High-sensitivity cardiac troponin and the early rule out of myocardial infarction: time for action

Andrew R Chapman , Nicholas L Mills

High-Sensitivity Cardiac Troponin

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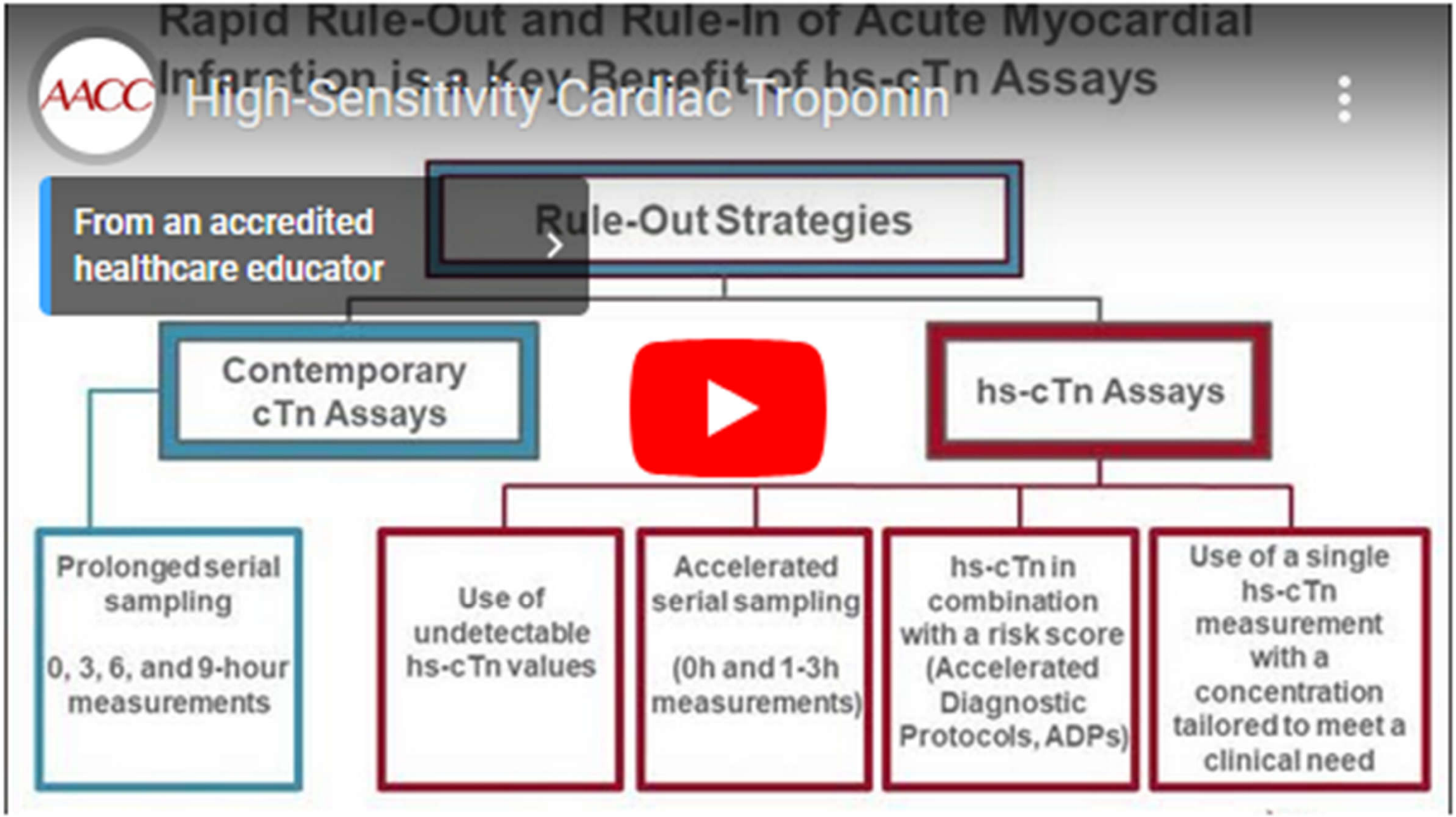
topics: Pathophysiology and Organ Systems, Cardiovascular



