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Coronary heart disease in young individuals: novel ways to detect, prevent and treat

Doença coronariana em jovens: novas formas de detecção, prevenção e tratamento

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ABSTRACT - In spite of major advancements in the management and prevention strategies of atherosclerosis, the prevalence of coronary artery disease has risen worldwide, and might start at an early age. Cardiovascular diseases among young adults are characterized as a heterogeneous group of disorders due to congenital or acquired causes. Multiple risk factors, such as dyslipidemia, premature coronary heart disease, diabetes mellitus and cigarette smoking potentiate the patient's risk for early coronary heart disease. Early assessment of patients with coronary artery disease can be performed using various non-invasive imaging methods, which facilitate early selection of effective and preventative therapies for coronary artery disease management; however, it is associated with several challenges due to limitations in risk calculators, and limited sensitivity of various screening methods. In this manuscript, we will discuss about pathophysiology, risk factors, invasive and non-invasive imaging methods, and various management strategies for the early prevention of coronary heart disease in young adults and, importantly, the future directions and preventing disease and sudden cardiac death.

Keywords: Coronary artery disease; Myocardial infarction; Computed tomography angiography; Risk factors; Atherosclerosis; Cardiovascular diseases

RESUMO - Apesar dos grandes avanços nas estratégias de manejo e prevenção da aterosclerose, a prevalência da doença arterial coronariana aumenta em todo o mundo, tendo início em idade precoce. As doenças cardiovasculares em adultos jovens caracterizam-se como um grupo heterogêneo de doenças que ocorrem por causas congênitas ou adquiridas. Múltiplos fatores de risco, como dislipidemia, doença coronária prematura, diabetes melito e tabagismo, potencializam o risco do paciente para a coronariopatia precoce. A avaliação precoce de pacientes com doença arterial coronariana pode ser feita por meio de vários métodos de imagem não invasivos, que facilitam a seleção precoce de condutas preventivas e terapêuticas efetivas para manejo da doença arterial coronariana; no entanto, ela está associada a várias dificuldades, devido às limitações dos escores de risco e à sensibilidade limitada de vários métodos de rastreamento. Neste manuscrito, discutimos sobre fisiopatologia, fatores de risco, métodos de imagem invasivos e não invasivos e várias estratégias de manejo na prevenção precoce da doença coronariana em adultos jovens e, mais importante, os rumos futuros e a prevenção de doenças e da morte súbita cardíaca.

Descritores: Doença arterial coronária; Infarto do miocárdio; Angiografia por tomografia computadorizada; Fatores de risco; Aterosclerose; Doenças cardiovasculares

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INTRODUCTION

Cardiovascular diseases (CVD), particularly coronary artery disease (CAD), have become prominent among children and young adults, with CAD being a primary global cause of death. Urban areas in India record incidence of CAD of 6.5 to 13.2%, surpassing rural rates of 1.6 to 7.4%.[1]

Approximately 20% of adult coronary heart disease (CHD) cases arise from non-atherosclerotic factors, such as autoimmune and connective tissue disorders. Young CAD patients exhibit different clinical findings from older individuals. Recent identification of risk factors like C-reactive protein and prothrombotic markers in healthy individuals has been significant. Coronary computed tomography angiography (CCTA) aids in the prevention of CAD in young adults.[2]

Sudden cardiac death (SCD) in youth is a major health concern, predominantly caused by CAD.[3] Children with CHD are at increased SCD risk due to severe cardiac arrhythmia from myocardial fibrosis or acute coronary syndrome (ACS).[4] The Covid-19 pandemic amplified this risk due to associated cardiac complications. After Covid-19 recovery, a high incidence of cardiac complications has been observed, and SCD risks escalated for patients with pre-existing cardiac conditions. Cardiovascular events, including myocarditis and pericarditis, have been observed after vaccination against coronavirus disease 2019 (Covid-19), mainly in young men.

Modifying risk factors, appropriate management, and prevention strategies can reduce CAD-related mortality. Despite advancements in prognosis, CAD-associated risk remains high. Further research is needed to identify improved diagnostic and intervention methods, especially for younger CHD patients.

PREVALENCE OF CORONARY HEART DISEASE IN YOUNG

Coronary artery disease, more common in those aged over 40 years, surprisingly affects younger individuals, even those who show no symptoms. Usually, ‘young’ is classified as under 40 years, while CAD is defined by atherosclerotic features, such as coronary revascularization, SCD, or acute myocardial infarction (MI).[5]

Asia faces significant challenges in preventing and managing CVD due to its vast population, cultural diversity, varied healthcare structures, and socioeconomic statuses. In 2019, CVD accounted for approximately 10.8 million deaths in Asia, comprising 35% of total deaths. Notably, 39% were premature, a higher rate than in the United States (23%), Europe (22%), and globally (34%). The majority of these deaths (87%) resulted from ischemic heart disease (IHD) (47%) or stroke (40%).[6]

In India, CVD is a major cause of mortality, affecting individuals earlier in life than their European counterparts.[7] For instance, in Europe, CVD accounts for 23% of deaths before 70, but in India, it is a staggering 52%. Early disease onset, rapid progression, and high mortality rates are alarming concerns. Over 80% of CVD deaths in India are attributed to IHD and stroke.[8]

Epidemiological data reveal that risk factors such as smoking, dyslipidemia, dysglycemia, and obesity significantly influence CVD incidence. Although cardiovascular risks are typically low in adolescents, they often increase in individuals aged 30-39 years. Primary risks for early CAD include a family history of premature CAD and smoking. Hypertension and diabetes are more common in later onset.[9]

Having a family history of premature CAD substantially elevates risk, but addressing these factors can significantly reduce mortality and morbidity in younger CAD patients.[10]

PATHOGENESIS OF CORONARY ARTERY DISEASE IN YOUNG

Atherosclerosis, involving lipid, fibrous, and inflammatory build-up in arteries, starts in childhood, silently advancing to CAD.[11] Its stealthy variant, subclinical atherosclerosis (SCA), is influenced by risk factors, like obesity and smoking. Early detection is crucial, as both non-obstructive and obstructive SCA plaques can lead to myocardial infarction (MI), with the latter being more dangerous.[12] Diagnostic methods, like CCTA and intravascular ultrasound (IVUS), identify atherosclerotic plaques, while biomarkers, such as carotid intima-media thickening, aid in SCA detection.[13]

Atherosclerosis initially appears as fatty streaks, evolving into fibrous plaques between ages 15 to 30, potentially causing MI and stroke. Primary contributors include smoking, obesity, and hypertension, while genetic factors, like proprotein convertase subtilisin/kexin type-9 (PCSK-9) mutations, amplify the risk.[14]

For younger patients, traditional CAD risk factors remain relevant. Smoking stands out, causing 80% of young adult CAD cases. Congenital coronary issues result in 4% of their heart attacks, while clots account for 5%. Other factors, including trauma and drug use, comprise 6%. Elevated triglycerides, low high-density lipoprotein (HDL), diabetes, and obesity are significant factors. Interestingly, positive remodeling in young individuals may indicate CAD potential.[15]

