CARDIO ROUNDS NEWSLETTER

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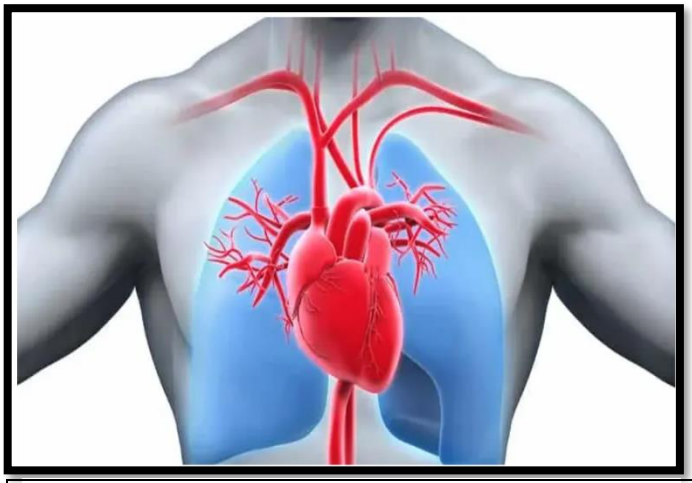
IN THIS ISSUE

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you "Cardio rounds" which contains latest and interesting news in the field of Cardiology

Association between the haemoglobin glycation index and the long-term prognosis of patients with coronary artery disease

INTRODUCTION- Coronary artery disease (CAD) is a serious cardiovascular condition caused by the buildup of plaque in blood vessels, resulting in decreased blood flow to the heart and chest discomfort. High blood pressure, smoking, diabetes, lack of exercise, alcoholism, high cholesterol, and a poor diet are all key contributors.[1] CAD remains a leading global cause of mortality, with patients undergoing percutaneous coronary intervention (PCI) experiencing variable long-term outcomes. Identifying reliable prognostic markers is crucial to improve risk stratification and management strategies. Traditional markers, such as haemoglobin A1c (HbA1c), have limitations in reflecting individual glycaemic variability. The haemoglobin glycation index (HGI), which quantifies the difference between measured and predicted HbA1c based on fasting plasma glucose, has emerged as a potential predictor for adverse outcomes in CAD patients. Therefore, this study investigates the association of HGI with all-cause mortality (ACM), cardiac mortality (CM), and major adverse cardiovascular events (MACEs) in a large cohort of CAD patients.[2]



Cardiovascular Disease

METHODS- This prospective cohort study involved a cohort of 10,598 patients with CAD who underwent PCI Participants were categorized into three HGI groups: Low HGI (< -0.506), Medium HGI (-0.506 to 0.179), High HGI (≥ 0.179). Demographic data (age, sex, smoking, etc.) and clinical variables (diabetes, hypertension, multiple vascular lesions) were recorded. Blood samples analyzed included FPG, HbA1c, lipid profiles, serum creatinine, and uric acid. Predicted HbA1c was derived using a linear regression equation based on FPG. The primary endpoints were ACM and CM. Secondary endpoints were MACEs and MACCEs (major adverse cardiovascular and cerebrovascular events). Patients were followed up for a median of 24 months through office visits, calls, and questionnaires. Cox proportional hazard models adjusted for confounders (age, sex, lipid profiles, etc.) were used to evaluate associations between HGI levels and clinical outcomes.

RESULTS- Over a median follow-up period of 24 months, 321 cases of all-cause mortality (ACM), 243 cardiac mortalities (CM), 774 major adverse cardiovascular events (MACEs), and 854 major adverse cardiovascular and cerebrovascular events (MACCEs) were recorded. Patients in the medium HGI group exhibited the lowest incidences of adverse outcomes compared to those in the low and high HGI groups. The medium HGI group had the lowest rates of ACM (2.1%), CM (1.6%), MACEs (6.0%), and MACCEs (6.9%). In contrast, the low and high HGI groups showed higher incidences of these outcomes, with the low HGI group

having a 3.4% ACM rate and the high HGI group having a 3.6% ACM rate. Similarly, the low and high HGI groups had higher MACE rates at 7.2% and 8.7%, respectively. Kaplan-Meier survival analyses revealed a U-shaped relationship between HGI levels and clinical outcomes, with the medium HGI group demonstrating the most favorable cumulative survival curves for all endpoints (Figure 1). Multivariate Cox regression analyses confirmed that low HGI significantly increased the risk of ACM, with a hazard ratio (HR) of 1.683, while high HGI significantly raised the risk of MACEs, with an HR of 1.247.

