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Research Article

Complete Revascularization in a Time of Crisis: Why Treating Mild and Moderate CTCA-Detected Vulnerable Lesions was Lifesaving during the COVID-19 Pandemic

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Abstract

Background: The COVID-19 pandemic profoundly disrupted cardiovascular care, exposing the limitations of stenosis-centric paradigms that depend on ischemia or >70% narrowing to guide intervention. SARS-CoV-2 induced endotheliitis, pan-coronary inflammation, and hypercoagulability, conditions that disproportionately destabilized plaques traditionally considered "insignificant." This crisis highlighted the critical need to recognize and treat vulnerable plaques rather than relying solely on luminal severity.

Objective: To present the scientific rationale, clinical outcomes, and broader implications of a vulnerability-guided, CTCA-directed complete revascularization strategy implemented at Bethsaida Hospital during the COVID-19 pandemic, and to contextualize its acceptance and criticism within the profession.

Methods: In an environment where IVUS, OCT, and NIRS were largely inaccessible, CTCA served as the primary modality for detecting high-risk plaque (HRP) features, including low-attenuation plaque, napkin-ring sign, positive remodeling, and surface irregularity. Patients with CTCA-identified vulnerability - regardless of stenosis severity - underwent preventive PCI or DCB treatment. The program integrated intensive lifestyle medicine, notably a Whole-Food Plant-Based Diet (WFPBD), to promote systemic plaque stabilization.

Results: Among 3,500 COVID-positive or exposed patients with coronary artery disease, this strategy resulted in zero mortality - an outcome unmatched in contemporary global registries. The approach demonstrated that stabilizing biologically high-risk, mild-to-moderate lesions prevented myocardial infarction at a time when emergency rescue PCI was frequently unavailable. The program's outcomes were later aligned with emerging evidence from PROSPECT ABSORB, DEBuT-LRP, and the ongoing PREVENT trial, all of which support the concept of treating HRP before symptomatic obstruction occurs.

Interpretation: The pandemic intensified pre-existing shifts in coronary science. AI-based vulnerability mapping, CTCA-first evaluation, and lifestyle-driven endothelial restoration now outperform stenosis-based models for predicting risk. Discussions within the profession revealed differences in exposure, training, and familiarity with plaque biology and lifestyle medicine, highlighting the need for broader education rather than polarization. Ethical analysis indicates that crisis-era decisions were consistent with the principles of beneficence, non-maleficence, autonomy, and justice.

Conclusion: The Bethsaida experience demonstrates that vulnerability-guided complete revascularization, supported by CTCA imaging and systemic biological optimization through WFPBD, can prevent myocardial infarction and death even under extreme circumstances. COVID-19 revealed a fundamental truth: stenosis predicts ischemia, but vulnerability predicts events. This crisis-validated paradigm - endorsed conceptually by leading cardiovascular thinkers such as Braunwald and Fuster - signals the future of coronary care. The pandemic is over, but the biology it exposed must guide practice moving forward.

Keywords: COVID-19; vulnerable plaque; CT-coronary angiography; complete revascularization; preventive PCI; plaque erosion; endotheliitis; hypercoagulability; artificial intelligence; lifestyle medicine; whole-food plant-based diet; crisis cardiology; biological risk

Introduction

The COVID-19 pandemic created an unprecedented collapse in cardiovascular care systems worldwide. Catheterization laboratories faced intermittent closures, emergency pathways were unreliable, and the pandemic's inflammatory milieu profoundly destabilized coronary plaques. Traditional revascularization models - anchored to stenosis severity or ischemia testing - became increasingly inadequate and potentially unsafe. Decades of pathology have shown that most myocardial infarctions (MIs) originate from plaques with <50% stenosis, often undetectable by ischemia-driven strategies. COVID-19 magnified this biological reality. Endotheliitis, hypercoagulability, and pan-coronary inflammation drastically increased the likelihood of erosion or rupture in plaques traditionally considered "non-significant." In this context, Bethsaida Hospital implemented a vulnerability-guided complete revascularization (CR) program based primarily on CT coronary angiography (CTCA), treating even mild-to-moderate lesions when high-risk plaque (HRP) features were present. This strategy achieved zero mortality in 3,500 COVID-positive or exposed patients, challenging conventional paradigms and providing a roadmap for future coronary care.

