CLEERLY CARE PATHWAY

Transforming heart health through a personalized approach to heart attack prevention.

cleerly

Cleerly Care Pathway

Introduction

The current approach to cardiovascular care is flawed for two reasons. One is the lack of a disease-based care paradigm with a focus on actual heart disease – atherosclerosis – in lieu of an emphasis on symptom-driven care that identifies only late-stage disease presentations and relies upon surrogates of heart disease rather than heart disease itself. The second is the lack of a personalized care pathway for coronary artery disease diagnosis and treatment. The result is an approach that leaves far too many high-risk patients undiagnosed because they don't present with stereotypical symptoms, whilst subjecting many symptomatic patients to expensive and invasive procedures that are in fact unnecessary because they have little buildup of arterial plaque.

Cleerly's personalized care pathway for heart attack prevention, backed by nearly two decades of clinical research as well as industry-leading AI technology, addresses both issues. Cleerly steadfastly focuses on measuring, characterizing, and tracking atherosclerosis instead of searching for less useful indirect markers of heart disease. The Cleerly Care Pathway provides a methodology for staging and treating heart disease that's modeled after the way healthcare has addressed cancer and common chronic conditions for decades. Through this care pathway, Cleerly is positioned to make high-value, personalized, and precision cardiovascular care available to far more patients - and effectively treat the disease that kills more people globally than any other.

"If you don't have chest pain, then you're probably OK."

Today's symptom-focused approach to cardiovascular care is dangerously flawed but we have the tools to change it

cleerly

A personalized approach to heart attack prevention

Heart disease is caused by atherosclerosis – accumulation of plaque (fat, cholesterol, calcium, and other materials) within the arteries. The plaque may lead to chronic narrowing of the arteries leading to a reduction in blood flow and ensuant chest pain and other symptoms, or acute events causing myocardial infarction, also known as a heart attack. For far too long though, healthcare providers have addressed heart disease by identifying and treating its indirect measures and risk factors– such as cholesterol, blood pressure and narrowing–rather than focusing on the actual disease itself that causes the narrowing.

Data shows that this approach isn't working. We miss more than half of patients who suffer a heart attack because they're considered "low risk" based on symptoms¹ (and may appear to be the picture of perfect health) but in fact have a plaque build-up. A stress test can aim to determine through indirect measures if an artery is more than 70% blocked, but it cannot determine whether a plaque will rupture, form a clot, and occlude an artery.² The average age of a sudden, fatal heart attack is only 50 years,³ compared to the average age of 65 for men and 72 for women for their first nonfatal heart attack.⁴

Current medical practice contributes to significant waste and inefficiency. The traditional approach to heart disease evaluation has focused on surrogates of disease (like cholesterol), symptoms of disease (like chest pain or shortness of breath), or sequelae of disease (like ischemia or stenosis), but not the actual disease process itself - atherosclerosis. Based on clinical research, the majority of coronary lesions that cause heart attack are unpredictably related to these surrogate markers, which results in waiting until end-stage disease begins for cardiovascular evaluation. This approach also mis-identifies the wrong patients: Nearly two of three referrals for invasive evaluation (invasive angiography) of the heart are unnecessary,⁵ 90% of stress tests come back normal,⁶ and roughly half of all stent placements in stable patients are either definitely or possibly inappropriate.⁷

Despite the billions of dollars spent on heart disease research annually, heart disease kills 700,000 Americans every year.⁸ It's the leading cause of death in the United States. It's the equivalent of nine fully loaded 737s crashing and killing everyone on board – every day. Globally, heart disease accounts for 32% of deaths (17.9 million) each year.⁹

"We were never taught to look[△] for disease, and that's really where things have to change. Now, we can not only look for disease, we can see disease, and we can define what kind of disease it is"

cleerly

WITHOUT AN EFFECTIVE AND EFFICIENT STANDARD OF CARE, HEART HEALTH OUTCOMES ARE GRIM

These grim outcomes beg the question: Why has healthcare accepted substandard cardiovascular care for so long? The answer is complicated, but there are five major reasons why.