AP&T Alimentary Pharmacology and Therapeutics

META-ANALYSIS

Meta-analysis: Chemoprevention of hepatocellular carcinoma with statins, aspirin and metformin

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accounting for concurrent aspirin and metformin consumption and lipophilic statins. Aspirin use was associated with reduced HCC risk overall (HR: 0.48; 95% CI: 0.27–0.87) (11 studies, 2,190,285 patients) but not in studies accounting for concurrent statin and metformin use. Metformin use was not associated with reduced HCC risk overall (HR: 0.57; 95% CI: 0.31–1.06) (3 studies, 125,458 patients). Most analyses had moderate/substantial heterogeneity, except in follow-up <60 months for aspirin (I^2 = 0%).

Conclusion

Although statin and aspirin use were associated with reduced HCC risk, only statin use was significant in subgroup analyses accounting for concurrent medications. Metformin use was not associated with reduced HCC risk. These data have implications for future clinical trial design.

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Metformin use history and genome-wide DNA methylation profile: potential molecular mechanism for aging and longevity

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Abstract

Background: Metformin, a commonly prescribed anti-diabetic medication, has repeatedly been shown to hinder aging in pre-clinical models and to be associated with lower mortality for humans. It is, however, not well understood how metformin can potentially prolong lifespan from a biological standpoint. We hypothesized that metformin's potential mechanism of action for longevity is through its epigenetic modifications.

Methods: To test our hypothesis, we conducted a post-hoc analysis of available genome-wide DNA methylation (DNAm) data obtained from whole blood collected from inpatients with and without a history of metformin use. We assessed the methylation profile of 171 patients (first run) and only among 63 diabetic patients (second run) and compared the DNAm rates between metformin users and nonusers.

Results: Enrichment analysis from the Kyoto Encyclopedia of Genes and Genome (KEGG) showed pathways relevant to metformin's mechanism of action, such as longevity, AMPK, and inflammatory pathways. We also identified several pathways related to delirium whose risk factor is aging. Moreover, top hits from the Gene Ontology (GO) included HIF-1α pathways. However, no individual CpG site showed genome-wide statistical significance ($p < 5E-08$).

Conclusion: This study may elucidate metformin's potential role in longevity through epigenetic modifications and other possible mechanisms of action.

NARRATIVE REVIEW

Charles J. Kahi, Sec

Emerging Tests for Noninvasive Colorectal Cancer Screening

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Colorectal cancer (CRC) is among the most common cancers globally and a major cause of cancer-related deaths. The American Cancer Society estimates that CRC will kill 1 in 60 Americans, and CRC screening is recommended for all Americans ≥45 years of age. Current CRC screening methods are effective for preventing CRC and have been shown to reduce CRC-related mortality. However, none of the currently available tests is ideal, and many people are not compliant with screening recommendations. Novel screening tests based on advances in CRC molecular biology, genetics, and epigenetics, combined with developments in sequencing technologies and computational analytic methods, have been developed to address the shortcomings of current CRC screening tests. These emerging tests include blood-based assays that use plasma-derived circulating tumor DNA and serum proteins to detect early CRC and advanced adenomas, assays that use stool DNA or mRNA, and methods for profiling the gut microbiome. Here we review current screening modalities, and we discuss the principles behind the most promising emerging CRC screening tests and the data supporting their potential to be used in clinical practice.