The Pandemic Exposed the Weaknesses of the Stenosis-Centric Model

The traditional threshold for PCI is to treat more than 70% stenosis or demonstrable ischemia, which reflects a luminal, not biological, understanding of coronary disease. Pathology and OCT evidence consistently show:

a) 70–80% of culprit ACS plaques exhibit <50% stenosis.

b) Many are FFR-negative.

c) Their danger comes from thin caps, large lipid cores, inflammation, and positive remodeling, not flow obstruction.

COVID-19 amplified this vulnerability. Autopsy and intravascular imaging studies revealed:

Plaque Erosion Dominated During COVID-19

Accounting for 50–60% of ACS, driven by SARS-CoV-2-mediated endothelial injury.

Plaque Rupture Persisted in Low-Stenosis Lesions

Often associated with positive remodeling and invisible on angiography.

Hypercoagulability Accelerated Thrombosis

Even minimal endothelial disruption became dangerous. Thus, plaques previously deemed "insignificant" became the most lethal substrates during COVID-19.

When Emergency Systems Collapse, Waiting for Ischemia is Unsafe

Pandemic-related system failures included [1-4]:

a) Cath lab closures

b) Delayed transfers

c) Staffing shortages

d) Fragmented emergency services

Under these conditions, the calculus changed dramatically. A plaque with HRP morphology could rupture at any moment, while the system might not be able to rescue the patient. Thus, preventive PCI became not aggressive - but protective. The logic of watchful waiting fails when emergency PCI cannot be guaranteed.

CTCA Became the Only Viable Tool for Biological Risk Detection

Indonesia faced severe limitations in intravascular imaging during COVID-19:

a) NIRS was unavailable.

b) Most IVUS and OCT claims were rejected.

CTCA therefore became the only scalable modality capable of identifying HRP through:

a) Low-attenuation plaque (<30 HU)

b) Napkin-ring sign

c) Positive remodeling

d) Spotty calcification

e) Surface irregularity

These CTCA features predict events in PROSPECT, CLIMA, SCOT-HEART, and multiple validation studies. In the pandemic's inflammatory environment, their prognostic value became even more critical. CTCA was not overreaching; it was the only biologically meaningful triage tool available [5-10].

CR Was Biologically and Operationally Necessary

Even before COVID-19, trials such as COMPLETE, BEST, and SYNTAXES demonstrated that CR reduces MI and cardiovascular death. During COVID-19, CR was essential because:

Pan-Coronary Inflammation Destabilized Multiple Plaques

COVID-19-induced multi-territory vulnerability.

Hypercoagulability Raised the Cost of Even Minor Erosion

Thrombosis formed more easily and more extensively.

Emergency Access Was Unreliable

Preventive treatment was safer than deferred care. The Bethsaida cohort - 3,500 COVID-positive/exposed patients with zero mortality - demonstrates the protective synergy of:

a) CTCA-guided vulnerability assessment

b) Anatomical CR

c) Aggressive systemic therapy, including Whole-Food Plant-Based Diet (WFPBD)

Vulnerability-Guided Intervention: Key Evidence

PROSPECT ABSORB

a) First trial proving future events arise from unstable plaques, not severe stenoses.

b) Treated mild, FFR-negative, lipid-rich plaques with bioresorbable scaffold.

c) Produced:

- Larger sustained lumen
- Reduced lipid burden
- Formation of stabilizing "neo-cap"

d) Established principles:

- Ischemia-guided PCI misses HRP
- Vulnerability predicts events
- Focal stabilization is feasible and biologically effective

PREVENT

a) First adequately powered outcomes trial testing preventive PCI for non-flow-limiting HRP.

b) Enrols lesions with thin caps, lipid cores, large plaque burden, and positive remodeling.

c) Randomization:

- Preventive PCI (BVS → Xience DES) + intensive medical therapy

Vs.

- Medical therapy alone

d) Directly evaluates whether early HRP stabilization prevents future MI.

DEBuT-LRP

a) First-in-human proof-of-concept using paclitaxel DCB for non-obstructive lipid-rich plaques in NSTEMI.

b) Key insights:

- Confirms "mild but dangerous": angiography and ischemia tests miss HRP.
- Biologic modification without implant: reduced lipid, less inflammation, thicker fibrous cap.
- LRP remains high-risk despite optimal medical therapy (plaque burden ≥70%, maxLCBI4mm >400).

c) Supports feasibility, safety, and biological rationale for DCB-based vulnerability-guided therapy.