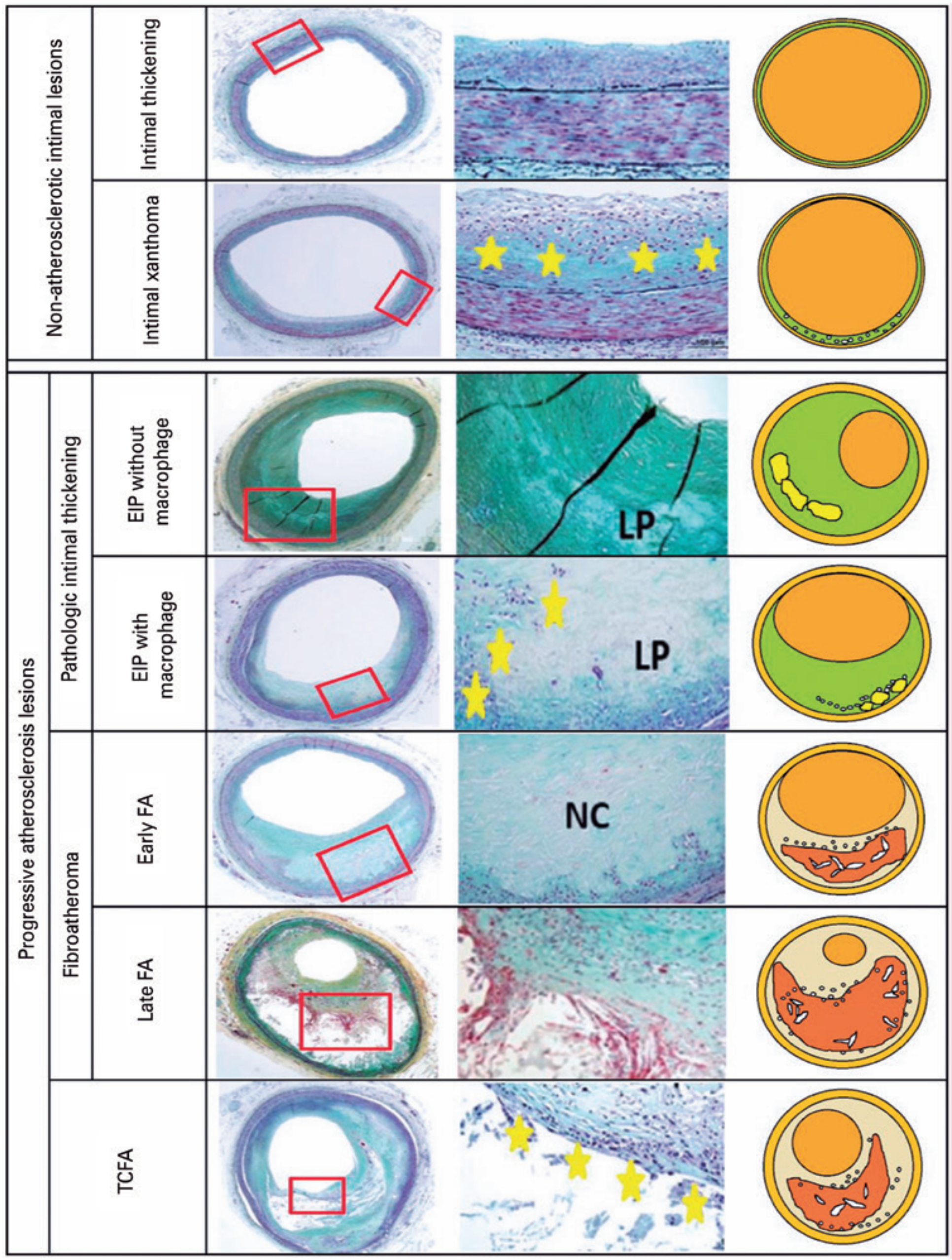
In contrast, older patients often experience severe CAD, characterized by multi-vessel disease, and reduced left ventricular function. Additionally, microvascular and endothelial dysfunctions are more common in this demographic group. Gradual progression of atherosclerosis is demonstrated in figure 1.

RISK FACTORS OF ATHEROSCLEROTIC CORONARY ARTERY DISEASE IN YOUNG

Key risk factors for CHD include diabetes, obesity, elevated lipoprotein (Lp) levels, family history of CHD, male gender, smoking, dyslipidemia, and intense exercise. Smoking, even less than 25 cigarettes a day, markedly increases CHD risk in young adults, leading to an eightfold increase in acute MI.[16]

Lipoprotein(a), a complex of low-density lipoprotein (LDL) particles and additional components, is strongly linked to CAD in younger demographic groups. A family history of CHD predicts CAD and acute MI, particularly in young adults, and is associated with a higher incidence of CAD. It is worth mentioning that 92.5% of young acute MI patients are male.[17]

Obesity doubles or triples the risk of CHD and acute MI in young patients, which is concerning given rising obesity rates. Diabetes, although prevalent in fewer people, is a



Source: the authors.
TCFA: thin-cap fibroatheroma; FA: fibroatheroma; PIT: pathologic intimal thickening; NC: necrotic core; LP: lipid pool.
Figure 1. Human coronary atherosclerosis gradual progression. Atherosclerotic lesions developed from various nonatherosclerotic lesions, including intimal xanthoma and intimal thickening, which start with thickening of arterial wall and further, lead to fibroatheroma and thin-cap fibroatheroma.

potent mortality predictor. Dyslipidemia is another significant risk factor; familial hyperlipidemia causes a 24-fold increase in acute MI risk.[18]

High-intensity exercise also influences CAD risk. A study involving middle-aged and older athletes found vigorous exercise strongly linked to the progression of coronary atherosclerosis and the development of coronary artery calcium (CAC) and plaques.[19] The relation between exercise and coronary atherosclerosis in athletes is demonstrated in figure 2.

RISK FACTORS OF NON-ATHEROSCLEROTIC CORONARY DISEASE IN YOUNG

Besides atherosclerosis, nonatherosclerotic factors contribute to CAD in young adults. Approximately 20% of MI cases in this demographic are attributed to some factors, such as coronary vessel inflammation, coronary artery embolism, connective tissue abnormalities, autoimmune disorders, and coagulation disorders.[20] Congenital CAD contributes to 5 to 35% of SCD cases in youth, with unusual coronary artery origins as one example.