Table 3. Colorectal Cancer Screening Test Type Strengths and Weaknesses

Screening test	Sensitivity/specificity for cancer	Sensitivity/specificity for advanced adenomas	Convenience	Safety	Cost
FIT	❙❙❙	❙	❙❙❙	❙❙❙❙	❙
Colonoscopy	❙❙❙❙	❙❙❙❙	❙	❙❙	❙❙❙❙
Stool DNA	❙❙❙	❙❙	❙❙❙	❙❙❙❙	❙❙
Stool RNA	❙❙❙	❙❙	❙❙❙	❙❙❙❙	[a]
ctDNA	❙❙❙	❙/[a]	❙❙❙❙	❙❙❙❙	❙❙/[a]
Serum proteome	❙❙/[a]	[a]	❙❙❙❙	❙❙❙❙	❙❙/[a]
Microbiome	❙❙❙/[a]	[a]	❙❙❙❙	❙❙❙❙	[a]

ctDNA, circulating tumor cell DNA; FIT, fecal immunochemical test

Conclusions

CRC is a common but preventable cancer. CRC screening is predominantly done using colonoscopy or stool-based tests, such as FIT and MT-DNA, and has been shown to prevent CRC-related deaths. However, the currently available tests have a variety of drawbacks making none of them ideal. Furthermore, compliance with CRC screening in the United States is well less than the target of 80%. Emerging CRC screening tests have the potential to address the drawbacks of current modalities and to improve compliance. These tests are the result of advancements in the technology used to detect cell free nucleic acids (eg, DNA, mRNA), analysis methods, and in the understanding of the molecular pathology of CRC. These tests are in different stages of development with plasma cfDNA-based assays being the class of assay that is most mature. The sensitivity and specificity of cfDNA-based assays from large clinical trials done in CRC screening populations are expected in the next year and likely will result in the addition of these tests to the menu of CRC screening options currently available. Screening assays that are based on the gut microbiome also seem to be promising but are likely a few years from being tested in large prospective observational studies in a CRC screening population. It is clear that there will be additional CRC screening tests available in the near future, although their place in the menu of screening options remains to be defined (Table 3).

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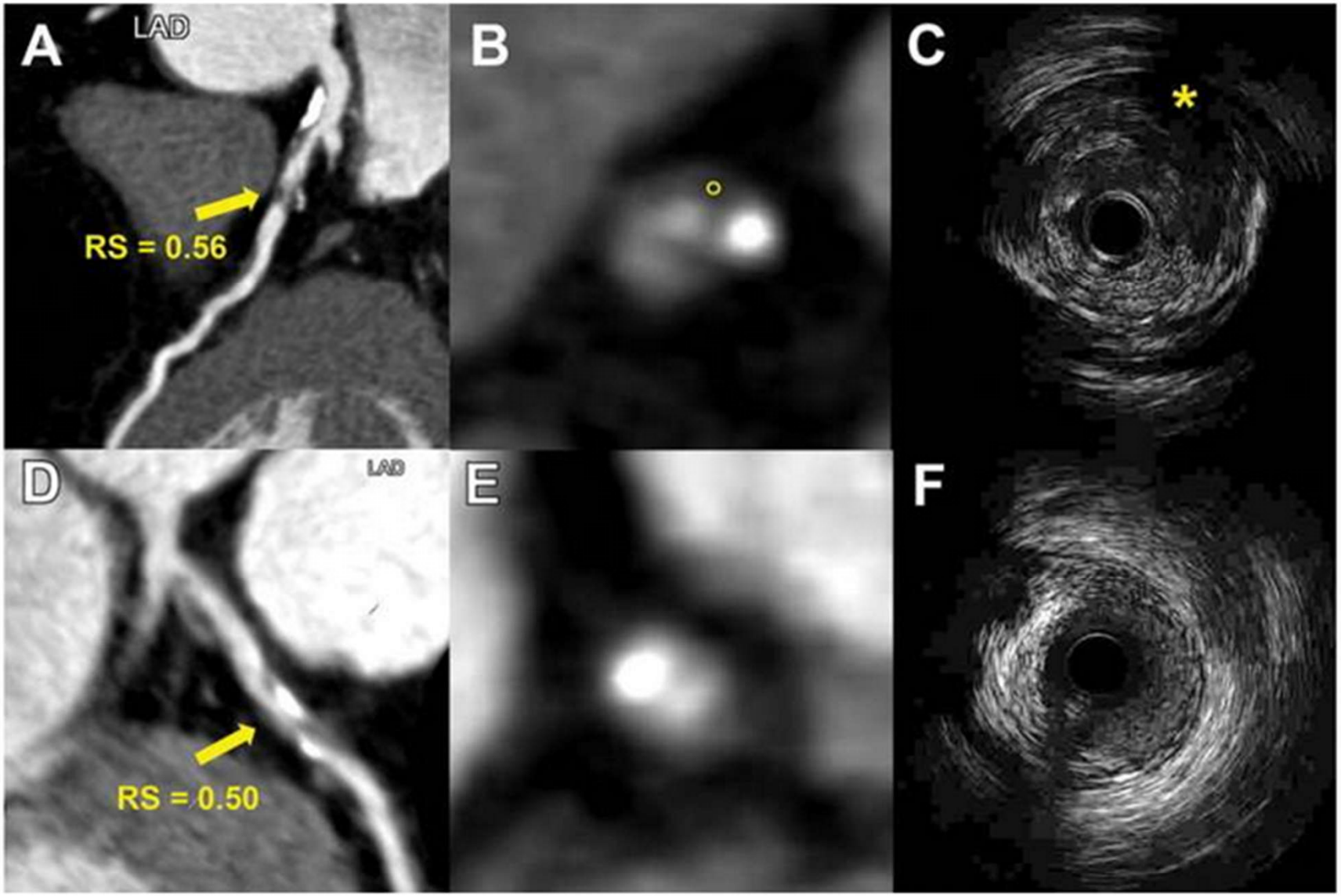
Researchers use radiomics to predict heart attacks