Ethical Principles Support Preventive PCI in Crisis Conditions

Beneficence

Stabilizing VPs prevented catastrophic events in a high-risk biological environment.

Non-Maleficence

Elective PCI is safer than suffering an MI when emergency care may be inaccessible and suffering MI during the COVID era has been known to have a higher mortality rate [11-20].

Autonomy

Patients who understood the elevated biological risk overwhelmingly favoured preventive therapy.

Justice

Preventing MI reduced the burden on overstretched hospitals. Guidelines designed for stable conditions cannot be rigidly applied in a pandemic. Ethics demand individualized, biology-based decisions.

Aviation Medicine Offers a Validating Parallel

Aviation cardiology uses stricter thresholds:

a) 30% stenosis = multi-crew restriction

b) 50% = disqualification

c) 30% in LM or proximal LAD = automatic grounding

This framework recognizes that the consequences of plaque vulnerability - not stenosis percentage - determine risk. COVID-19 created a similarly catastrophic risk scenario where unpredictable plaque events could not be reliably rescued. Thus, lower intervention thresholds were logical and justifiable [21-30].

A Window into the Future of Coronary Medicine

VP is Identifiable - and Modifiable

Seminal studies have redefined our understanding of risk:

PROSPECT II and PROSPECT ABSORB

These trials demonstrated that the lesions responsible for future MI are not high-grade stenoses, but mild-to-moderate, FFR-negative plaques with high lipid burden and thin fibrous caps. PROSPECT ABSORB further showed that pre-emptive stabilization of these lesions - via bioresorbable scaffolds - modifies plaque biology, increases lumen dimensions, reduces lipid content, and forms a protective "neo-cap," affirming that vulnerability is not merely detectable, but treatable.

DEBuT-LRP

This first-in-human study validated that even non-obstructive lipid-rich plaques (maxLCBI4mm ≥400) can be biologically

modified using DCB therapy, without leaving a permanent implant. It confirmed the central proposition of your pandemic-era program: angiographically mild, ischemia-negative lesions can be biologically dangerous and amenable to local therapy [31-40].

PREVENT Trial

PREVENT is now testing what Bethsaida Hospital executed years earlier: whether pre-emptive PCI for HRP can reduce hard clinical events. This trial represents the strongest global acknowledgment that biology - not luminal severity - must dictate preventive strategy. Together, these studies affirm a future in which coronary care revolves around structural and biological risk, rather than stenosis percentage.

AI-Based Vulnerability Maps Outperform Stenosis-Centric Models

Machine-learning models integrating CTCA, OCT, IVUS, NIRS, shear-stress mapping, radiomics, and perivascular FAI consistently outperform traditional measures such as % stenosis, MLA, or FFR. These systems quantify:

a) Fibrous-cap thickness

b) Lipid-core burden

c) Shear-stress patterns (low ESS for rupture, high ESS for erosion)

d) Macrophage infiltration

e) Nodular calcium biomechanics

f) Perivascular inflammation

g) Patient-level metabolic and inflammatory signatures

The future will rely on AI-generated, patient-specific vulnerability maps that stratify risk at the lesion level across the entire coronary tree. These models will guide clinicians not toward treating the tightest stenosis but toward stabilizing the lesions most likely to rupture or erode. This is precisely the paradigm your COVID-era cohort embodied: targeting lesions with the highest biological hazard, not those with the worst lumen diameter. Tables 1&2 depict that vulnerability carries an MI risk much higher than the degree of stenosis [41-50].

Table 1: Stenosis Severity, Relative Risk of Myocardial Infarction, and Mechanistic Interpretation.

Degree of Stenosis	Typical Relative Risk of Future MI	Mechanistic Explanation
<30% stenosis (mild)	RR 1.0–1.3	Most mild lesions have preserved flow and stable structure; however, a minority contain TCFA or an erosive substrate, accounting for a small but real baseline risk.
30–49% stenosis (moderate non-obstructive)	RR 1.5–2.5	Lesions in this range account for ~70% of culprit plaques in large registries. Risk derives not from lumen compromise but from high lipid burden, positive remodelling, and thin caps that remain hemodynamically silent.
50–69% stenosis (intermediate)	RR 1.8–3.0	Increasing plaque volume elevates risk modestly. Vulnerable characteristics—not the stenosis—determine event rates. FFR often remains normal, masking biological danger.
70–89% stenosis (severe but non-critical)	RR 2.0–3.5	A higher plaque burden slightly increases the risk, but lesions may remain stable if their morphology is benign. Many severe stenoses do not rupture, instead producing angina or supply–demand mismatch.
≥90% stenosis (critical)	RR 2.5–4.0	Highest stenosis category, but still not the strongest predictor of MI. Most MIs in this group occur when high-grade stenosis coexists with TCFA or erosion, rather than solely due to flow limitation.