- △ Current testing strategies lack diagnostic accuracy. Relying on indirect markers of heart disease as opposed to its underlying root cause means that many patients are regarded as high risk when they are actually low risk, and vice versa. This means that patients may need to undergo multiple procedures some invasive, some expensive, and many unnecessary to receive an accurate diagnosis and assessment of their heart health. All too often, patients think they have a clean bill of health when, in fact, they are high risk. Earlier this year, comedian Brad Upton had what he described as a "significant" heart attack a 100% blockage of his right coronary artery just eight months after a treadmill stress test told him he "had the heart of a 20-year-old college soccer player."¹⁰
- Patients don't know enough about heart health. Only 40% of Americans discuss heart health with their primary care physician (PCP), and only 25% know that arterial plaque is what causes a heart attack.¹¹ On the other hand, PCPs tend to have limited knowledge of heart health beyond identifying indirect markers or symptoms, and they likewise have limited experience reading and interpreting radiology reports. Further, many believe there are limited options for treatment (statins, lifestyle modifications) when in fact within the last several years many new and very effective additional medications have become available.
- **Patients need to see several providers to get heart health answers.** When patients talk to their PCP, they're typically referred to a cardiologist for follow-up care. From there, they may have multiple different tests and eventually be referred to an invasive cardiologist to go to the catheterization laboratory for imaging, after which they may be asked to schedule another cardiology appointment to discuss overall results and therapy. This is a fragmented experience, as it requires several patient touchpoints with the healthcare ecosystem to simply determine if they face an elevated risk of heart attack or heart disease.

Personalized care is nearly impossible without a cardiovascular disease staging system. The most prevalent forms of cancer and the most common chronic conditions all have staging systems that provide both a prognosis (disease burden, impact on quality of life, and average life expectancy for someone at that stage of disease progression) and a suggested treatment plan (which can range from lifestyle intervention to drug therapy to surgery). This hasn't been the case for coronary artery disease, and it leaves patients and their care teams on their own to assess disease burden, overall risk, and frequented treatment options.

Fragmented technology adoption leaves many patients unaware of their risk. In today's healthcare system, the technology necessary to administer computer tomography (CT) scans, analyze the results of CT scans, and provide clinical decision support for all members of the care team is largely limited to specialized cardiology centers. While hospital and community imaging centers can conduct CT scans, few offer analysis and decision support specifically tailored to cardiovascular care. As a result, coronary imaging tests are largely reserved for symptomatic patients at tertiary care centers, leaving a significant unmet need for patients who are asymptomatic but at highly elevated risk.

CARDIOVASCULAR CARE **NEEDS A PERSONALIZED APPROACH**

Together, the current system is fragmented, ineffective and inefficient. The diagnosis of heart disease often occurs far too late in the disease process, diagnostic testing is inefficient with too many false positives, and the opportunity to intervene effectively is lost. Reliance on indirect markers of disease misses the opportunity to detect, diagnose, characterize, and personalize treatment of the disease itself. Current standards and methods are ineffective, leading up to 700,000 heart disease deaths per year and adversely impacting nearly 20 million more.¹⁰

Simply put, this is unacceptable for the wealthiest nation in the world and the most well-funded healthcare system. Our physicians – and especially our patients – deserve an approach to cardiovascular care that uses advanced technology to identify patients at risk and leverages a personalized care pathway to identify, define, educate, treat, and track disease, ultimately preventing heart attacks.

Cleerly believes the new standard for cardiovascular care should be coronary CT angiography (CCTA)-based evaluation for atherosclerosis. This aligns with the American College of Cardiology's raising CCTA to a Level 1A in their guidelines for chest pain evaluation.¹² CCTA is a noninvasive method that uses advanced CT technology to determine if plaque has built up in the arteries, what amount of plaque is present, and what type of plaque it is.

