicated. Taken together, these patterns suggest that while CAD might appear to be declining in the general population, a significant and growing risk is emerging among younger individuals—one that deserves much closer attention. [14,15]

4. Traditional VS Non Traditional Risk Factors

Young patients who experience myocardial infarction share with older individuals the classic cardiovascular risk factors, such as smoking, obesity, hypertension, diabetes mellitus, and dyslipidemia. However, a significant proportion of these younger patients differ from their older counterparts in terms of emerging risk factors. Young patients are frequently users of recreational drugs, and may present with various autoimmune diseases, familial hypercholesterolemia, elevated lipoprotein levels, as well as psychosocial factors such as stress, depression, and burnout, all of which play an increasingly recognized role in the pathogenesis of myocardial infarction in this age group.[14,15]

4.1. Conventional Cardiovascular Risk Factors Associated with Young AMI:

4.1.1. Dyslipidemia

Dyslipidemia is an important risk factor in young people who suffers AMI, with over 80% having at least one anormal lipid along other risk factors [5]. Some studies data reveal that lipid profiles have improved in some European young adult population, but AMI in this patients continues to rise [4].

In a cohort of adults under 40 age who suffers an AMI, 40 percent of them have abnormal levels of lipid, most commonly hypertriglyceridemia, high LDL-c and low HDL-C [16].

A Korean study found that statin use implicated a higher AMI risk than non-using. Non statin users how have LDL-C >120mg/dL faced a 33% higher AMI risk vs those with <80mg/dL, and the statin users with LDL-C <80mg/dL had a 66% higher risk then non user with similar LDL-C value. Also, the HDL-C remains a consistent risk marker in younger adults.[16–19].

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4.1.2. Hypertension

Hypertension contributes significantly to the development of atherosclerosis in the young. While often asymptomatic, elevated blood pressure is frequently underdiagnosed and untreated in this age group, exacerbating cardiovascular risk.[20]. Results shows that young people received a diagnosis slower compared to older patients.

Delayed diagnosis allows vascular damage to progress silently, amplifying long term cardiovascular risk [21].

Global, the prevalence of undiagnosed hypertension is high. A Indonesia study reveal that 55% of men and 44% of women age 26-35 age were undiagnosed [22].

4.1.3. Smoking

Cigarette using promote endothelial inflammation and dysfunctions followed by thrombosis and lipid oxygenation, accelerating atherosclerosis without an important plaque burden.

Smoking remand one of the most common risk factor for AMI among all people. In a recent study, 52.5% from individual were smokers and in a Danish register data of patients, age 30-49, 74% were current smokers comparing with the rest of traditional risk factors (10% hyperlipemia, 15% hypertension, 7% diabetes). Recent studies reveals that a 9 fold in man to 13 fold in women increased AMI risk [14].

Multiple studies confirm that active smoking is an important cardiovascular risk factor for younger women than man. In an UK cohort study revealed that women had an 13 higher risk of AMI comparing to 8,5% in man [23].

The smoking cessation also have an important role, young people who quits smoking with one year post AMI had 70% lower all causes of mortality and 80% lower cardiovascular mortality over 11 year. [14,24]

4.1.4. Obesity

Recent studies shown a strong association between obesity and AMI in young people. Data from numerous studies with AMI reveal that obesity is present in 78% of the patients who suffers an AMI at a young age. In young women, a BMI >30 increased the risk of AMI nearly by 4,7 fold (HR 4,71, 95% CI: 3,88-5,72) and also associated with higher cardiovascular mortality.[25,26]

4.1.5. Diabetes Mellitus

Diabetes mellitus is an important modify risk in young people who suffer AMI. A study from 2024 reveals that glycemic variability in patients with AMI is correlated with worse outcomes and higher rate of in-hospital mortality. The mortality of patients who suffers from diabetes mellitus with high glycemic values is increased with 1,25—3,40 [27]. Glycemic fluctuations were associated with higher in-hospital mortality, most notably among AMI patients whose admission blood glucose was within the normal range.