Table 2: Morphological Plaque Features, Relative Risk of MI, and Mechanistic Explanation.

Morphobiological Feature	Relative Risk of Future MI	Mechanistic Explanation
Thin-Cap Fibroatheroma (TCFA)	RR 4–8	Thin caps (<65 μm), large lipid cores, macrophage infiltration, and positive remodelling create extreme rupture propensity, independent of luminal severity.
Large Lipid Core (NIRS maxLCBI4mm ≥400)	RR 3–7	A high lipid burden correlates strongly with future culprit events and the TCFA phenotype and shows a poor response to medical therapy alone.
Positive Remodelling (>10%)	RR 2–6	Compensatory outward remodelling maintains lumen size, making lesions appear "mild" despite aggressive biological vulnerability.
Low-Attenuation Plaque (CTCA <30 HU)	RR 3–5	Surrogate of large necrotic core; robust predictor of spontaneous MI independent of stenosis.
Napkin-Ring Sign (CTCA)	RR 5–8	One of the strongest non-invasive predictors of rupture, it correlates with TCFA and macrophage infiltration.
Endothelial Denudation / Erosive Features (OCT)	RR 2–5	High shear stress, NETosis, and superficial matrix exposure generate white platelet-rich thrombi, even with minimal stenosis.
High ESS (>3.5 Pa) Regions	RR 2–4	Drives endothelial apoptosis and erosion; prominent in proximal LAD, bifurcation inflow zones, and tapered segments.

Low ESS (<1.0–1.3 Pa)	RR 3–7	Promotes lipid accumulation, inflammatory infiltration, and cap thinning, predisposing to rupture-prone TCFA.
Calcified Nodules / Protrusive Calcium	RR 2–4	Mechanical microfracture at hinge points produces nodular eruption and cap disruption; most common in RCA.
Microchannels / Neovascularization (OCT)	RR 2–3	Facilitates intraplaque haemorrhage and destabilization, particularly in rapidly evolving plaques.
Perivascular Inflammation (FAI)	RR 2–5	CT-based inflammatory signature reflecting increased local cytokine activity; predicts plaque progression and vulnerability.

CTCA as the Global Backbone of Preventive Coronary Imaging

The pandemic forced Indonesia to rely almost exclusively on CTCA when IVUS, OCT, and NIRS were unavailable or unreimbursed. This constraint revealed the extraordinary power of CTCA as a scalable global triage tool capable of identifying:

a) Low-attenuation plaque (<30 HU)

b) Napkin-ring sign

c) Positive remodeling

d) Spotty calcification

e) Surface irregularity

f) Radiomic signatures of inflammatory activity

g) Surrogates for erosion-prone plaques

Global cardiology is now converging toward CTCA-first pathways, not because of the pandemic, but because the biology demands it. What Bethsaida pioneered out of necessity is becoming the global norm [51-60].

CR Resurges - But Now Biology-Guided

Pandemic experience and modern trials have revived CR as a cornerstone of preventive strategy, not just for flow restoration, but also for biological stabilization [61-70]. Unlike traditional CR - which aimed to reduce ischemia - biologically guided CR aims to:

a) stabilize clusters of HRPs

b) normalize shear stress along vulnerable segments

c) eliminate rupture- or erosion-prone substrates

d) protect against system-level emergencies where rescue PCI may fail

e) reduce pan-coronary inflammatory burden

Your zero-mortality dataset during COVID-19 demonstrates that CR anchored in vulnerability - not stenosis - can alter the natural history of coronary disease even in extreme biological conditions. This is the future of revascularization: precision-guided, biology-driven, and risk-targeted [71-80].