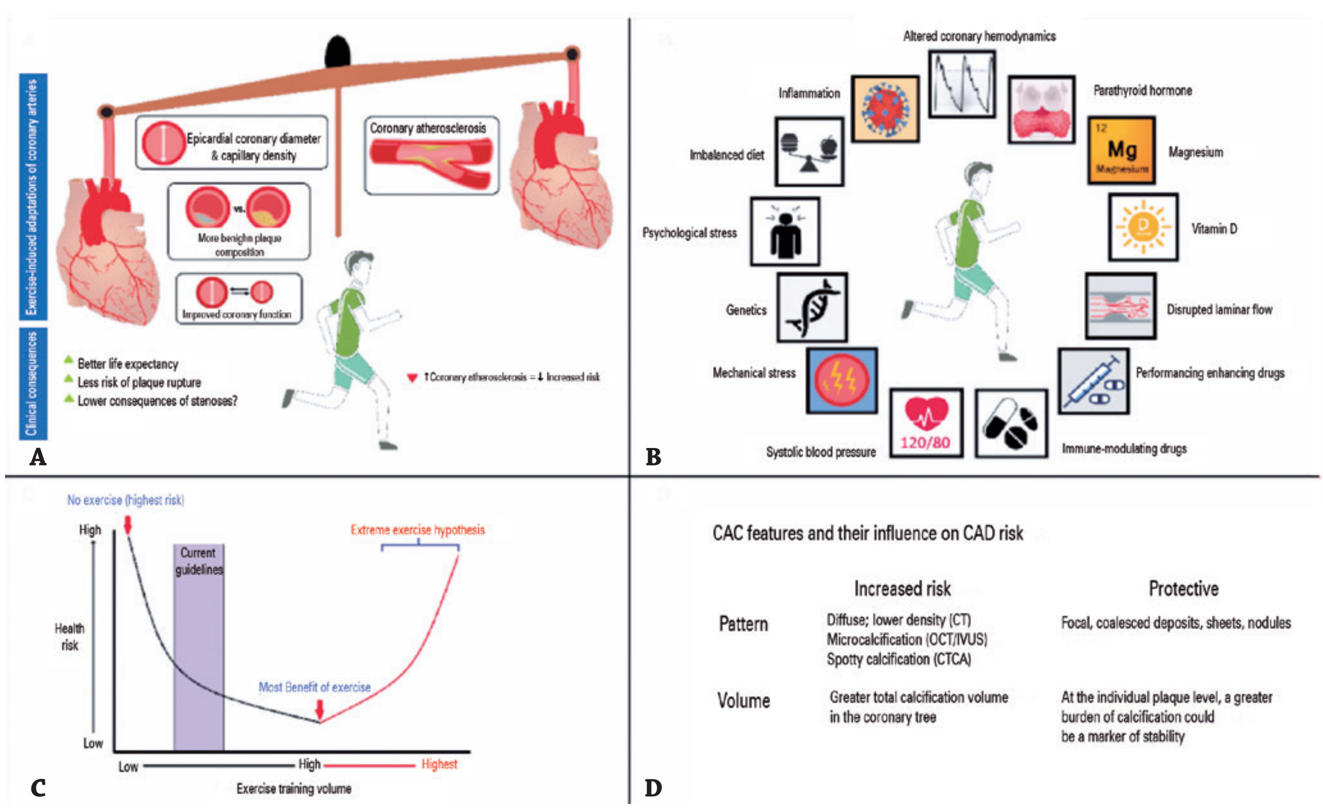
Coagulation abnormalities account for around 5% of acute MI cases in young individuals. Some conditions, such as myocardial bridging and coronary vasospasm, are associated with CAD.[21] Genetic imbalances affecting fibrinolysis and coagulation can trigger CHD in the young. Kawasaki disease narrows coronary artery walls, leading to childhood CHD, while spontaneous coronary artery dissection (SCAD) is a rare cause of ACS in young adults.[22]

Drug abuse, including cocaine and amphetamines, promotes atherosclerosis through mechanisms like thrombosis, vasoconstriction, and hypercoagulability. The factor V Leiden mutation, associated with a procoagulant state, also contributes to young CHD.[23]

Autoimmune diseases, such as systemic lupus erythematosus and antiphospholipid syndrome, induce CHD. Systemic infections by organisms like mycoplasma, *Helicobacter pylori*, and chlamydia cause inflammation, while irradiation for malignancies can lead to scar formation and intimal damage.[24] A comprehensive list of atherosclerotic and non-atherosclerotic risk factors for young adult CAD is detailed in table 1.

ATHEROSCLEROSIS IMAGING IN STABLE CORONARY DISEASE BY NON-INVASIVE IMAGING MODALITIES IN YOUNG

Non-invasive imaging techniques, like computed tomography coronary artery calcium (CTCAC), CCTA, and computed tomography angiography (CTA), are pivotal for early evaluation of asymptomatic SCA.[25] These methods augment risk stratification in CAD, offering vital diagnostic insight into ACS, cardiovascular outcomes, and ischemia.



Source: the authors.
CAC: coronary artery calcium; CAD: coronary artery disease; CT: computed tomography; OCT: optical coherence tomography; IVUS: intravascular ultrasound; CTCA: computed tomography coronary artery.
Figure 2. Relation between exercise and coronary atherosclerosis in athletes. (A) Risks and benefits associated with effect of long-term exercise on coronary morphology and function and atherosclerosis. (B) Potential reasons for modulation of risk of coronary atherosclerosis in athletes. (C) Relation between volume of exercise and risk of coronary atherosclerosis. (D) Features of coronary artery calcium and their effect on risk of coronary artery disease.

A strong link exists between plaque burden and CAC. The CARDIA study demonstrated that high CAC levels are tied to a significant increase in CHD and CVD events. Even minimal CAC in young adults elevates risks.[26] While CAC is predictive of cardiovascular events, CCTA offers a more in-depth view of atherosclerotic plaque, capturing stenosis severity and non-calcified plaque.

Carotid intima-media thickness, an imaging biomarker measured via ultrasound, is indicative of atherosclerotic load. The perivascular adipose tissue surrounding coronary arteries, which can be assessed through CTA's perivascular fat attenuation index, is critical in CAD onset. Low fat attenuation index (FAI) signals increased perivascular adipose tissue inflammation,[27] reinforcing CTA FAI's role in gauging CAD intensity.

Certain proteins and biomarkers linked to oxidation, inflammation, and metabolic syndrome provide insights into CAD progression. Combining these with traditional risk factors enhances CAD risk prediction accuracy.[28] Emerging biomarkers, such as lipoprotein-associated phospholipase-A2, highlight CAD risks in the younger population.

The polygenic risk score further refines CAD risk predictions for the young. The study by Khera et al. emphasized the role of polygenic risk score, especially for those with a familial history of early CAD.[29] Quantitative plaque imaging offers deep insights into stable coronary disease and plaque progression. CTA plaque quantification, majorly via CCTA, evaluates coronary artery plaque burden severity, outshining traditional risk assessments in predicting cardiovascular events.[30]

Modern advancements champion CCTA as a premier non-invasive imaging tool for CAD assessment. CCTA not only predicts plaque dynamics but also furnishes invaluable data on CAD progression, informing treatment approaches for CAD patients.

Atherosclerotic lesions evolve from early non-atherosclerotic intimal lesions to high-risk, rupture-prone thin-cap fibroatheromas (TCFA) or 'vulnerable plaques'.[31] These plaques, marked by large necrotic cores, thin fibrous caps, and macrophage infiltration, have high rupture potential. Detecting these is crucial for risk assessment in CAD individuals.[32] CCTA is essential to evaluate these plaques and the overall coronary artery state. Studies show that culprit lesions in ACS have certain high-risk features, such as positive vessel remodeling and spotty calcification.[33] CCTA used for illustration of combined SCA by groups is demonstrated in figure 3.