This last point is critical: Not all atherosclerosis is the same. Similar to cancers, there are many different types of heart disease. Hard, calcified plaque causes a narrowing of the artery, whereas soft, low-density plaque is the most dangerous, it may rupture and cause a blood clot to form guickly obstructing blood flow and causing a heart attack and even sudden death.^{13, 14} These present different heart health risks and require different treatment options. More traditional methods of diagnosing heart disease, such as stress testing are both less sensitive (therefore miss early disease) and less specific (lead to false positive results) than CCTA, stress testing therefore both gives providers and patients a false sense of security that they are "normal" when they may actually have advanced atherosclerosis, and at other times give false positive results leading to unnecessary invasive testing. CCTA can detect the earliest stages of heart disease, when it is most easily treated and is more accurate in later stage disease, so patients are not subjected to unnecessary invasive imaging at the high rate that stress testing causes.

Shifting diagnosis from symptom-driven to disease-based preventive care is an important step that requires buy-in from clinicians and patients. Both need to be able to understand the results of a CCTA-based evaluation, which requires explanations in plain language and images. They also need to know what those results mean for their care, which requires both a staging system to describe heart disease risk and evidence-based

A personalized approach to heart attack prevention

treatment recommendations that can be tailored to the stage of disease progression and other personal health factors. And they need this information at the point of care, in the moment when a conversation about heart health is already taking place.

Getting all this right requires state-of-the-art technology that comes in two primary forms. First is CCTA scanning that can capture whole-heart imaging in a matter of seconds. Next is cloud-based machine intelligence that can transform the data generated by CCTA scans into actionable insights for clinicians and patients with a turnaround time of less than one hour. With these solutions in place, the healthcare industry will be empowered to implement personalized cardiovascular care enabled by a new care pathway.

INTRODUCING CLEERLY'S PERSONALIZED CARE PATHWAY FOR HEART ATTACK PREVENTION

Prevent

The new Cleerly Care Pathway for cardiovascular care gives healthcare a closed-loop, step-by-step approach for early diagnosis, informed decision-making, and personalized treatment and tracking of coronary heart disease. Clinicians are no longer forced to rely on indirect disease markers and inaccurate diagnostic tools as they speculate on patients' heart disease risk and make "best-guess" care plan recommendations.

Cleerly and its founders have spent more than a decade researching the effectiveness of CCTA and advanced analytics compared to other methods of measuring atherosclerosis. This body of extensive clinical evidence will enable Cleerly to develop a personalized care pathway for heart attack prevention that is adopted as a standard of care. The intention of the care pathway is to identify more at-risk patients sooner and support a closed-loop healthcare journey for those patients – all with the goal of preventing heart attacks from happening in the first place.



01

Cleerly Care Pathway

A personalized approach to heart attack prevention

• Identify nensive, wholeheart™ uantification and

haracterization of plaque

Identify

The first step in addressing heart disease is identifying the existence of atherosclerosis using comprehensive and accurate coronary artery disease detection. Unlike existing approaches that evaluate indirect markers or symptoms like cholesterol or shortness of breath, Cleerly's analysis delivers comprehensive coronary phenotyping of all coronary arteries and their branches - allowing for quantification of the strongest predictor of future heart attack risk.¹

Based on two decades of clinical research, Cleerly's AI-enabled CCTA analysis yields high diagnostic accuracy. Our published clinical data from multi-centered clinical trials proves that Cleerly has high diagnostic performance as compared to multiple invasive gold standards, including, expert (Level III) clinical readers, quantitative coronary angiography (QCA), fractional flow reserve (FFR), intravascular ultrasound (IVUS) and invasive near-field infrared spectroscopy (NIRS) for coronary artery disease evaluation.¹⁵

Similar to breast cancer, the ability to non-invasively enable direct visualization of actual heart disease early is the most critical step in reducing mortality risk.





 \triangle

 \triangle

ranslate advanced imaging science and data nto actionable clinical insights for all stakeholders

 \triangle

^{step} 02 <u>·</u>

 \triangle

Cleerly Care Pathway

 \triangle

Once patients at risk are identified, the next step is to characterize the extent, severity, and type of atherosclerosis present and translate advanced imaging science into actionable clinical insights.