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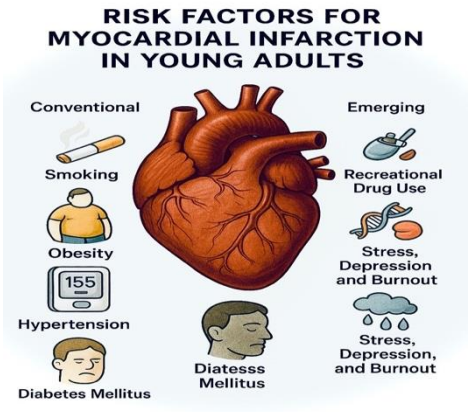

Figure 1. Traditional and novel cardiovascular risk factor in young**.**

4.2. Novel Cardiovascular Risk Factors in Young

4.2.1. Recreational Drug Use

In the last years, the recreational drug use is recognized as an independent factor for AMI among young people, especially cannabis and cocaine use [28].

Cocaine stimulates alpha-1 and beta-1 adrenergic receptors, increasing heart rate and systemic blood pressure, which in turn elevates myocardial oxygen demand. It can also induce coronary vasospasm, hours after use, particularly in epicardial vessels, reducing myocardial oxygen supply. Furthermore, it activates platelets and plasminogen, contributing to thrombus formation [29–31]. Chronic use and the acute use have a different impact on cardiovascular system, unlike its chronic consequences, the acute cardiovascular impact of cocaine has been extensively documented. As a powerful stimulant, cocaine use has been linked to electrocardiographic changes, heightened blood pressure, arrhythmias, and AMI. The likelihood of MI in cocaine users is shaped by both underling cardiac risk factors and high-risk behaviors. Mechanistically, cocaine can provoke acute events through multiple pathways, including inhibition of cardiac sodium and potassium channels and promotion of coronary artery spasm or vasoconstriction. By contrast, the long-term cardiovascular effects of cocaine remain less clearly defined, with previous studies reporting inconsistent results [29].

Cannabis increases heart rate and blood pressure and contributes to platelet aggregation, endothelial dysfunction, and coronary vasospasm.

In AMI registries, 10.7% of young patients reported cocaine and/or cannabis use. A French study found 12.6% of AMI patients tested positive for drug use, 34% of whom were under 50. [32,33]

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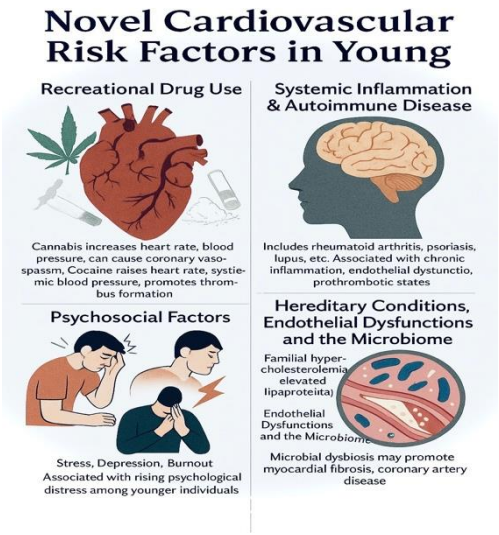

Figure 2. Novel cardiovascular risk in young.

4.2.2. Systemic Inflammation and Autoimmune Disease

Systemic inflammation and autoimmune disease make an important impact in the patient's life, and a more important impact in the life of a young patients who suffers AMI.

Young AMI registry data reveal that 2,5% of patients under age 50 had an autoimmune disease or systemic inflammation (SID), such as rheumatoid arthritis, psoriasis, systemic lupus erythematosus or multiple sclerosis. These patients where more often women and had hypertension comparing to others. Patients under age 50 with SID suffers 2 more higher all-cause mortality over 11 years [34].