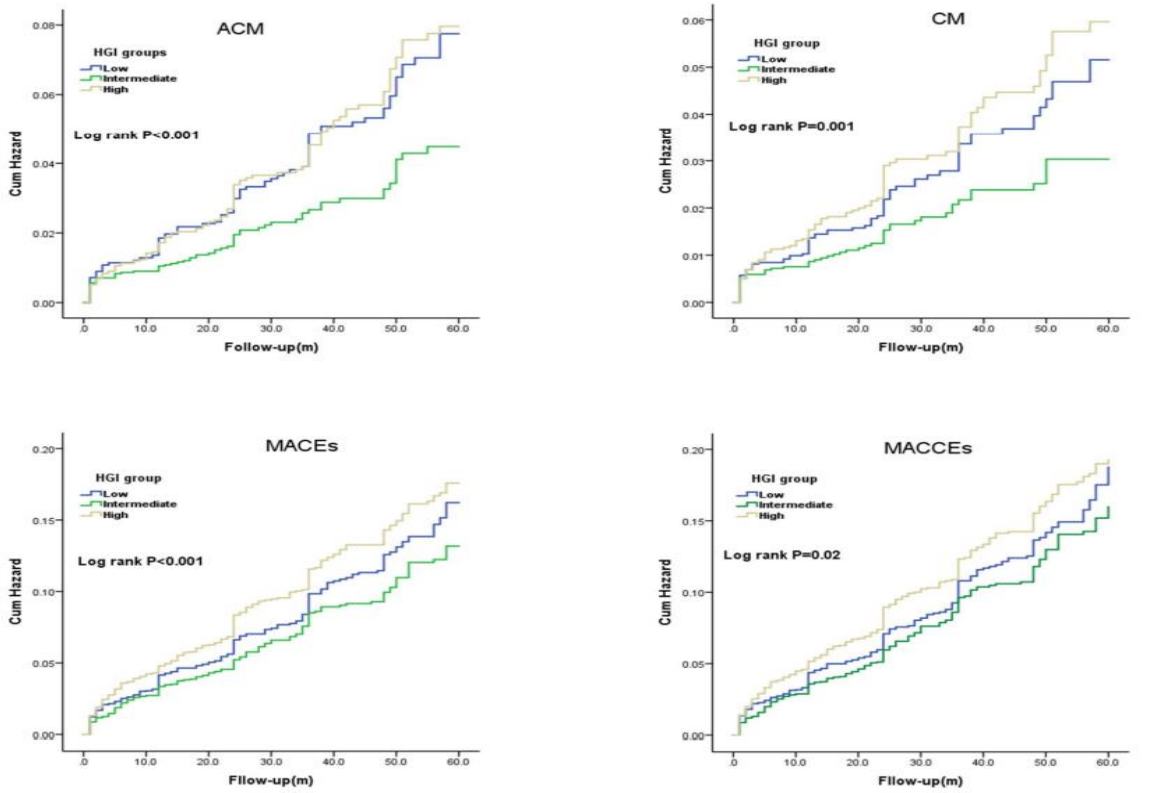


Figure 1. Cumulative Kaplan-Meier graphs showing the three HGI categories and the time to clinical outcomes for each patient. All-cause mortality, or ACM; Major adverse cardiovascular events (MACCEs) are major unfavourable cardiovascular and cerebrovascular events; cardiac mortality (CM) is the term for MACEs. The p-Values that are bolded indicate statistical differences.

DISCUSSION- This study confirms that both low and high HGI levels predict adverse outcomes in CAD patients post-PCI, with medium HGI associated with better survival.[2] These findings are consistent with Cheng MD et al. analysis which identified similar U-shaped associations in a smaller cohort. The mechanistic link may involve advanced glycation end-products (AGEs), which are elevated in high HGI states and contribute to endothelial dysfunction, vascular stiffness, and inflammatory responses.[3]

CONCLUSION- HGI serves as a robust independent predictor of adverse outcomes in CAD patients undergoing PCI. Both low and high HGI levels indicate higher risks of ACM, CM, and MACEs, emphasizing the need for individualized management strategies for these patients.