Cleerly analysis provides vessel-by-vessel detail with more precise phenotyping for each coronary artery and its branch. Comprehensive plaque assessment offers an at-a-glance view of characterized plaque volume by coronary region and delivers a clear and concise summary of identified stenosis by severity. Existing approaches like invasive procedures and outdated technologies that prioritize indirect markers or symptoms fail to meet the needs of patients and providers who need to understand individual plaque burden and determine optimal treatment.

This was the case for Terry Schemmel, a 58-year-old with no symptoms of heart disease and no family history of heart health problems. However, Schemmel's Cleerly analysis showed a 95% blockage in his left anterior descending artery. Instead of suffering a widowmaker heart attack because his high risk could not be detected through indirect markers, Schemmel had a stent implanted and was prescribed an anticoagulant. He also sees a cardiologist every six months to monitor his heart health and adheres to his treatment plan, which includes lifestyle modifications and low-cost medical therapy.¹⁶

Fast, accurate, and comprehensive disease phenotyping is critical to early identification and characterization of a patient's heart attack risk. Clinical evidence indicates that CCTA technology, coupled with artificial intelligence that has been cleared by the U.S. Food and Drug Administration, is superior to other methods for identifying and defining arterial plaque.^{17, 18, 19}



Define

The multi-center, international CLARIFY 1²⁰ and CLARIFY 2²¹ studies have demonstrated that Cleerly's technology is very close in performance to invasive coronary angiography (ICA) technology superior to individual expert CCTA readers. Additional research has shown that CCTA is very similar to invasive intravascular ultrasound (IVUS) for estimating luminal area, percentage of area stenosis, plaque volume, and plaque area.²² Again, it's worth noting that CCTA is non-invasive compared to both ICA and IVUS. 03



Improve patient health literacy through innovative tools that meet them where they are



Empower

Education and empowerment are critical components of any care pathway, and cardiovascular care is no exception. Health literacy has been linked to a 67% increased risk of mortality and a 20% increased risk of hospitalization for patients who have been diagnosed with heart failure.²³

Efforts to improve heart health education are numerous and varied, emphasizing medication adherence, symptom monitoring, self-management, and nutrition and lifestyle modification. Success rates for these programs are mixed, with one-off, in-person programs shown to have low adherence and limited effectiveness.²⁴ In fact, traditional methods of patient education don't contribute to decreases in deaths, heart attacks, invasive procedures, or hospitalizations for heart disease. Put another way: Those who participate in education programs fare no better than those who don't.²⁵

Cleerly's personalized care pathway for heart attack prevention addresses education on two fronts. Providers receive an easy-to-read data visualization that color-codes and scores stenosis based on its severity, allowing them to clearly communicate with patients about their risk of a heart attack and guide appropriate treatment. Patients receive personalized reports that pair the results of their CCTA scan with personalized resources to help them understand their risk factors.



This approach benefits patients such as Steven Rowell, 63, who had a Cleerly analysis following a procedure to repair an abdominal aortic aneurysm.²⁶ This analysis found a severe atherosclerotic plague burden of 987mm³, the presence of non-calcified plague, and stenosis ranging from 5% to 100%. The Cleerly report gave Rowell a complete breakdown of his heart health – and it helped his cardiologist decide on a treatment plan that avoided an invasive procedure in place of aggressive medical therapy and a modified diet.27

^{step} **04**

_Treat

Enable personalized cardiovascular care through a new disease staging system





Until recently, heart disease didn't have a staging system – a critical missed opportunity for providing a prognosis or treatment plan. The lack of a staging system stemmed from the lack of a reliable way to measure and treat heart disease risk given the current standard of cardiovascular care.

That's why Cleerly has developed a four-stage system for measuring the disease burden of coronary artery disease based on atherosclerotic plaque, which describes patients based on either the total plaque volume or percent atheroma volume, which is the proportion of arterial volume occupied by plaque. Stages are defined as normal (no plaque), mild, moderate, and severe.²⁸ This staging system provides a first-of-its-kind methodology to describe the severity of heart disease risk. This is possible because CCTA can quantify the total atherosclerotic plaque burden, which technology such as ICA and IVUS cannot do and which even expert CCTA readers cannot reliably do without Cleerly's advanced AI technology.