Rheumatoid arthritis (RA) is a chronic autoimmune disease that increases cardiovascular (CV) mortality by up to 50%, with a risk of acute coronary syndromes comparable to type 2 diabetes [35]. Beyond traditional factors, persistent systemic inflammation drives endothelial dysfunction, accelerates atherosclerosis, and promotes unstable plaque formation. The distinct CV profile in RA includes myocardial infarction, sudden death, and silent ischemia [36]. The "lipid paradox" — low lipid levels despite high CV risk — further reflects the central role of inflammation, while targeted anti-inflammatory therapy can reduce this burden [37].

In systemic lupus erythematosus (SLE), young patients—particularly women under 45—carry a disproportionately high risk of myocardial infarction, with incidence rates up to ten times greater than in the general population [38]. This vulnerability is fueled not only by conventional risk factors such as hypertension and dyslipidemia, but also by disease-specific drivers: persistent systemic inflammation, immune-mediated vascular injury, high disease activity, long-term corticosteroid exposure, and antiphospholipid antibodies. These mechanisms accelerate atherosclerosis, destabilize plaques, and heighten thrombotic potential, enabling severe coronary events to occur even in the absence of traditional risk profiles. Prompt control of inflammation and proactive cardiovascular surveillance are therefore critical to reducing the burden of premature AMI in SLE [38].

In the last 5 years, multiple cohort studies and meta-analyses have confirmed that young adults with ankylosing spondylitis (AS) or axial spondylarthritis face a significantly higher risk of myocardial infarction—even after adjusting for traditional factors [39]. Persistent systemic inflammation (TNF-α, IL-17), endothelial dysfunction, arterial stiffness, and frequent NSAID use accelerate atherosclerosis, while metabolic syndrome and smoking amplify this risk. TNF inhibitors appear protective [40], with real-world data linking effective inflammation control to fewer acute coronary events. Early cardiovascular screening and aggressive disease management are essential to reduce premature MI in AS patients.

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Psoriasis is a systemic, immune-mediated disease that accelerates atherogenesis and raises ASCVD risk beyond traditional factors, with signal strongest in moderate–severe skin disease. Mechanistically, chronic IL-17/TNF-α–driven inflammation promotes endothelial dysfunction, arterial stiffness, and pro-thrombotic pathways—biologic plausibility that aligns with higher MI/ACS rates in observational cohorts and contemporary reviews [41]. Recent evidence links disease severity and duration to coronary microvascular dysfunction—an early substrate for type 1 MI—supporting the concept of "premature" coronary disease in younger patients with long-standing psoriasis [42]. Therapeutically, large real-world and meta-analytic data suggest patients treated with modern biologics (anti-TNF, anti-IL-17, anti-IL-23) experience lower incident cardiovascular events versus oral/non-biologic therapy, consistent with the inflammation-hypothesis; signals are not uniform across all agents (eg, anti-IL-12/23) [43].

Medium–large-vessel inflammation can directly involve coronaries—causing ostial stenoses, aneurysms, thrombosis, and rapid restenosis—on top of diffuse endothelial injury and pro-thrombotic signaling. The result is acute coronary events at ages where atherosclerosis alone would be unlikely. Takayasu arteritis (teens–young women): Contemporary reviews show frequent coronary involvement (esp. ostial/proximal lesions) with MI as a major cause of TAK-related death; multimodality imaging (CTCA/CMR) refines detection [44]. Kawasaki disease (KD) (childhood) → young-adult MI: Persistent or giant coronary aneurysms carry long-term atherosclerotic change and MI risk years after the acute illness [45]. ANCA-associated vasculitis (AAV): Recent cohort/meta-analytic data show substantially higher cardiovascular events, including MI; risk peaks in the months after diagnosis and remains elevated [46]. Polyarteritis nodosa (PAN): Medium-vessel necrotizing vasculitis with documented coronary arteritis/occlusions and MI—even in young patients—though uncommon overall [47].

Systemic inflammation can profoundly affect lipid metabolism, exemplified by the paradoxical LDL-C rise seen after inflammation control in rheumatoid arthritis. In the Young-MI registry, patients with SID had similar overall lipid profiles to those without SID but showed a tendency toward higher triglycerides ($P = 0.04$). Despite comparable renal function at presentation, SID patients had significantly lower peak troponin levels during the index MI ($P = 0.003$), suggesting possible differences in myocardial injury patterns [34,48].