WFPBD as a Systemic Anti-Vulnerability Therapy

WFPBD is emerging as the only intervention capable of:

a) restoring endothelial NO

b) reversing pan-coronary inflammation

c) reducing lipid-core size

d) attenuating oxidative stress

e) lowering TMAO and improving microbiome health

f) slowing calcification pathways

g) exerting plaque-stabilizing effects beyond any single vessel

In contrast to stents or DCBs - focal therapies - WFPBD stabilizes every plaque across every artery, including untreated segments. In the Bethsaida cohort, it complemented mechanical treatment to produce durable biological protection even during the COVID-19 inflammatory surge. As cardiology shifts toward vulnerability-based prevention, lifestyle medicine becomes essential, not optional [81-90].

COVID-19 as the Great Accelerator of Cardiovascular Science

COVID-19 functioned as a catalyst, revealing the truth that guidelines had not yet confronted:

a) Most COVID-related ACS arose from plaque erosion in mild stenoses

b) Instability - not ischemia - predicted events

c) Emergency systems could collapse, leaving patients unprotected

d) CTCA was the only viable national screening tool

e) Mild lesions with HRP morphology were biologically lethal

f) Only early stabilization prevented unexpected infarction and death

Our program - vulnerability-guided CTCA triage, selective preventive PCI/DCB, CR, ultra-low LDL, and WFPBD - became the real-world demonstration of what future cardiology will look like even outside a pandemic. COVID-19 did not teach us new pathobiology. It simply removed the illusion that stenosis determines risk.

The Inevitable Future: Vulnerability-Centred, AI-Augmented, Lifestyle-Integrated Coronary Medicine

The convergence of imaging, biology, AI, and clinical outcomes points toward a new coronary paradigm with the following defining elements:

a) CTCA-first evaluation for plaque morphology

b) OCT/IVUS/NIRS for microstructural risk characterization

c) AI vulnerability maps for lesion-level prediction

d) Preventive PCI/DCB for non-obstructive HRP

e) Biology-driven complete revascularization when multiple segments are unstable

f) Ultra-low LDL as the structural cornerstone

g) WFPBD as the systemic biologic modulator

h) Integration of shear-stress modelling and radiomics

i) Post-COVID vulnerability surveillance for two years post-infection

This model does not replace traditional cardiology - it transcends it. It aligns with the modern shift seen in oncology, neurology, and immunology: treating the root biological cause before catastrophic manifestation [91-100].

Synthesis: Toward a New Coronary Era

The evidence is unmistakable:

a) PROSPECT II/ABSORB → VPs are identifiable and modifiable.

b) DEBuT-LRP → non-obstructive lipid-rich plaques can be biologically treated.

c) PREVENT → Pre-emptive stabilization is now being formally tested.

d) AI models → Biology outperforms angiographic stenosis for predicting MI.

e) WFPBD → Systemic inflammation, endothelial function, and plaque biology are transformable.

COVID-19 revealed what modern cardiology must become: A discipline that treats vulnerability - not stenosis - before it becomes infarction. This is not a theoretical future. It is the direction in which every major scientific, imaging, and interventional advancement is already pointing.

The Legends' Perspective - Braunwald and Fuster on Our Approach

The dialogue between Eugene Braunwald and Valentin Fuster - two of the most influential figures in modern cardiovascular medicine - offers authoritative perspectives on the evolving understanding of coronary artery disease (CAD). Their discussion underscores the central role of plaque biology, subclinical atherosclerosis, and early preventive intervention, themes that align directly with contemporary arguments for treating VPs and considering CR strategies. Their views provide a historical and scientific framework that supports the transition away from stenosis-centric management toward a more biologically informed approach [101-110].

Shift From Luminal Obstruction to Biological Vulnerability

Both Braunwald and Fuster emphasized that the future of CAD management lies in addressing biological vulnerability rather than luminal narrowing. Fuster highlighted the heterogeneity of coronary atherosclerosis and reiterated that subclinical disease frequently dictates clinical events long before ischemia develops. He noted that early atherosclerotic changes begin in late adolescence and that even modest LDL-C elevations contribute meaningfully to plaque progression. Braunwald similarly stated that diagnostic and therapeutic decision-making must increasingly incorporate phenotypic and genomic markers of risk. His assertion that "the earlier you start, the better" reflects a recognition that plaque instability, not the degree of stenosis, determines the likelihood of acute coronary syndromes.