Measuring plaque using CCTA is just the first step, though. The next step is developing an appropriate treatment plan that varies based on the stage of disease progression – not on cholesterol or other indirect markers. This is similar to the use of other disease staging systems to determine the type and intensity of medical management; the more severe the disease the more aggressive the medical intervention. To address this need, disease treatment algorithms that integrate coronary atherosclerosis stages as defined by CCTA combined with the presence of additional risk factors (lipid disorders, diabetes, hypertension, obesity, and tobacco use) are under development and peer-review to provide effective personalized treatment recommendations for everyone.²⁹

In addition, Cleerly's upcoming TRANSFORM trial will determine whether preemptive screening for asymptomatic patients at high risk due to atherosclerosis combined with a treatment strategy emphasizing prevention will improve health outcomes and reduce heart attacks and cardiac death compared to the historical standard of care that treats risk factors alone. With the positive results of this trial, Cleerly hopes to eventually attain guidance recommendations for universal CCTA screening from organizations such as the American Heart Association and the American College of Cardiology. (CCTA has already received Class 1, Level A recommendations from AHA and ACC, among others, for diagnosing symptomatic patients.³⁰)





step 05 Track

Improving outcomes for any chronic condition is more than a matter of putting patients on a care plan. Clinical teams need to be able to track patients to demonstrate the success of a given therapy over time. If the disease continues to progress, providers will know that the treatment plan is ineffective, and that different or additional therapies are warranted. If the atherosclerosis stabilizes or regresses (gets lower in volume), then they can be assured that the patient is receiving the correct regimen. Since the goal of the new standard of cardiovascular care is to treat the disease and not its symptoms or surrogates, Cleerly's personalized care pathway for heart attack prevention focuses on tracking atherosclerosis, not cholesterol or blood pressure.

The PARADIGM, EVAPORATE, and DISCO trials demonstrated that quantitative analysis of CCTA can accurately indicate whether lifestyle interventions and/or medications have either stopped atherosclerosis progression or transformed high-risk plaque into low-risk plaque.³¹ Cleerly has special software that will compare two CCTA exams performed in the same patient at two different timepoints, such as before and following the initiation of therapy. This will then directly compare the volume and type of plaque as well as the presence and degree of any stenoses (blockages) and thereby help the physician determine the effectiveness of therapy and make modifications if needed.

Cleerly's staging system and disease treatment algorithm addresses tracking as well as treatment, providing recommendations for frequency of future scans based on a patient's current stage of disease stabilization or progression and the results of baseline treatment options.



Page

20

THE GOAL IS PREVENTION

Prevent

The ultimate goal of the Cleerly Care Pathway for heart attack prevention is to empower physicians with the insights to prevent heart attacks – for Terry Schemmel, Steven Rowell, and hundreds of thousands of others in the United States and around the world.

To date, there has only been one large-scale, randomized control trial that has shown how non-invasive CCTA can save lives. The SCOT HEART trial showed a 41% reduction in deaths and non-fatal heart attacks at a five-year endpoint.³² Patients in the experimental arm underwent CCTA in addition to a standard of care testing; because the CCTA was able to depict atherosclerosis in many patients where the stress test was read as "normal", those patients were prescribed and adhered to primary prevention (medication) at a significantly higher rate. There was no difference between the control group and the CCTA group in the number of angiograms, stents, or bypass surgeries.³³ Detection and treatment of non-obstructive atherosclerosis saves lives.

Cleerly is picking up where SCOT-HEART left off. Through multiple studies, Cleerly has shown extraordinary ability to detect and classify atherosclerosis. Cleerly uncovers high-risk arterial plaque in 58% more patients as compared to expert human readers,³⁴ reduces referrals for invasive coronary angiography by up to 87%,³⁵ and affirm the value of Cleerly's AI-enabled CCTA approach over invasive methods for heart disease evaluation.³⁶

Through the adoption of the Cleerly personalized care pathway for heart attack prevention, healthcare will no longer be overlooking the more than 50% of patients who will suffer heart attack or death without any prior symptoms or the 90% of patients who undergo an unnecessary stress test.³⁷ That's the power of the new standard of care.