Coronary artery disease plaque progression results in calcification. Coronary computed tomography angiography excels in visualizing this calcification, from micro to nodular forms. Studies like EVINCI highlighted CCTA's superiority in predicting CAD compared to other tests. Further, PROMISE and SCOT-HEART (Scottish Computed Tomography of the Heart) trials[34] affirmed CCTA's advantage in predicting cardiovascular events. While CCTA outperforms coronary artery calcium score (CACS) in predicting future events, it comprehensively assesses plaque morphology, composition, and treatment efficacy. CCTA's analysis helps pinpoint fast-progressing plaques and treatment resistance. Advantages associated with the CCTA method in comparison to CAC are illustrated in figure 4.

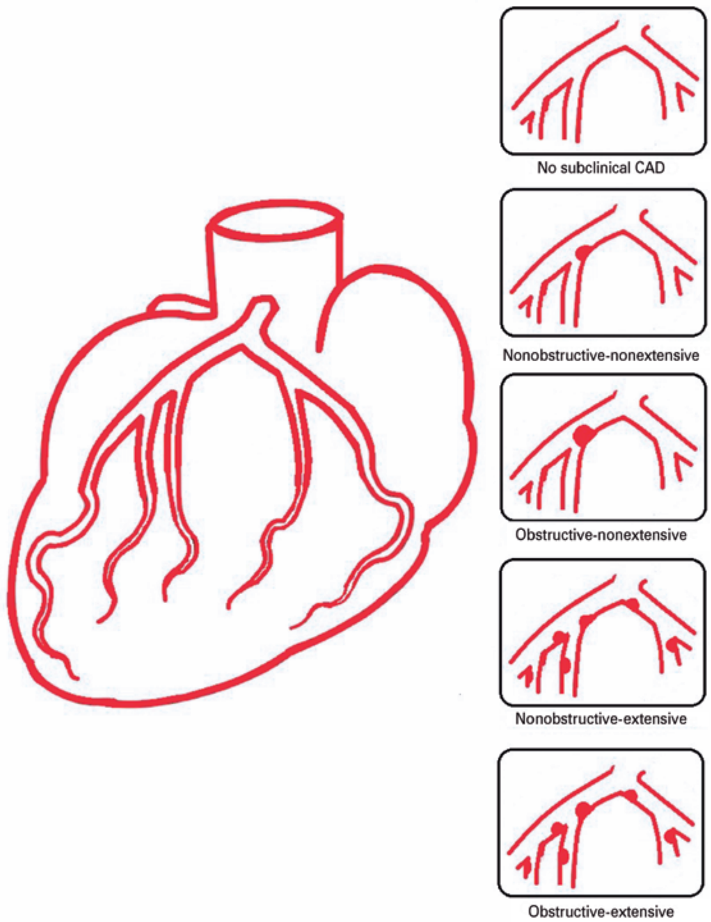
Patients with low attenuation plaque or positive remodeling face increased CAD risks, as shown in the SCOT-HEART trial.[35] Although valuable in outcome prediction, these plaques have limited negative predictive value. CAC, with minimal involvement, predicts SCA in asymptomatic patients, guiding treatment. However, for symptomatic MI patients, CAC is not the primary imaging choice. The Agatston method measures the CAC score. Challenges with CCTA include its time-intensive nature and expertise requirement. Hence, software applications like perivascular fat attenuation index and wall shear stress promise automated high-risk plaque assessment. Moreover, advances in CCTA have amplified its diagnostic capacity. The modulation of plaque characteristics demonstrated by CCTA is illustrated in figure 5.

Table 1. Various atherosclerotic and non-atherosclerotic risk factors responsible for coronary artery disease in young adults

Atherosclerotic risk factors	Non-atherosclerotic risk factors
CHD family history	Coronary arteries abnormal origin
Reduced HDL	Myocardial bridging
Obesity and overweight	Disorders of connective tissue, like giant cell arteritis, Takayasu disease
Reduction in HDL	Overuse of tobacco and other drugs
Elevation in LDL	Spontaneous dissection in coronary artery specifically in pregnant women and patients with connective tissue disorders
Secondary or primary dyslipidaemia	Use of oral contraceptives
Male gender	Various bacterial infections such as mycoplasma, Helicobacter pylori
Use of tobacco	Disorders associated with coagulation system

Source: the authors.

CHD: coronary heart disease; HDL: high-density Lipoprotein; LDL: low-density lipoprotein.

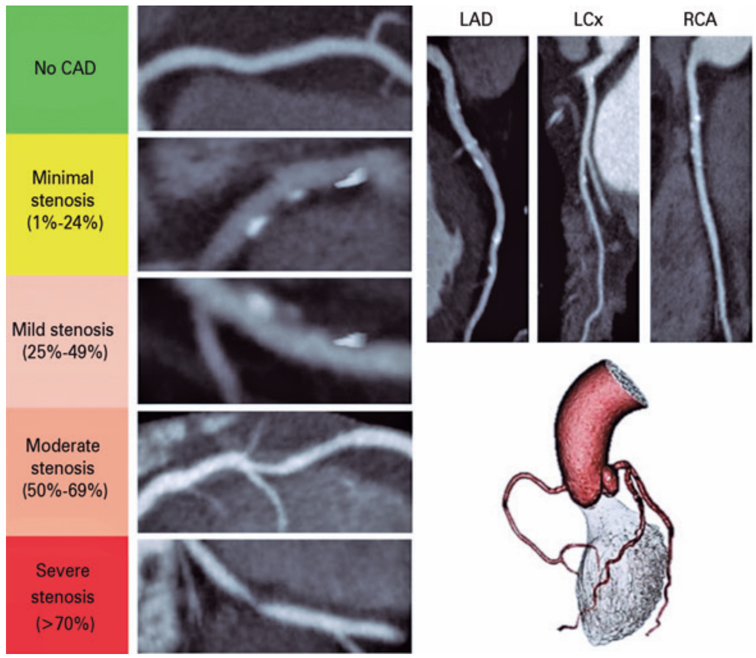


Source: the authors.
CAD: coronary artery disease.
Figure 3. Coronary computed tomography used for illustration of combined subclinical coronary atherosclerosis by groups. Obstructive (<50% stenosis) or non-obstructive stenosis (>50% stenosis) were the two categories in which coronary luminal diameter stenosis was classified. Patients were classified as non-obstructive stenosis, no atherosclerosis, non-obstructive extensive, obstructive extensive and non-obstructive non-extensive.