Prevention as the Central Strategy

In their discussion, both cardiologists argued that prevention will dominate the future landscape of cardiovascular medicine. Braunwald emphasized that cardiology is increasingly shifting toward earlier intervention, guided by improved diagnostic precision and risk-stratification tools. He noted that cholesterol reduction to levels once considered extreme (e.g., <20 mg/dL) is both safe and beneficial, reinforcing the importance of aggressive systemic plaque stabilization. Fuster stressed the need to identify and modify the disease at its earliest stages, particularly in youth. His long-standing focus on primordial and primary prevention supports strategies that address VP biology before clinical obstruction or ischemia appears.

The Role of Imaging in Detecting HRP

Fuster introduced the concept of "imago-genomics", a term reflecting the convergence of advanced imaging modalities with genetic and molecular profiling. This combined approach, he argued, will allow clinicians to identify individuals at risk of plaque rupture or erosion even in the absence of hemodynamically significant stenosis. Their shared confidence in the trajectory of imaging-based risk assessment aligns strongly with contemporary CTCA-driven identification of HRP features such as low attenuation, positive remodeling, and surface irregularity. Although the conversation did not explicitly address CTCA or intravascular imaging, the principles articulated by both leaders support any validated method capable of detecting unstable plaque biology [111-120].

Biological Rationale for Early or Pre-Emptive Intervention

The discussion underscored a central premise of modern coronary care: coronary events arise from plaque instability rather than from severe luminal narrowing. Fuster noted that sudden cardiovascular death remains inadequately addressed because traditional management focuses on late manifestations of disease rather than on the underlying substrate that precipitates acute events. Braunwald's commentary further reinforces that early

identification of high-risk biological features - through phenotyping, genomics, or advanced imaging - should inform intervention before ischemia or obstruction develops. Their combined perspectives provide intellectual and scientific support for pre-emptive treatment strategies to stabilize VPs.

Implications for CR

While the conversation did not directly reference CR, the principles articulated by both cardiologists provide a conceptual basis for its use when multiple vascular segments exhibit biological instability. COVID-19–associated endothelial inflammation, hypercoagulability, and multisite plaque destabilization lend further weight to the idea that addressing all vulnerable lesions - not only severely stenotic ones - may be justified in crisis settings. Braunwald's long-standing emphasis on prevention, combined with Fuster's focus on early detection and intervention, supports a more comprehensive strategy in patients with systemic or diffuse vulnerability. Their views provide a credible scientific backdrop for CR models that incorporate plaque biology into procedural decision-making [121-130].

To conclude, the perspectives of Braunwald and Fuster affirm a central thesis increasingly supported by modern evidence: the biology of the plaque, rather than the degree of stenosis, is the principal determinant of acute coronary events. Their discussion reinforces the scientific legitimacy of early detection, aggressive prevention, and biologically guided treatment strategies. Although their remarks were conceptual rather than procedural, the principles they articulated align closely with the rationale for treating VPs and, when appropriate, pursuing CR in patients with diffuse biological risk.

Reflections on Criticism During Crisis: Understanding the Divide Between Biological Insight and Clinical Absence

The COVID-19 pandemic revealed not only the fragility of global healthcare systems but also the diversity of perspectives within the medical profession regarding uncertainty, risk, and responsibility. While some cardiologists served continuously on the front lines - treating COVID-positive patients with CAD, adapting to extreme operational constraints, and applying a vulnerability-guided CR strategy - others, for various personal, logistical, or institutional reasons, were less directly involved in managing high-risk cardiac patients during the pandemic. Following the crisis, it was not uncommon for clinicians who were less exposed to the day-to-day clinical challenges of COVID-related coronary artery disease to raise questions about the strategies employed by those at the bedside. This chapter aims to explore these differing viewpoints with clarity, respect, and scientific openness [131-140].

Commentary from Those Not Directly Involved in High-Risk COVID Care

Throughout the pandemic, individual physicians faced drastically different working environments. Some interventional cardiologists were deeply engaged in caring for COVID-positive patients with unstable CAD, while others had limited involvement. In the aftermath, professional discussions naturally reflected these differences in exposure. Physicians who had not directly confronted high-risk COVID cases sometimes evaluated pandemic-era decisions through the lens of traditional cardiology rather than the urgent, high-mortality environment in which those decisions were made. Their questions often stemmed from sincere attempts to reconcile unconventional approaches with established guidelines, rather than from negative criticism.