Both low and high HGI levels are associated with increased risks of all-cause mortality (ACM), cardiac mortality (CM), and major adverse cardiovascular events (MACEs).

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Association of metabolomic biomarkers with plaque burden and instability in Coronary Atherosclerotic Disease

INTRODUCTION- Coronary atherosclerotic disease (CAD) is a major global health challenge, driven by risk factors such as hypertension, diabetes, and dyslipidemia.[1] The elevated levels of low-density lipoprotein cholesterol (LDL-C) are one of the primary risk factors for CAD. Nonetheless, CAD may develop in those without high LDL-C levels.[2] While lipid-lowering therapies form a cornerstone of CAD management, their effectiveness in mitigating cardiovascular risks remains incomplete. Recent advances in nuclear magnetic resonance (NMR)-based metabolomics offer promising insights into the role of metabolic disturbances, particularly dyslipidemia, in CAD progression. Even though metabolic markers have been examined in relation to the risk of cardiovascular disease in Western populations, there are few extensive studies that concentrate on the direct correlations between metabolite profiles and the degree of coronary atherosclerosis, as well as the metabonomic traits of Asian populations with CAD. Therefore, this study aims to investigate the associations between metabolomic biomarkers and plaque burden and instability in patients undergoing moderate lipid-lowering therapy.[1]

METHODS- This cohort study analysed 2560 newly diagnosed CAD patients from the GRAND cohort who received moderate lipid-lowering therapy. Serum samples were profiled using NMR spectroscopy, quantifying 175 metabolites, including lipoprotein subfractions and low-molecular-weight metabolites. The Gensini score evaluated plaque burden, while cardiac troponin T (cTnT) levels assessed plaque instability. Multivariate linear regression determined metabolite associations with CAD severity, and a Mendelian randomization approach explored potential causal relationships. Composite metabolomic indices were constructed to predict major adverse cardiac events (MACEs) during a median follow-up of 3.8 years.

RESULTS- LDL components, especially triglycerides and apolipoprotein B, exhibited a robust positive association with both the Gensini score (plaque burden) and cTnT levels (plaque instability). These markers displayed stronger correlations with CAD severity than traditional LDL cholesterol measurements. HDL components such as cholesterol esters, apolipoprotein A1, and apolipoprotein A2 were inversely associated with CAD severity. These finding highlights HDL's protective role, with larger HDL particles (HDL2, HDL3, and HDL4) showing stronger inverse associations compared to smaller HDL1 particles. Amino acids such as glycine and histidine were inversely associated with cTnT levels, while phenylalanine showed a positive correlation. Fatty acid composition revealed that a higher proportion of polyunsaturated fatty acids (PUFAs) was inversely associated with both plaque burden and instability, whereas mono-unsaturated fatty acids (MUFAs) showed a positive association with instability. The Gensini score–based metabolomic index was significantly associated with an increased risk of MACEs, including all-cause death, non-fatal myocardial infarction, stroke, ischemia-driven revascularization, and progression of coronary atherosclerosis. Per standard deviation increase in this index corresponded to a 14.8% higher risk of MACEs (HR, 1.148; 95% CI, 1.018–1.295) (Figure 1). Sensitivity analyses excluding patients with diabetes or reduced kidney function (eGFR <60 mL/min) confirmed consistent findings, supporting the robustness of the observed associations. A genetically higher level of apolipoprotein B was strongly associated with increased Gensini scores. In contrast, dihydrothymine was inversely associated with plaque burden.

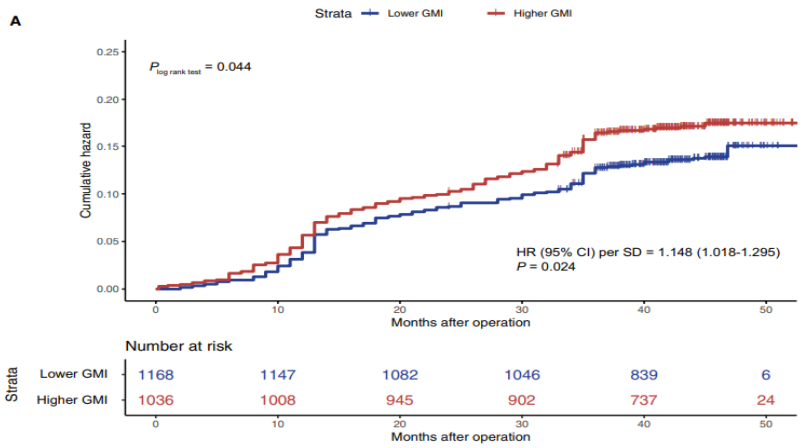

Figure 1. Associations of metabolomic indices of Gensini score with risk of major adverse cardiac events.

