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EDITORIAL COMMENT

Tertiary Cardiovascular Manifestations of the (Not So) Forgotten Disease

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In the 1990s, intensification of management and heightened public health awareness driven by the AIDS epidemic nearly eradicated syphilis in the United States, thus marking a significant triumph in disease control. However, epidemiologic data reveal signals of a troubling resurgence of this disease within recent years.[1] The cause is undoubtedly multifactorial. Underfunding of sexually transmitted disease prevention and monitoring programs within our public health sector that resulted in limited access to confidential clinics, while concurrently stifling medical awareness and perpetuating a stigma around sexually transmitted infections, lies at the core of the issue.[2] Decreasing rates of condom use in the era of alternative contraceptive therapies and antiretroviral medication have further fueled the rise in syphilis cases. The recent COVID-19 pandemic, which effectively diverted resources away from other public health initiatives and restricted access to already limited screening services, only worked to worsen the already long-standing inequalities within our health care system.[3] Given this landscape, it is not unreasonable to posit that we may be at the forefront of an increase in syphilis-related cardiovascular disease in the future.

Tertiary syphilis, which can manifest 10 to 30 years after the initial infection, is well known for its severe complications, particularly its cardiovascular sequelae of aortitis, aneurysms, and valvulopathies. However, one of its more insidious manifestations is coronary ostial stenosis. This rare condition, seen in less than one-fourth of patients with syphilitic aortitis, involves the often life-threatening narrowing of the coronary artery origins secondary to aortic wall thickening caused by syphilitic aortitis.[4] Unlike atherosclerotic disease, this condition typically manifests with a normal distal arterial bed. Whereas anginal symptoms are common, myocardial infarction (MI) is rare in syphilitic coronary stenosis because of the gradual narrowing that permits formation of collateral circulation, although sudden death has still been reported. Coronary ostial stenosis can stem from various causes, such as atherosclerosis, congenital disease, or inflammatory conditions (eg, Kawasaki disease and Takayasu arteritis), thereby making it difficult to tie its origin back to syphilis, especially with disease's long latency period. In this issue of *JACC: Case Reports*, Nakamura et al[5] highlight the case of a 51-year-old man without traditional cardiac risk factors who presented with severe left main (LM) coronary artery ostial stenosis, aptly accredited to undertreated syphilis. Although the rarity of ostial stenosis makes this case an interesting read, one could argue that the true importance of this case lies not only in the diagnosis itself, but also in the choice of intervention used.

The standard of care for unprotected LM atherosclerotic coronary artery disease, which includes ostial lesions, has been coronary artery bypass grafting (CABG).[6] However, percutaneous coronary intervention (PCI) is also considered a viable alternative in cases of lower-complexity disease, particularly when it can achieve outcomes comparable to those of CABG, especially in isolated ostial or shaft lesions without distal LM coronary artery involvement.[7,8] The decision between these approaches is often guided by risk assessments such as the SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) scoring system (which incorporates anatomical disease complexity in its stratification) and the clinical variables of diabetes, chronic kidney disease, and

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ejection fraction.[9-11] In acute settings such as ST-segment elevation MI or cardiogenic shock, PCI, aided by mechanical circulatory support, is typically favored when patients are deemed to have prohibitively high operative risks.[12] Randomized trials have shown comparable survival outcomes between PCI and CABG for ostial and shaft LM coronary artery lesions, although CABG has consistently demonstrated lower rates of spontaneous MIs and need for repeat revascularizations.[6]

In contrast, syphilitic ostial lesions pose a unique challenge because of their distinct pathophysiology, leaving the optimal treatment strategy open to debate. Single-center retrospective studies and case reports have shown that CABG, especially with the use of the left internal mammary artery, provides superior long-term outcomes, such as lower rates of restenosis and major adverse cardiac events, when compared with PCI.[13] In patients with concurrent valvular heart disease and aortopathy with root dilation, CABG is clearly advantageous.

Nakamura et al[5] preferred CABG over PCI given the inherent risk of accelerated in-stent restenosis in an inflammatory milieu. PCI has emerged as a viable alternative strategy for managing syphilitic ostial stenosis, particularly in clinical scenarios such as acute MI or in patients experiencing acute hemodynamic instability.[14,15] However, the risk of in-stent restenosis is a major challenge that remains poorly understood. Limited data are available, but 1 observational study suggested that the use of a shorter stent length and successful treatment of syphilitic infection could reduce the risk of in-stent restenosis.[16]

This case report brings to light the importance of recognizing cardiovascular complications of untreated syphilis. However, in the absence of clear, standardized treatment guidelines for syphilis-related coronary ostial lesions, we recommend a patient-centered approach that takes into account the coronary anatomy, concomitant cardiac disease, and clinical comorbidities. The unique risk posed by coronary ostial lesions (and cardiovascular complications in general) merits greater educational efforts at the primary care levels in screening, early diagnosis, and management of syphilis. Left undiagnosed or untreated, these lesions can lead to life-threatening complications that could have been avoided with earlier detection and appropriate antibiotic therapy. By filling this gap in our understanding, we can improve outcomes for patients affected by this potentially growing epidemic.