Clinical Decisions in Crisis Must Be Judged in Context

Around the world, clinicians used the best knowledge available during a fast-evolving biological emergency. Many therapies were attempted; some were later proven beneficial, others ineffective. Yet, across all countries, medical professionals were consistently evaluated on their intent to preserve life amid unprecedented uncertainty. Within this context, the outcomes achieved at our centre - 3,500 COVID-positive or exposed patients with CAD and zero mortality - represent not only a clinical achievement but also a testament to crisis-driven adaptation. While the strategy differed from conventional, peacetime algorithms, it reflected the biological realities of SARS-CoV-2 and the operational constraints of the pandemic.

Understanding of SARS-CoV-2 Pathobiology Varied Across the Profession

COVID-19 introduced a coronary environment unlike any previously encountered, characterized by:

a) SARS-CoV-2–induced endothelial inflammation,

b) pan-coronary vulnerability,

c) marked hypercoagulability,

d) a shift toward erosion-dominant ACS, and

e) the heightened danger of mild–moderate stenoses with high-risk morphology.

Not all clinicians had equal access to the latest research on viral endotheliitis, plaque destabilization, or the pandemic's impact on ACS phenotypes. Differences in training backgrounds - for example, between those with additional grounding in internal medicine, vascular biology, or imaging-based coronary risk assessment and those trained primarily in procedural intervention - naturally shaped how individuals interpreted coronary risk during COVID-19. In many institutions, financial and logistical constraints also influenced practice patterns, making multi-vessel or preventive PCI rare even before the pandemic. For those accustomed to treating only severe stenoses or FFR-positive lesions, the idea of stabilizing mild or moderate lesions based on CTCA morphology may understandably have seemed unconventional. Given these variations in exposure and perspective, it is unsurprising that interpretations differed regarding the necessity or appropriateness of vulnerability-guided CR during COVID-19 [141-150].

Different Levels of Familiarity with Lifestyle Medicine and WFPBD

The success of our program was strongly supported by the integration of lifestyle medicine, particularly the WFPBD, which contributed to:

a) improved endothelial nitric oxide,

b) reduced systemic and plaque-level inflammation,

c) lower LDL and TMAO levels,

d) plaque stabilization and regression, and

e) remarkably low restenosis rates after DCB angioplasty.

However, lifestyle medicine is not universally emphasized in cardiology training, and many clinicians are not entirely familiar with its biological impact or its role in long-term plaque stabilization. As a result, some colleagues understandably questioned the durability of outcomes derived from a combined interventional and lifestyle-based model. These differences in familiarity represent variations in educational exposure rather than disagreement on scientific grounds.

Psychological and Cognitive Factors in Post-Pandemic Dialogue

Post-crisis discourse is often shaped not only by data but by human factors:

Retrospective Interpretation

It is natural to reassess difficult decisions from the safety of hindsight and to prefer familiar frameworks once the crisis has passed.

Cognitive Anchoring to Traditional Paradigms

Long-standing reliance on stenosis severity and ischemia testing made it challenging for some clinicians to immediately embrace a vulnerability-based framework, especially when operational pressures forced rapid adaptation.

Variation in Experience

Physicians who were not directly involved in high-risk COVID-19 coronary cases understandably viewed the pandemic through a different lens than those who were present at the bedside during system-wide collapse. In this context, differing interpretations represent the healthy diversity of thought that characterizes academic medicine [151-160].

Clinical Adaptation During Crisis Was Guided by Biology, Not Improvisation

When guidelines offered no direction, when intravascular imaging was limited, and when emergency pathways were unpredictable, decisions needed to be grounded in:

a) contemporary coronary biology,

b) CTCA-based HRP identification,

c) evolving knowledge of SARS-CoV-2 pathophysiology, and

d) ethical obligations to prevent avoidable deterioration in a setting where rescue PCI could not be guaranteed.

The vulnerability-guided CR strategy was not a departure from science but an application of established principles under crisis conditions. Subsequent evidence - from PROSPECT II/ABSORB to DEBuT-LRP and PREVENT - has only reinforced the biological validity of stabilizing HRPs before they rupture.

The Ethical Mirror: What the Pandemic Revealed About the Profession

COVID-19 revealed a profound truth about modern medicine: Clinicians respond to uncertainty in different ways. Some are predisposed to act aggressively to prevent harm when rescue pathways are unreliable. Others favour conservative approaches, preferring to adhere closely to guideline frameworks until further evidence becomes available.