by Radiological Society of North America



Representative images from two patients demonstrate the use of a radiomic signature (RS) to discr...

Researchers are using an approach called radiomics to predict future cardiac events like heart attacks, according to a study published in *Radiology*. Radiomics allows researchers to extract quantitative, or measurable, data from CT images that can reveal disease characteristics not visible in the images alone.

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COMMENTARY | ARTICLES IN PRESS

Clinical Utility of Routine Use of Fungal Blood Cultures

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autopsy-proven infection. [1] This knowledge is useful in addressing the general misconception that *Candida spp* are slow-growing. At the present time, routine blood-culture techniques and the previously described lysis-centrifugation method are essentially equivalent in the clinical assessment of suspected candidemia.[6]

In modern clinical practice, a clinician might consider ordering fungal blood cultures as part of a comprehensive infectious evaluation for fever or a systemic inflammatory syndrome, often seeking an answer when routine blood cultures do not isolate a causative pathogen by attempting to identify a pathogenic fungus. Another reason that fungal blood cultures might be ordered is for diagnostic evaluation in certain immunocompromised hosts, when *Cryptococcus*, *Histoplasma capsulatum* or other opportunistic molds might cause disease more frequently. However, fungal blood cultures are often ordered without knowledge of the culture process, indications, and limitations when interpreting test results. As described earlier, *Candida spp* can be readily identified via routine blood cultures. Other fungal infections such as histoplasmosis and coccidioidomycosis can be diagnosed by utilizing a thorough history and physical exam, laboratory and radiographic findings, targeted advanced diagnostics, such as fungal antigen and serological testing, and, in certain instances, histopathological examination of tissue specimens.[1] For example, *Histoplasma capsulatum* can be diagnosed with the urine antigen test with high sensitivity, and the sensitivity and specificity of the serum *Cryptococcus* lateral flow assay for antigen detection are both 98%.[7] In addition, a negative fungal blood culture can also provide false reassurance during clinical assessment. The test result might be a false-negative, as the

THE END