Studies also reveal that autoimmune disease contributes to AMI risk with the endothelial disfunction made from the inflammation, the immune complex deposition and the prothrombotic states. [34,49]

Among inflammatory markers, high-sensitivity C-reactive protein (hsCRP) has uniquely transitioned into routine cardiovascular risk assessment, reflecting hepatic response to IL-6 stimulation. While CRP itself is not a causal driver of atherothrombosis, upstream mediators such as IL-1 and IL-6 actively promote plaque development and destabilization. Other candidates — myeloperoxidase (MPO), lipoprotein-associated phospholipase A_2 (Lp-PLA_2), and trimethylamine-N-oxide (TMAO) — highlight diverse inflammatory and metabolic pathways linking immune activation to vascular injury. MPO fosters oxidative modification of LDL and impairs HDL function, Lp-PLA_2 amplifies oxidative stress within plaques, and TMAO, generated from gut microbial metabolism of red meat and eggs, accelerates foam cell formation, platelet activation, and thrombosis. Despite strong mechanistic evidence, these markers remain largely research tools; their integration into everyday risk stratification for young AMI patients awaits effective targeted interventions and broader validation across populations [50,51].

Post-AMI autoimmune responses such as Dressler syndrome is an important factor to reveal the importance of autoimmune system responses against myocardial neo-antigens formed as a respond to AMI [52].

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4.2.3. Hereditary Conditions: Hypercholesterolemia and Lipoprotein(A)

The prevalence of genetic lipid disorders makes an important role and relation to an early AMI due to the importance of an early diagnosis to initiation the treatment and prevent the AMI.

Familial hypercholesterolemia has a high prevalence among young AMI cohort, 1-5% are heterozygous for familial hypercholesterolemia (comparing to 0,5% in the rest of population). This pathology increases the risk of AMI in young age with 15-20 more comparative with the patients who doesn't have familial hypercholesterolemia, and the patients who have it, have a 2.3 more risk of recurrence. A study with 690 patients reveal that patient with familial hypercholesterolemia have more likely a three vessel disease (p=0.007), and a higher thrombus burden and final TIMI slow/no-flow (p=0.027) comparing to the unlikely patient who suffer from the disease (p=0,006). [53–55]

Lipoprotein A (LpA) is a stronger independent risk factor in young people with AMI due to pro-atherogenic and pro-thrombotic properties, being the particle who carries cholesterol molecules. High levels of LpA are correlated to 2-3 much higher risk of AMI comparing to normal levels. Also, levels >50mg/dL affects 20-25% of global individuals, and a value more than 180 mg/dL place the patients at a very high risk of AMI. US multi-ethic cohort revels that high levels of lipoprotein(A) is linked to a very high risk of AMI. This lipoprotein may be in the future a screening test for preventing the AMI in patients of any age [56–58].

Other genetics lipid disorder implicated in AMI at young age are represented by ApoA5 polymorphism who is linked to higher values of triglycerides and like that, they increase the risk of AMI making also a predictor of yearly AMI. [56,58,59]

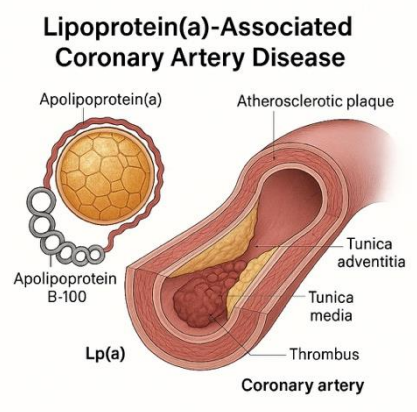

Figure 3. structure of Lipoprotein(a)**.**

4.2.4. Psychosocial Factors: Stress, Depressions, Burnout

Increased responsibilities, academic and career pressures, and social isolation contribute to rising psychological distress in younger populations

Meta-analyses found that depression has an 24% prevalence in patients who suffer an AMI, 12% have anxiety and 10% of them suffers from PTSD. Early psychological intervention has a very important role in prevention and recovery to those who suffers an AMI. [60,61].