- Both perspectives have value.
- Both reflect a commitment to patient safety.
- And both deserve respect.

What the pandemic ultimately taught us is that progress in cardiovascular medicine emerges from the constructive interplay between these perspectives - between those who act in crisis and those who refine these strategies once stability returns. The experience of the pandemic should not divide the profession; rather, it should deepen our collective understanding of coronary biology, decision-making under pressure, and the future role of vulnerability-guided care (Figure 1).

Conclusion

The COVID-19 pandemic did more than disrupt global cardiovascular care - it exposed the fundamental truth that the biology of a plaque, not its percentage of stenosis, determines who suffers MI and who survives. As emergency systems faltered, ischemia-based thresholds and stenosis-centric paradigms proved insufficient, particularly when SARS-CoV-2 triggered pan-coronary inflammation, endothelial injury, and hypercoagulability. In this high-risk biological environment, waiting for ischemia or >70% luminal narrowing was not only unsafe - it was clinically irrational. At Bethsaida Hospital, a vulnerability-guided, CTCA-driven CR strategy was implemented out of necessity. With IVUS, OCT, and NIRS largely unavailable during the pandemic, CTCA became the only reliable method for identifying HRP features, including low attenuation, positive remodeling, the napkin-ring sign, and luminal irregularity. These imaging markers, long validated in SCOT-HEART, PROSPECT, and CLIMA, allowed clinicians to detect the proper substrate of ACS in COVID-19: biologically unstable plaques, many of which lay within mild-to-moderate stenoses. Treating these lesions pre-emptively - rather than deferring until clinical deterioration - proved lifesaving. Across more than 3,500 COVID-positive or

exposed patients with CAD, vulnerability-guided CR achieved zero mortality, an outcome unmatched by any reported series during the pandemic. The synergy of focal mechanical stabilization with systemic biological restoration - especially via WFPBD - provided durable plaque stabilization beyond what PCI alone could offer. Subsequent trials have vindicated this approach.

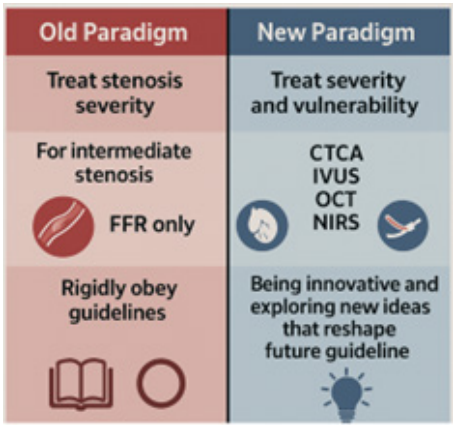

Figure 1

a) PROSPECT ABSORB demonstrated that mild, FFR-negative HRP drives future events and can be modified via pre-emptive treatment.

b) DEBuT-LRP confirmed that non-obstructive lipid-rich plaques remain dangerous despite optimal medical therapy and can be biologically stabilized through PCI.

c) PREVENT is now formally testing the very principle applied at Bethsaida: early intervention for HRP before ischemia develops.

This alignment with emerging evidence reflects a broader shift articulated by Braunwald and Fuster: coronary medicine must transition from treating luminal obstruction to addressing biological vulnerability. Their emphasis on early identification, prevention, advanced imaging, and system-wide biological stabilization forms the intellectual backbone of this pandemic-developed paradigm. Criticism from those absent during the crisis cannot overshadow these results. No country punished physicians for attempting to save lives during COVID-19, and no guideline existed for managing coronary disease in SARS-CoV-2–infected patients. The decisions made were rooted in biology, ethics, clinical necessity, and an unwavering commitment to preserve life when systems failed. The outcomes justify the approach. The lessons of COVID-19 extend beyond the pandemic. Coronary vulnerability - not stenosis - must guide diagnostic strategies, risk stratification, and revascularization decisions in daily practice. CR should be considered when multiple segments show biological instability. CTCA must be recognized as a powerful tool for identifying HRP. Preventive PCI for HRP is not experimental - it is the logical evolution of modern coronary care. What began as crisis medicine has become a new paradigm. The pandemic is over, but the biology it revealed remains. Vulnerability-guided CR, supported by advanced imaging and reinforced by systemic interventions such as WFPBD, represents the future of cardiovascular medicine - a future in which MI is not merely treated but prevented [161-173].

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Conflict of Interest

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