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REFERENCES

1. National Academies of Sciences Engineering and Medicine. In: Crowley JS, Geller AB, Vermund SH, eds. *Sexually Transmitted Infections: Adopting a Sexual Health Paradigm*. National Academies Press; 2021:750.

2. Why STDs are soaring in America: rash behaviour. *The Economist (Online). The Economist Newspaper NA*. Inc; June 14, 2018.

3. Nazir A, Masood W, Ahmad S, et al. Rise of syphilis surge amidst COVID-19 pandemic in the USA: a neglected concern. *Ann Med Surg (Lond)*. 2022;80:104239. https://doi.org/10.1016/j.amsu.2022.104239

4. Heggtveit HA. Syphilitic aortitis. A clinicopathologic autopsy study of 100 cases, 1950 to 1960. *Circulation*. 1964;29:346-355. https://doi.org/10.1161/01.cir.29.3.346

5. Nakamura K, Kim K, Yamamoto H, et al. Left main coronary artery ostial stenosis caused by syphilitic aortitis presenting with syncope. *JACC Case Rep*. 2025;30(1):102720.

6. Davidson LJ, Cleveland JC, Welt FG, et al. A practical approach to left main coronary artery disease. *J Am Coll Cardiol*. 2022;80(22):2119-2134. https://doi.org/10.1016/j.jacc.2022.09.034

7. Naganuma T, Chieffo A, Meliga E, et al. Long-term clinical outcomes after percutaneous coronary intervention for ostial/mid-shaft lesions versus distal bifurcation lesions in unprotected left main coronary artery: the DELTA Registry (drug-eluting stent for left main coronary artery disease): a multicenter registry evaluating percutaneous coronary intervention versus coronary artery bypass grafting for left main treatment. *JACC Cardiovasc Interv*. 2013;6(12):1242-1249. https://doi.org/10.1016/j.jcin.2013.08.005

8. Guo CL, Yu XP, Yang BG, et al. Long-term outcomes of PCI vs. CABG for ostial/midshaft lesions in unprotected left main coronary artery. *J Geriatr Cardiol*. 2017;14(4):254-260. https://doi.org/10.11909/j.issn.1671-5411.2017.04.004

9. Farooq V, van Klaveren D, Steyerberg EW, et al. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. *Lancet*. 2013;381(9867):639-650. https://doi.org/10.1016/s0140-6736(13)60108-7

10. Takahashi K, Serruys PW, Fuster V, et al. Redevelopment and validation of the SYNTAX score II to individualise decision making between

percutaneous and surgical revascularisation in patients with complex coronary artery disease: secondary analysis of the multicentre randomised controlled SYNTAXES trial with external cohort validation. *Lancet*. 2020;396(10260):1399-1412. https://doi.org/10.1016/s0140-6736(20)32114-0

11. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360(10):961-972. https://doi.org/10.1056/NEJMoa0804626

12. Zeitouni M, Marquis-Gravel G, Smilowitz NR, et al. Prophylactic mechanical circulatory support use in elective percutaneous coronary intervention for patients with stable coronary artery disease. *Circ Cardiovasc Interv*. 2022;15(5):e011534. https://doi.org/10.1161/CIRCINTERVENTIONS.121.011534

13. Berhil T, Radi FZ, El Boussaadani B, Raissouni Z. Tertiary syphilis and cardiovascular disease: the united triad: case report. *Eur Heart J Case Rep*. 2024;8(3):ytae013. https://doi.org/10.1093/ehjcr/ytae013

14. Nakazone MA, Machado MN, Barbosa RB, Santos MA, Maia LN. Syphilitic coronary artery ostial stenosis resulting in acute myocardial infarction treated by percutaneous coronary intervention. *Case Rep Med*. 2010;2010:830583. https://doi.org/10.1155/2010/830583

15. Li X, Wang X, Wang Z, et al. Cardiovascular syphilis-associated acute myocardial infarction: a case report. *Medicine (Baltimore)*. 2021;100(7):e24788. https://doi.org/10.1097/md.0000000000024788

16. Zhang L, Wang Y, Zhang Z, et al. Risk factors of in-stent restenosis among coronary artery disease patients with syphilis undergoing percutaneous coronary intervention: a retrospective study. *BMC Cardiovasc Disord*. 2021;21(1):438. https://doi.org/10.1186/s12872-021-02245-6

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