4.2.5. Endothelial Dysfunctions and the Microbiome

The idea that microbiome is a important factor in development the cardiovascular disease increase in the last decade due to the influence of the metabolic system. Microbiome can use trimethylamine N-oxide, short chain fatty acids and bile acid pathways causing heart failure, atherosclerosis, hypertension, myocardial fibrosis and coronary artery disease [58,62].

Viral (e.g., cytomegalovirus, influenza A, hepatitis C) [63] and bacterial (e.g., Chlamydia pneumoniae, Helicobacter pylori) infections have been implicated in atherosclerosis via endothelial activation, cytokine upregulation, and heat shock protein expression [64,65]. While infection-driven

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inflammation is a plausible contributor, evidence from the Tsimane population — with high hsCRP prevalence but minimal coronary calcification — suggests that inflammation alone, in the absence of conventional risk factors, may be insufficient to promote coronary artery disease [66].

A 2025 study found AMI patients had blood samples enriched in Firmicutes, Bacteroidota, Actinobacteriota and Bacteroides, however, the clinical significance of those in AMI remained unclear and warrant for further investigation. [62]

Dysbiosis, including reduced microbial diversity and a shift toward Bacteroides-dominant profiles, may promote myocardial fibrosis and coronary artery disease. Further studies are needed to clarify the microbiota's role in AMI. [67]

HIV infections have an important role in AMI in young patients. Despite modern antiretroviral therapy, young people living with HIV face a 1.5–3× higher risk of myocardial infarction than HIV-negative peers, often occurring a decade earlier. The culprit is not simply atherosclerosis, but a triple hit [68]

1. Immune dysregulation – persistent monocyte/macrophage activation and cytokine release (IL-6, TNF-α) destabilize plaques even when viral load is undetectable [68,69].
2. Endothelial injury – HIV proteins and chronic inflammation drive microvascular dysfunction, creating fertile ground for both type 1 and type 2 MI [69].
3. Therapy-related effects – while integrase inhibitors are generally safer, certain regimens, especially recent abacavir exposure, have been linked to abrupt rises in MI risk [69].

5. Clinical Presentations and Diagnostic Challenges

Typical symptomatology of presentations are representation of chest pain with or without radiating in arms or jaw, diaphoresis, dyspnea and dizziness. The atypical symptoms are representation of digestive symptoms like epigastric pain, indigestion, nausea or vomiting; neurological symptoms like fatigue, neck or back pain, or even syncopal episode are more often present in young women (90% of women are having atypical symptoms) [70].

Some meta-analysis found that 11,6% of all gender patients who suffers AMI are presenting atypical symptoms and 33,6% are having no chest pain. Small studies reveal that 69% of young patients with AMI have no chest pain before the event [70].

These atypical symptoms of presentation lead to misdiagnosis of this patients, which can increase in-hospital mortality (19% in atypical symptoms vs 3% in typal symptoms) due to the time of interventions, and because of that, is very important to know the non-specific symptoms for making a more rapidly intervention [71].

The different batwing symptomatology is related to neural modulation and acute inflammation or ischemic changes cause by the epicardial coronary artery ischemic patterns [72].

Duet o the atypical symptoms on presentation, time to diagnosis is often delayed, and the time to PCI is more often longer.

A South Asian registry showed that young patients with AMI have 125 minutes longer waiting time of the medical service presentation comparing to elderly patients and a European study reveal that the uncertainty diagnosis in primary care lead to longer time of waiting in younger patients [73].

In Japanese studies reveal that this problems persist, and because of that, the patients fail to meet the guideline-recommended benchmarks for early intervention: <10 minutes door-to-ECG and <90 minutes door-to-PCI [74].