DISCUSSION- There was a positive association between LDL components, particularly apolipoprotein B and triglycerides within LDL, and plaque burden.[1] This finding aligns with Boekholdt SM et al. which demonstrated that apolipoprotein B outperformed LDL cholesterol as a predictor of CAD severity and cardiovascular events.[3] Similarly, Varbo A et al. highlighted that higher triglyceride-rich lipoproteins, rather than LDL cholesterol alone, were strongly associated with myocardial infarction risk. These findings support the notion that metabolomic profiling offers a more granular view of lipid abnormalities contributing to CAD progression.[4]

CONCLUSION- This study demonstrates the potential of metabolomic biomarkers in non-invasive risk assessment for CAD patients. Triglycerides and apolipoprotein B within LDL significantly predict plaque burden and instability, while HDL components exhibit protective associations. These biomarkers may serve as valuable tools in CAD prognosis and therapeutic targeting, reducing reliance on invasive diagnostic techniques.

Triglycerides and apolipoprotein B within LDL significantly predict plaque burden and instability, while HDL components exhibit protective associations.

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Impact of Nonculprit Lesions location on major clinical outcomes in ST-segment elevation myocardial infarction patients

INTRODUCTION- ST-segment elevation myocardial infarction (STEMI) is the most severe form of coronary artery disease (CAD), with significant morbidity and mortality. The most common cause of STEMI is a complete thrombotic blockage caused by an atherosclerotic plaque in an epicardial coronary artery.[1] Approximately 50% of STEMI patients have severe non-culprit lesions (NCLs) associated with worse outcomes. The COMPLETE (Complete vs Culprit-Only Revascularization to Treat Multi-Vessel Disease After Early PCI for STEMI) trial demonstrated that angiography-guided complete revascularization significantly reduced the risk of cardiovascular (CV) death or myocardial infarction (MI) compared to culprit-only PCI. Since LAD supplies up to 50% of the myocardium and is associated with high-risk features, such as lipid-rich plaques, but may cause less myocardial damage in non-culprit scenarios. Prior studies in stable CAD, including the recent ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial, showed no significant benefit of PCI over medical therapy for proximal LAD disease. However, the influence of NCL location, particularly in the left anterior descending (LAD) artery, on outcomes remains unclear. This sub-analysis of the COMPLETE trial aimed to evaluate the impact of NCL location and the benefit of complete revascularization versus culprit-only PCI on major outcomes, including CV death, MI, and ischemia-driven revascularization.[2]

METHODS- The COMPLETE trial was a multinational randomized study comparing culprit lesion-only PCI with complete revascularization in STEMI patients with multivessel disease (MVD). A total of 4,041 subjects were enrolled in this trial across 140 centers, with a median follow-up of 35.8 months. After successful primary PCI, eligible patients with at least one qualifying NCL were randomized to complete revascularization or culprit-only PCI. Randomization was stratified by the timing of NCL PCI (during hospitalization or within 45 days post-discharge). Qualifying NCLs had ≥70% stenosis (or 50%-69% with FFR <0.80), a diameter ≥2.5 mm, and were suitable for PCI. Outcomes included two coprimary endpoints: (1) CV death or new MI, and (2) CV death, new MI, or ischemia-driven revascularization

(IDR), with additional secondary outcomes such as MI, stroke, new onset NYHA functional class IV heart failure, and stent thrombosis.