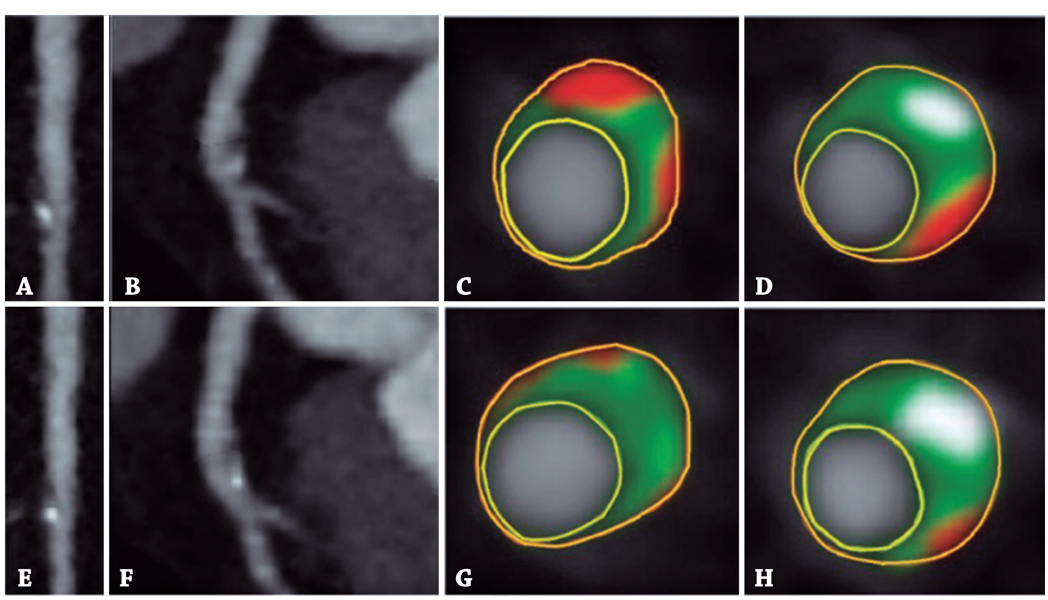
There are concerns about cancer risks from CCTA radiation exposure, but technological advancements have cut down radiation doses. From these advancements, the imaging biomarker perivascular fat attenuation index has emerged, which is crucial for visualizing coronary artery inflammation. The FAI helps identify high-risk plaques and forecast future heart attack risks.[36]

Coronary computed tomography angiography with FAI unveils phenotypic alterations in coronary arteries due to atherosclerosis, aiding early detection of subclinical CAD. VascuCAP is one promising commercial software that facilitates this task. Emerging CCTA applications, like fractional flow reserve (FFR), non-invasively estimate coronary artery pressure, as evidenced by investigations, such as the FAME study,[37] which revealed that a smaller proportion of patients undergoing coronary angiography (CAG) had obstructive CAD and FFR-positive lesions. The correlation between CCTA-derived plaque features, FFR, and myocardial perfusion are pivotal in diagnosing ischemia, with technologies like fractional flow reserve-computed tomography (FFR-CT) creating patient-specific blood flow models. These, along with wall shear stress, identify high-risk plaques and assess the physiological implications of CAD. CCTA and IVUS method used to investigate the coronary artery plaque features are shown in figure 6. CCTA derived imaging technologies are demonstrated in figure 7.

18F-fluorodeoxyglucose (FDG), positron emission tomography (PET), and magnetic resonance imaging (MRI) are instrumental in predicting CAD risk, particularly in younger individuals, by evaluating metabolic activity and providing cardiovascular insights. When combined with inflammatory biomarkers and traditional risk factors, they enhance CAD risk prediction. Cardiac MRI, despite its limitations like low spatial resolution, is crucial in assessing IHD and high-intensity plaques.[38] Exercise stress testing is invaluable for symptomatic CAD patients, assessing known



Source: the authors.
LAD: left anterior descending artery; LCx: left circumflex artery; RCA: right coronary artery.
Figure 4. Comparison of coronary computed tomography angiography imaging modality with coronary artery calcium score. As to the coronary artery calcium score, unique imaging benefits are provided by coronary computed tomography angiography, including high resolution imaging of atherosclerotic plaque features, such as stenosis severity characterization, plaque prone to rupture and non-calcified plaque.



Source: the authors.
Figure 5. Modulation of plaque characteristics demonstrated by coronary computed tomography angiography in response to biological therapy in psoriasis. Before biological therapy, psoriasis was identified (A to D) and after biological therapy, (E to H) in left anterior descending artery plaque of a patient, which suggested decline in total atheroma volume and non-calcified plaque burden. (A) Longitudinal planar and (B) curved planar reformat. (C, D) For plaque subcomponents, representative cross-sectional view with color overlay. Encircling of the lumen is done in yellow, and orange is used for vessel wall encircling, with the subcomponents in between dense calcified (white), necrotic (red), fibro-fatty (light green) and necrotic (red). (E) Longitudinal planar and (F) curved planar reformat. (G, H) For plaque subcomponents, representative cross-section view with color overlay.

cardiac disease through various parameters, but faces challenges in youth due to developmental factors.

Myocardial perfusion imaging (MPI), evolving from single photon emission computed tomography and PET, is a vital tool for risk stratification, diagnosing angina, or MI, and predicting future CAD events. It offers valuable prognostic information, especially for those with limited exercise capability and electrocardiogram (ECG) abnormalities. Optical imaging technologies, like optical coherence tomography (OCT) and near-infrared spectroscopy (NIRS), offer high-resolution imagery of vulnerable plaques. OCT analyses fibrous cap structures, and NIRS, as validated by trials, identifies cardiovascular event risks through lipid core measurements. Developments in OCT-NIRS hybrid systems and near infra-red fluorescence aim for enhanced risk stratification.[39]

Traditional methods for CAD risk assessment in youth have their limitations. The introduction of machine learning algorithms and radiomics has significantly improved the accuracy of CAD risk forecasting in this demographic group. Advanced imaging techniques and their role in youth risk prediction are summarized in table 2.[40] The amalgamation of these advanced techniques and emerging technologies continues to refine and amplify our capabilities in early diagnosis and risk stratification, paving the way for timely interventions and more tailored therapeutic strategies for individuals at risk of CAD.