These delays in diagnosis and PCI increase the risk of major adverse cardiac events, and may lead to long-term reductions in quality of life [75–77].

The mortality rate in-hospital in young patients who suffer AMI is between 0,7% to 7%, typically lower than older people, but in short-term (30 days), young patients without standard risk factors has 30 more higher risk mortality. A cohort study found that the mortality rate is 120% higher in patients with STEMI comparing with N-STEMI where the risk is 12 more higher [5,78]

On long term mortality (one year), the patients <40 age have similar all-cause mortality comparing to those of 41-50 age [78]. The STEMI and N-STEMI mortality rate is different to the short

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term risk: the STEMI patients have 2 more higher risk of mortality comparing to the general population, and the NSTEMI have 2,5-2,8 much higher risk of mortality. [5,73–77,79–81]

6.1. Atherothrombotic Pathways

Classical mechanism: The classic mechanism of atherosclerosis in AMI involves:

1. The endothelial dysfunctions and the response to the injury [82]. The first factors who leads to this are represented by the high LDL, high systolic arterial blood pressure, smoking and the oxidative stress, this is leading to increase permeability of the endothelia from where the LDL particles enter in the intima of the artery, lead the process of oxidation and increase the inflammation. From that point, macrophage apoptosis contributes to increased inflammation and endothelial dysfunction.[83].
2. Plaque progression: Chronic inflammation sustained by cytokines representing by IL 6, IL 1, TNF alpha, hs-CRP,promotes the growth and destabilization of plaque. Autoimmune diseases may contribute to this inflammatory process and accelerate plaque development in young individuals [84,85].
3. Intimal remodelation: The vascular smooth muscle cells respond to inflammation by proliferating and producing extracellular matrix leading to fibrous cap formation and also by transforming into foam cells contributing to plaque bulk and potentially necrotic formation [86].
4. Calcification and plaque stability.: The instability plaque use to have microcalcifications comparing to stability plaque who have macrocalcification, and by that is more frequent the rupture of the unstable plaques and the promotion of a possible ischemic event [87].

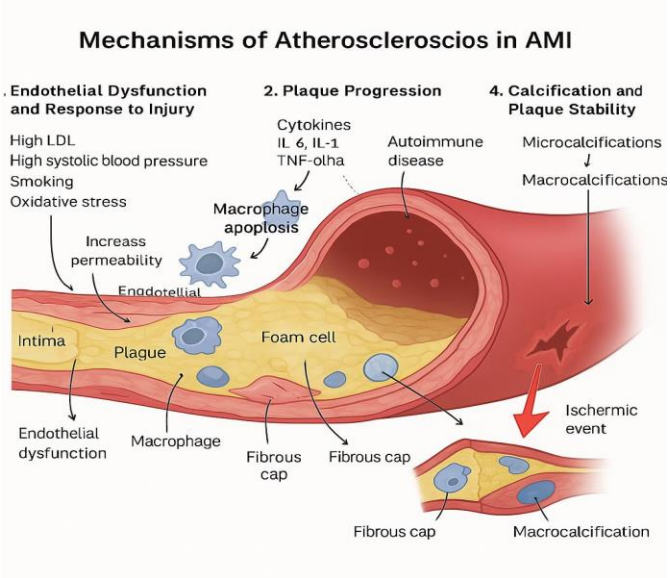

Figure 4. Mechanism of Atherosclerosis in AMI**.**

6.2. Non-Atherosclerotic Mechanism:

MINOCA is defined by AMI without >50% obstruction of the epicardial coronary artery and is a common cause of ischemic event, more often in young people, especially in young women. Is considerate a syndrome, not a single event because it includes: coronary plaque disruption and erosion, epicardial spasm, spontaneous coronary artery dissection(SCAD), microvascular dysfunction [88]. Long term studies in young patients reveal 12% mortality over 7 years follow and a <30% reduction of the ventricular ejection fraction in young people who suffer from MINOCA [89].