RESULTS- The current study results showed that 1,666 patients had proximal or mid-LAD NCLs and 2,185 did not. Patients with proximal/mid-LAD NCLs were older, more likely female, and less likely to be current smokers. Procedural characteristics showed similar primary PCI rates, but those with proximal/mid-LAD NCLs had higher baseline left ventricular ejection fraction and SYNTAX scores, and more often had ≥2 vessels with NCLs. The first coprimary outcome (CV death or new MI) occurred in 8.5% of patients with proximal/mid-LAD NCLs compared to 9.9% with other NCL locations (HR: 0.83; 95% CI: 0.67-1.03). The second coprimary outcome (CV death, new MI, or IDR) occurred in 12.7% versus 13.2% respectively (HR: 0.95; 95% CI: 0.8-1.14). Similar patterns were observed for proximal LAD NCLs alone, with no significant differences compared to other NCL locations. Complete revascularization reduced the first coprimary outcome in patients without proximal/mid-LAD NCLs (HR: 0.65; 95% CI: 0.50-0.86) but showed no significant benefit in those with proximal/mid-LAD NCLs (HR: 0.85; 95% CI: 0.61-1.18; interaction P=0.235) (Figure 1). For the second coprimary outcome, complete revascularization reduced events in both groups with consistent benefit (interaction P=0.897). The secondary outcome (CV death, MI, IDR, unstable angina, or class IV heart failure) showed similar benefits with complete revascularization irrespective of NCL location (interaction P=0.909). Stratification by stenosis severity showed differential effects favoring complete revascularization in proximal/mid-LAD NCLs with stenosis ≥60%.

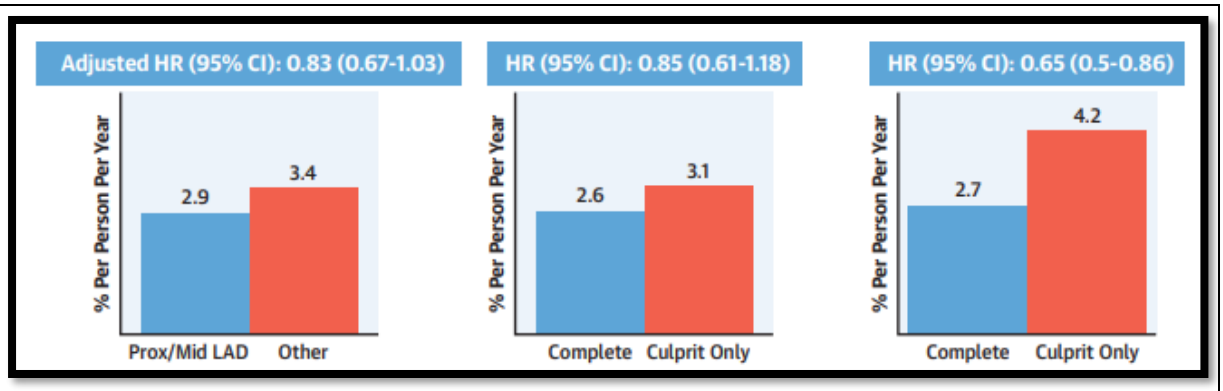

Figure 1. Proximal/mid-LAD NCL Vs other NCL Comparison

DISCUSSION- This sub-analysis demonstrated that complete revascularization provided consistent benefits in patients with and without proximal or mid-LAD NCLs, with no significant differences in major clinical outcomes between the two groups.[2] These findings are aligned with Lee JM et al., which showed that complete revascularization using physiology-guided strategies significantly reduced clinical events in patients with acute myocardial infarction (AMI), regardless of NCL location.[3] Both trials underline the importance of addressing nonculprit lesions to improve long-term outcomes.

CONCLUSION- Patients with/without proximal/mid-LAD NCLs exhibited comparable clinical outcomes when they presented with STEMI and multivessel CAD. Complete revascularization had a similar effect for patients with and without proximal/mid-LAD NCL

site, and there was no indication that coprimary and secondary outcomes differed. Regardless of the location of the NCL, the current findings support full revascularization.

Patients with a proximal/mid-LAD NCL had comparable event rates to those without among those who presented with STEMI and multivessel CAD.