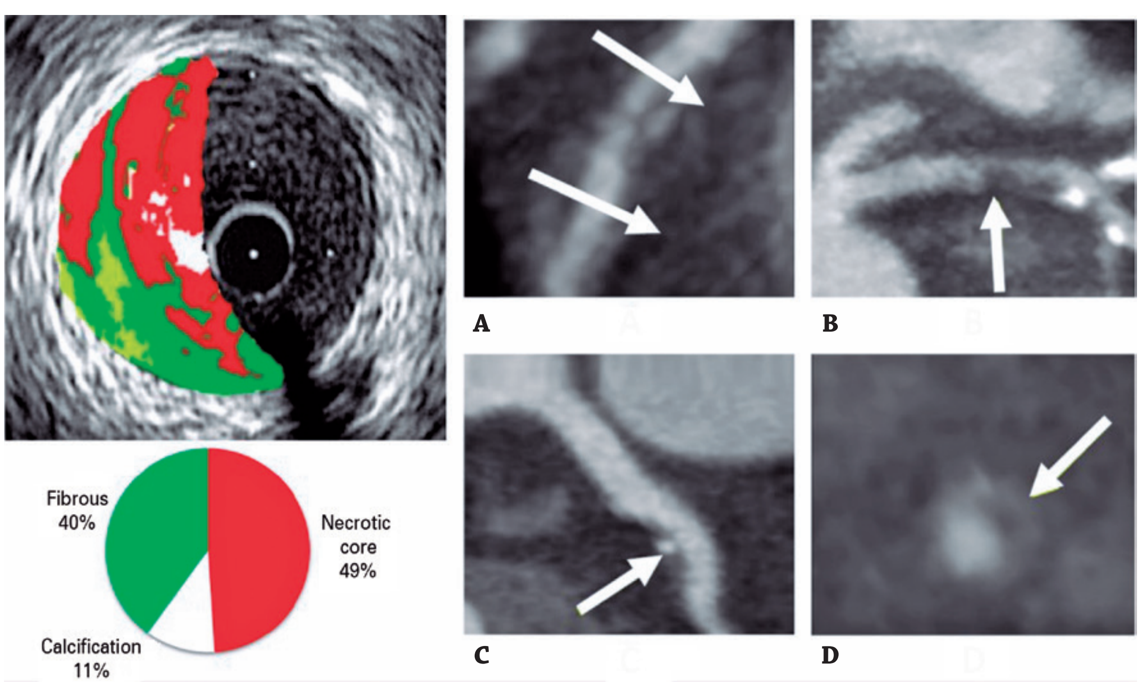
DIAGNOSIS OF NON-ATHEROSCLERTIC CORONARY ARTERY DISEASE IN YOUNG

Myocardial infarction with non-obstructive coronary arteries (MINOCA) accounts for 6 a 8% of acute MI cases, distinctively lacking obstructive CAD. Assessing MINOCA necessitates differentiating between ischemic and non-ischemic MI sources. Cardiac magnetic resonance (CMR) non-invasively identifies these injuries and their origins.[41] Invasive techniques, like OCT and IVUS, provide deeper insights of coronary lesions.

For SCAD, initial evaluation uses CAG to classify it based on angiographic traits. However, CAG's limited arterial wall visualization necessitates intracoronary imaging: IVUS helps in unclear SCAD situations, OCT reveals luminal details, CCTA identifies hematomas and dissection flaps, and CMR spots late gadolinium enhancement in suspicious arteries.

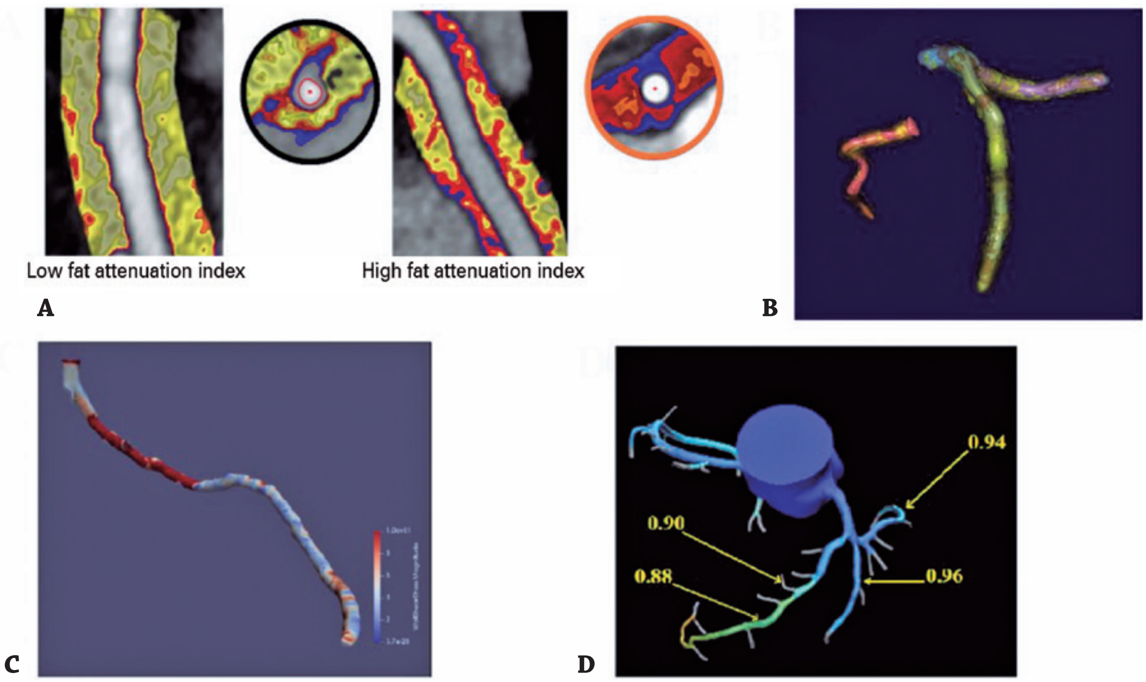
Intraplaque hemorrhage is central to plaque evolution and rupture. Some diagnostic tools, such as CCTA, NIRS, and non-contrast MRI, target intraplaque hemorrhage, with MRI being particularly sensitive for recent thrombus or hemorrhage detection.

Coronary artery spasm (CAS) plays a role in MI onset. Diagnosing CAS involves recognizing chest pain without exertion, related ECG changes, and using tests like CAG, Holter monitoring, and exercise testing.[42] Sometimes,



Source: the authors.

Figure 6. Coronary computed tomography angiography and intravascular ultrasound used to assess the coronary artery plaque features. On coronary computed tomography angiography, a huge risk of vulnerability was observed in various coronary plaque morphological features, including (A) positive remodeling, (B) low-attenuation plaque, (C) spotty calcification and (D) napkin-ring sign from SCOT-HEART trial.



Source: the authors.

Figure 7. Coronary computed tomography angiography derived emerging technologies. (A) Coronary computed tomography angiography was used for the identification of two patients present with low and high perivascular fat attenuation index. (B) Three-dimensional view of right and left coronary arteries is demonstrated using vascuCAP (Elucid Bioimaging, Boston, Massachusetts, USA) from coronary computed tomography angiography used for the characterization and quantification of plaque. (C) Example of coronary computed tomography angiography used for demonstrating superimposed profile of wall shear stress on a coronary artery tree (D) coronary computed tomography angiography used for extraction of fractional flow reserve-computed tomography calculations.

ergonovine injections assist in CAS assessment, adhering to strict guidelines.

MANAGEMENT OF CORONARY ARTERY DISEASE IN YOUNG

Both young and old CHD and ACS patients often receive similar treatments. For acute ST-elevation myocardial infarction (STEMI), initial measures include aspirin, nitrates, oxygen, morphine, and beta-blockers.[43] Statins play a pivotal role in managing atherosclerosis or CHD by lowering mortality rates and transforming plaques. The CCTA PARADIGM (Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography Imaging) study showcased that statin users exhibited fewer vulnerable plaques, more calcification, and stabilized atherosclerotic diseases. CCTA illustrates the comparison of coronary artery plaque characteristics in patients using or not statins as shown in figure 8.

Young STEMI patients benefit from treatments like percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), and thrombolytic therapy. Evidence suggests PCI significantly improves STEMI outcomes across all ages, with younger patients often faring better. For a young smoker suspected of CAD, OCT is advised post-stabilization. If OCT is not viable, intracoronary lysis can be used, with subsequent OCT directing potential stenting decisions.