1. SCAD primarily affects young women, often without traditional risk factors (23-36% in women who suffer AMI). In SCAD the most come mechanism is represented by intimal tear who allowing the blood into the media and the rupture of the vasa vasorum causing intramural

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hematoma. This two events compressing the true lumen of the vessel and make a obstruction of the lumen. SCAD is associated with fibromuscular dysplasia (as pregnancy related vascular changes and connective tissues disorder, and emotional or physical stressors). The main treatment strategy is represented by conservative management (aspirin+beta-blockers), and the PCI strategy is reserved only for high risk patients [90–92].

2. Vasospasm is a very frequent cause of MINOCA in young people, 20% of them have vasospasm. The main mechanism is represented by automatic overstimulation, endothelial dysfunction, oxidative stress and hyperreactivity of smooth muscle contractility. The main treatment strategy is represented by calcium channel blockers and nitroglycerin, avoid beta-blockers, and life style intervention [93].
3. The microvascular dysfunction is cause by distal embolization of thrombus during PCI, ischemia-reperfusion injury who leads to endothelial swelling, pericyte contraction, glycocalyx shedding and capillary obstruction or microvascular inflammation and oxidative stress who leads to chronic dysfunction and remodeling. The main ways of diagnosis are represented by invasive index of microvascular resistance, hyperemic microvascular resistance and resistance reserve ration, and the non-invasive diagnosis ways are represented by PET imaging detect microvascular obstruction and quantify flow reserve. The main treatment strategy is represented by beta-blockers, calcium channel blockers, ACE inhibitors/ARBs, statin, SGLT-2, colchicine. [4,93,94]

7. Conclusions and Future Directions

Young adults experiencing AMI represent a distinct and increasingly recognized clinical subgroup, in whom classical cardiovascular risk factors—such as smoking, obesity, hypertension, diabetes, and dyslipidemia—often coexist with unconventional and age-specific contributors. Emerging literature from the past five years emphasizes the complex interplay between genetic predispositions (e.g., familial hypercholesterolemia, elevated lipoprotein(a)), psychosocial stressors (burnout, depression), recreational drug use, systemic inflammation, and autoimmune disease.

In contrast to older patients, young MI cases frequently lack obstructive coronary artery disease, with mechanisms like coronary vasospasm, spontaneous coronary artery dissection (SCAD), microvascular dysfunction, and MINOCA (Myocardial Infarction with Non-Obstructive Coronary Arteries) playing a central role. This etiologic diversity is matched by clinical heterogeneity—ranging from atypical symptomatology and delayed presentation to variable prognoses driven by microvascular injury and neurohormonal activation.

Diagnosis in young MI requires a high index of suspicion and often extends beyond conventional angiography, incorporating advanced imaging, intracoronary functional testing, and biomarker profiling. Management, too, must go beyond standard secondary prevention to address individualized needs—whether through calcium channel blockers for vasospasm, immunomodulatory therapy in autoimmune-mediated cases, or mental health support in stress-driven presentations.

Ultimately, MI in young adults is not simply a premature expression of an old disease; it is a multi-dimensional syndrome rooted in biology, behavior, and context. Future research and clinical strategies must adopt a more personalized, mechanism-oriented approach—one that integrates cardiovascular science with the evolving realities of a younger, more complex patient population.

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Abbreviations

MI	Myocardical infarction
CAD	Coronary artery disease
MINOCA	Myocardical infarction with non-obtrustive coronary arteries
CHD	Coronary heart disease
AMI	Acut myocardical infarction
BMI	Body mass index
SID	Systemic inflammation
RA	Rheumatoid arthritis
CV	Cardiovascular
SLE	Systemic lupus eerythematosus
AS	Ankylosing spondylitis
hsCRP	High-sensitivity C-reactive protein
MPO	Myeloperoxidase
Lp-PLA2	Lipoprotein-associated phospholipase A2
TMAO	Trimethylamine-N-oxide
LpA	Lipoprotein A
SCAD	Spontaneous coronary artery dissection
DOAJ	Directory of open access journals
TLA	Three letter acronym
LD	Linear dichroism

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