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Co-Occurrence of Deep Vein Thrombosis and Vascular Aneurysms: A Rare Case Report

INTRODUCTION- Deep vein thrombosis (DVT) is one of the common venous thromboembolic (VTE) disorders, with an incidence rate of 1.6 per 1000 yearly.[1] DVT and vascular aneurysms are distinct conditions with separate pathophysiological mechanisms. DVT involves the formation of thrombi in deep veins, typically of the lower limbs, while aneurysms represent localized vascular dilations, often occurring in arterial walls. Rarely, these two conditions co-occur, with aneurysms compressing adjacent veins and disrupting blood flow, leading to thrombus formation. This case report describes a young female patient with a history of DVT who subsequently developed a ruptured iliac artery aneurysm, highlighting the rare intersection of these conditions and the associated clinical challenges.[2]

CASE PRESENTATION- A 20-year-old female with a history of left lower limb DVT at age 19 was treated with rivaroxaban for six months following negative evaluations for coagulation factor abnormalities, including factor V Leiden mutation. A year later, she presented with severe abdominal and flank pain, pallor, and hypotension (BP 85/50 mmHg; HR 120 bpm), raising suspicion of acute haemorrhage. Laboratory tests revealed anaemia (haemoglobin 6 g/dL), mild leucocytosis, and normal C-reactive protein (CRP). A CT angiography confirmed a ruptured right common iliac artery aneurysm with mural thrombi

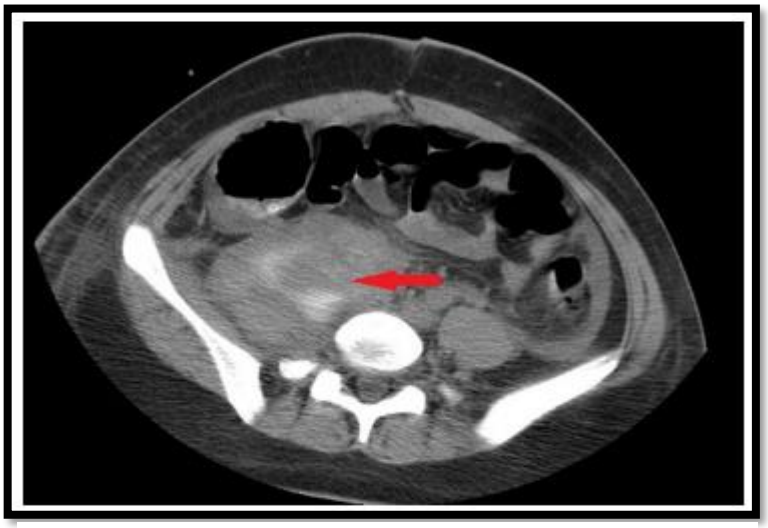

Figure 1. Right iliac artery aneurysm ruptured alone (red arrow)

(Figure 1). Emergency surgery was performed, involving the placement of an 8-mm Dacron graft from the right common iliac to the right external iliac artery. Postoperatively, the patient recovered hemodynamically but experienced persistent abdominal pain relieved by corticosteroids. Six weeks later, she developed small bowel obstruction secondary to a large pancreatic pseudocyst, which was drained surgically. Despite this, high output drainage persisted, prompting oral pancreatin therapy. Two months post-surgery, graft thrombosis was detected via CT imaging, but the patient remained asymptomatic, without signs of ischemia. Pathology of the aneurysm sac indicated an inflammatory process. Coagulation assessments and rheumatological tests remained negative throughout her follow-up.

DISCUSSION- This was the case report of a young female without typical risk factors, presenting with a ruptured right common iliac artery aneurysm following a prior episode of DVT, an atypical and challenging scenario.[2] Similar findings were reported by Malli F et al., who described a case of an iliac artery aneurysm leading to DVT and pulmonary embolism.[3] Additionally, Pazur et al. presented a case of an abdominal aortic aneurysm causing venous compression and DVT. While their case involved older patients with common risk factors such as smoking and cardiovascular disease, the mechanism of compression and the clinical presentation were comparable.[4] The uniqueness of this case report lies in the patient's young age and absence of these risk factors, emphasizing the need to consider inflammatory or systemic causes.

CONCLUSION- It is uncommon for vascular aneurysms and deep vein thrombosis to coexist. When assessing patients who have both aneurysms and deep vein thrombosis at the same time, it's critical to consider the compressive effects on veins and flow disruptions caused by aneurysms. This connection may also be influenced by chronic traumatic arteriovenous fistula, Behçet's disease, Hughes-Stovin syndrome, and recurrent nontyphoidal Salmonella bacteraemia.

The rare co-occurrence of DVT and arterial aneurysms requires a high index of suspicion, particularly in atypical patients without conventional risk factors.

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