KEY TAKE-HOME MESSAGES

- *Post-mortem* studies and intravascular imaging (especially high-resolution OCT) provide mechanistic insights in ACS.
- Plaques with ruptured caps cause ACS in over half of cases, while plaque erosion accounts for one-third.
- Small, non-randomized studies favour a no-stenting, antithrombotic therapy approach for eroded plaques, warranting further large, randomized clinical trials.
- Intracoronary OCT aids in diagnosing and managing rare ACS causes, like eruptive calcified nodules, coronary spasms, or embolism.
- Mechanistic studies give insight into additional interventions, such as immune system modulation, along antithrombotic therapies and coronary interventions, in ACS caused by lesions with OCT-defined IFC.

Table 2. Various novel imaging approaches to personalize the risk prediction in young individuals

Various novel imaging methods	Biomarkers/novel risk score
CTA perivascular fat attenuation index	Micro RNA
CTA plaque quantification	Polygenic risk score
Coronary artery calcium score	Various inflammatory biomarkers
Machine learning and radiomics	Improvement in the risk calculator
18F-FDG PET ± MRI	

Source: the authors.

CTA: computed tomography angiography; FDG: fluorodeoxyglucose; PET: positron emission tomography; MRI: magnetic resonance imaging.

- Current data supports intravascular OCT use to optimize primary PCI in ACS, advocating for testing in long-term, randomized controlled trials.
- OCT helps identify vulnerable plaques, like TCFA and macrophages, potentially predicting future events.
- Both young and old CHD and ACS patients can receive comparable treatments. For acute STEMI, standard treatments include aspirin, nitrates, oxygen, morphine, and beta-blockers. Statins are pivotal in CHD management, reducing mortality by arresting atherosclerotic plaque growth and altering plaque composition. The CCTA study, which examined 2,252 patients with potential or confirmed CAD, investigated statin effects. It found that statin users had reduced low-density cholesterol, fewer low-attenuation plaques, and increased calcium-rich plaques. There was also pronounced calcification progression in these patients, underscoring the role of statins in atherosclerosis stabilization.[44]
- Young STEMI patients see benefits from revascularization techniques like PCI, CABG, and thrombolytic. Evidence indicates PCI outperforms fibrinolysis in treating STEMI for all ages, but younger patients frequently experience superior outcomes.
- For young smokers, like a 30-year-old with possible non-obstructive CAD, post-stabilization OCT is advised. If imaging is unattainable, intracoronary lysis can be initiated, with OCT potentially directing stenting decisions. Use of multipronged approach to break the cycle of CAD in young adults is demonstrated in figure 9. Various invasive and non-invasive imaging methods to detect sub-clinical atherosclerosis in young are shown in figure 10.

WHAT WE KNOW SO FAR

Due to various risk factors, such as obesity, smoking, family history of CAD and hyperlipidemia, young adults are at huge risk of CAD.

Several invasive and non-invasive imaging methods CCTA, carotid intima-media thickening and CTCAC can be used for the early assessment of CAD in young adults.

Primary PCI, CABG and fibrinolytic therapy can be used as treatment approaches for the management of CAD in young adults.

FUTURE DIRECTIONS

Various other novel risk factors, such as plaque burden, FAI, TCFA and MINOCA, should be taken into consideration, and future trials are required to find their importance in prevention.

Non-invasive methods, like quantitative CCTA, wall shear stress, quantification of CAC score, CCTA derived characteristics, FFR-CT, PET, MRI, and invasive methods, such as OCT, NIRS and intravascular photoacoustic, play a potential role in understanding plaque characteristics and tools to prevent and/or treat these plaques in young patients.

In performing primary PCI, the role of intracoronary lytic agents, intracoronary suction, or management with OCT, aid identifying and managing the plaque.

Most importantly, the future lies in prevention of ACS and SCD for young patients rather than treatment.

CONCLUSION

Coronary artery disease is a severe chronic inflammatory disease with a high incidence rate in young adults. The coronary artery disease cycle in young adults can be broken by adopting the multipronged approach, which involves the early identification of young adults, who are at huge risk of development of coronary artery disease, by using various imaging modalities. The objective is to improve adherence to developed preventative therapeutic approaches. Furthermore, the risk of coronary artery disease and long-term complications in young adults can also be reduced by early assessment, proper counselling, and appropriate modification of various risk factors. As to etiology, treatment and prognosis, physicians must know the differences that exist among younger and older patients. Future research must focus on identifying effective and quite safer imaging methods for the prediction of sudden cardiac death in young adults.

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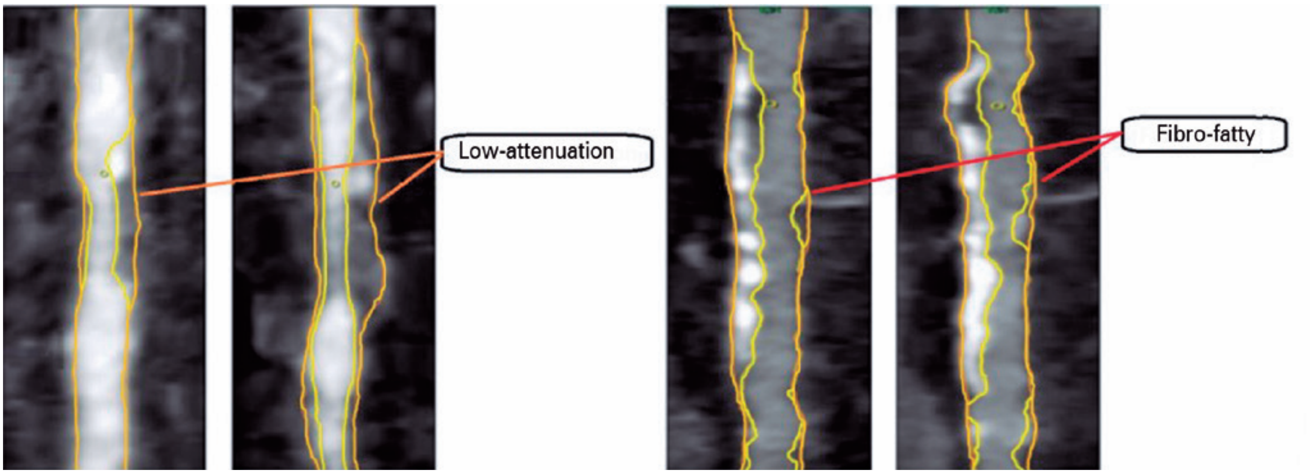
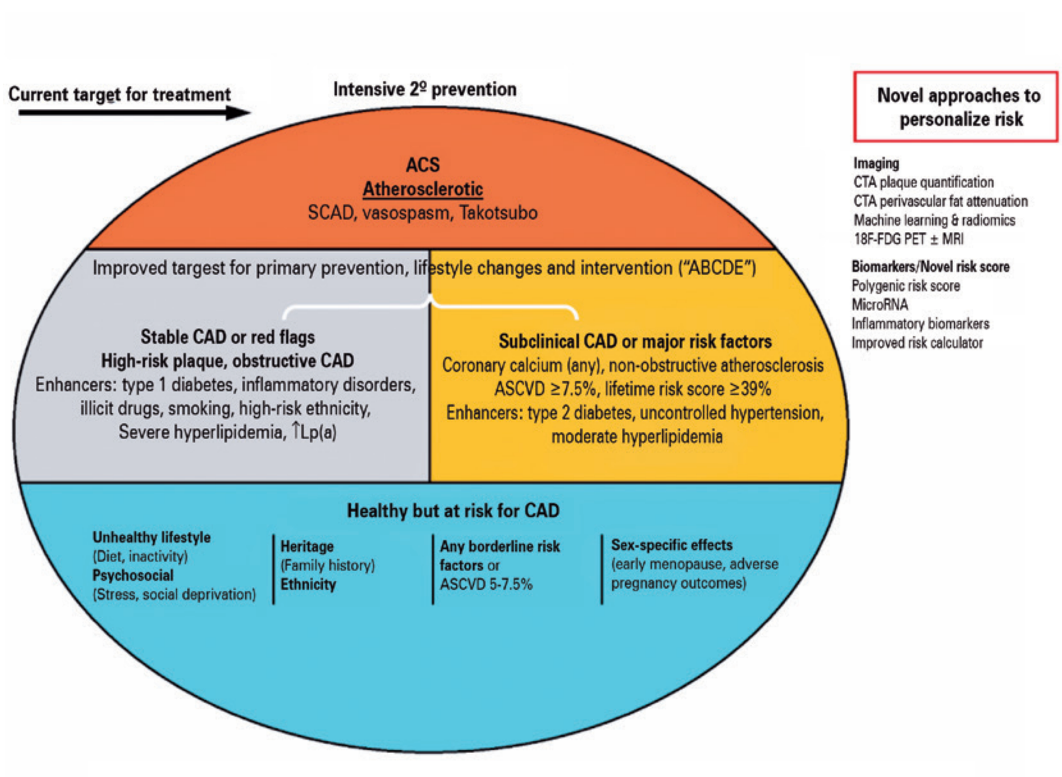


Source: the authors.

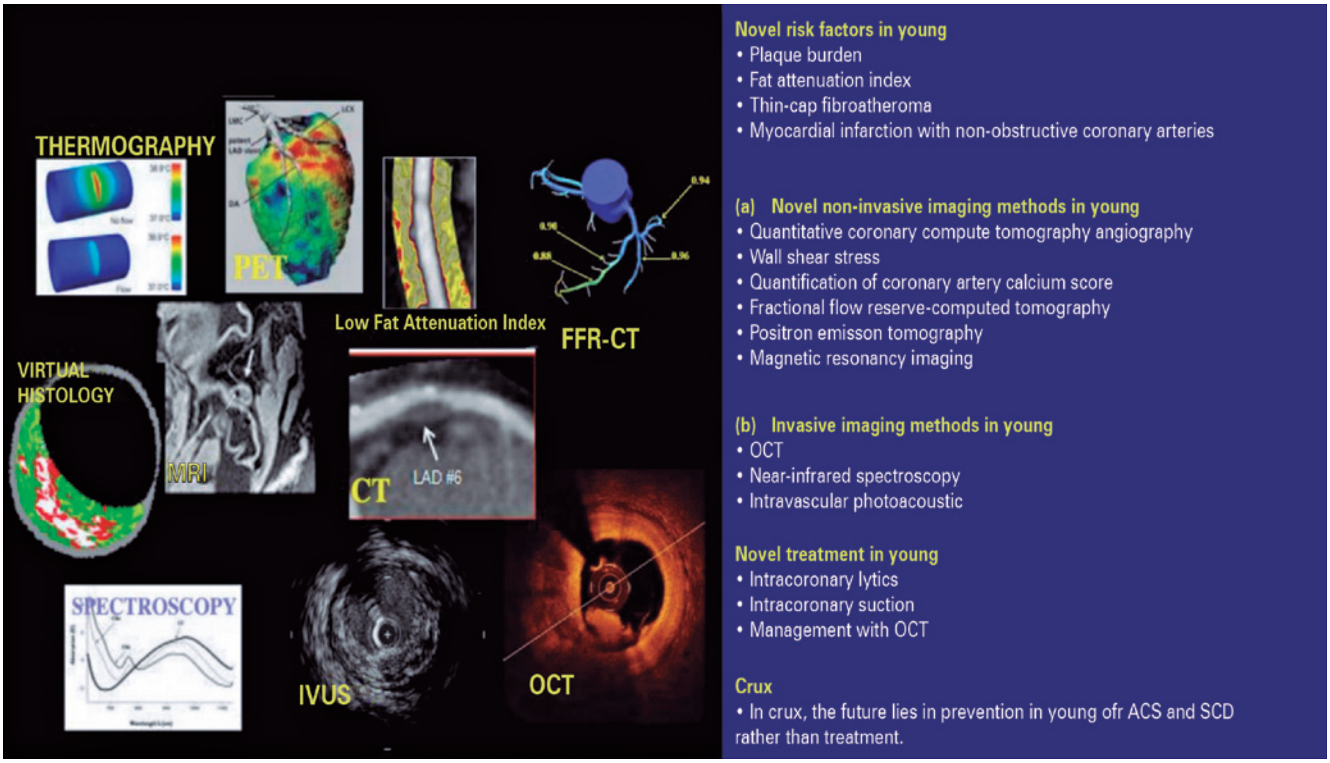
Figure 8. According to statin use, assessment of coronary artery plaque characteristics by coronary computed tomography angiography method (Supplementary material). Modulation of non-calcified burden susceptible to rupture in patients on statins in comparison to those not taking statins is demonstrated by the study PARADIGM (Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography Imaging). This study demonstrates the use of coronary computed tomography angiography in the assessment of patient response to treatment.



Source: the authors.

ACS: acute coronary syndrome; SCAD: spontaneous coronary artery dissection; CAD: coronary artery disease; Lp(a): lipoprotein (a); ASCVD: atherosclerotic cardiovascular disease; CTA: computed tomography angiography; FDG: fluorodeoxyglucose; PET: positron emission tomography; MRI: magnetic resonance imaging.

Figure 9. Use of multipronged approach to break the cycle of coronary artery disease in young adults. To break the cycle from coronary artery disease at huge risk to acute coronary syndrome in young adults, a multipronged approach is required. Screening of patients for conventional atherosclerotic cardiovascular disease risk should be done and should be managed by using "ABCDE" approach. Personalized risk prediction can be modulated by using novel imaging methods, novel biomarkers, and various scoring methods.



Source: the authors.
PET: positron emission tomography; FFR-CT: fractional flow reserve-computed tomography; MRI: magnetic resonance imaging; CT: computed tomography; IVUS: intravascular ultrasound; OCT: optical coherence tomography; ACS: acute coronary syndrome; SCD: sudden cardiac death.
Figure 10. Various non-invasive and invasive modalities, which can identify sub-clinical atherosclerosis and its risk. Various invasive and non-invasive imaging methods to detect sub-clinical atherosclerosis in young coronary artery disease.

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None.

CONFLICTS OF INTEREST

The authors declare there are no conflicts of interest.

CONTRIBUTION OF AUTHORS

Conception and design of the study: RM, DD and BM; data collection: RM, DD and BM; data interpretation: RM, DD and BM; text writing: RM, DD and BM; approval of the final version to be published: RM, DD and BM.

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