5 KEY IMPACTS OF THE CLEERLY CARE PATHWAY FOR HEART ATTACK PREVENTION

The Cleerly Care Pathway enables a care process that is...



Standardized. There is a clear digital process for providing care and a clinical staging system that offers providers a familiar model for describing disease prognosis and informing treatment.



Personalized. Comprehensive analysis backed by artificial intelligence provides insights to guide treatment plans that target a patient's individual heart disease risk, not indirect markers.



A personalized approach to heart attack prevention

Accessible. CCTA scanning is available at imaging centers throughout the country, and not limited to hospital-based cardiac care units, which means far more patients can be scanned and treated.



Appropriate. Invasive procedures are reserved for the patients who truly need them. Lower-risk patients are treated with therapeutics and/or lifestyle interventions.



Preventive. Early identification, treatment, and tracking of the true cause of heart disease makes it possible for physicians to prevent heart attacks and save lives.

										Care Pathway	
		JOIN US IN TRANSFORMING HEARI HEALIH For far too long, cardiovascular care has suffered from inefficient and ineffective methods for diagnosing and treating patients with suspected heart disease. Far too many patients have experienced preventable heart									

heart disease. Far too many patients have experienced preventable heart attacks because they were deemed low risk by traditional factors and lived their everyday lives not knowing they had a severe buildup of non-calcified arterial plaque. Far too many other patients have also experienced a gamut of tests and procedures based solely on the presence of indirect risk factors for heart disease.

Cleerly's care pathway provides the personalized approach to cardiovascular care that healthcare has been seeking for decades. It combines readily available and clinically-proven technology – CCTA – with advanced artificial intelligence to assess individual patient risk, educate patients and their care teams, and enable providers to offer personalized treatment options and tracking strategies. It is poised to improve clinical outcomes (through early detection and prevention) as well as financial outcomes (through reduced utilization of high-cost and unnecessary services).

Adopting this pathway enables hospitals, health systems, and independent practices to provide patients with a new standard of proactive and precision heart care that prevents heart attacks and improves their quality of life.

LEARN MORE ABOUT CLEERLY BY VISITING OUR WEBSITE OR SENDING US AN EMAIL.

CLEERLYHEALTH.COM info@cleerlyhealth.com

Page 24



Cleerly, Inc. 2022 | All rights reserved | https://cleerlyhealth.com/indications-for-use | Reproduction, adaptation, or translation of this document is prohibited without prior written permission of Cleerly, Inc. The information, including but not limited to, text, graphics, images and other material contained in this report are for informational purposes only. No material on this report is intended to be a substitute for professional medical advice, diagnosis or treatment.

¹ <u>Preventing Myocardial Infarction in the Young Adult in the First Place</u>. Journal of the American College of Cardiology. May 2003.

²Cardiac exercise stress testing: What it can and cannot tell you. Harvard Health Publishing. April 15, 2020.

³ <u>Coronary Risk Factors and Plaque Morphology in Men with Coronary Disease</u> <u>Who Died Suddenly</u>. *The New England Journal of Medicine*. May 1, 1997.

⁴<u>Older Americans and Cardiovascular Disease</u>. *American Heart Association*. Released 2021.

⁵Low Diagnostic Yield of Elective Coronary Angiography. New England Journal of Medicine. March 11, 2010.

⁶ <u>Temporal Trends in the Frequency of Inducible Myocardial Ischemia During</u> <u>Cardiac Stress Testing</u>. *Journal of the American College of Cardiology*. March 12, 2013.

⁷<u>Trends in U.S. Cardiovascular Care: 2016 Report from 4 ACC National</u> <u>Cardiovascular Data Registries</u>. *Journal of the American College of Cardiology.* March 2017.

⁸Leading Causes of Death. National Center for Health Statistics. Last reviewed Jan. 13, 2022.

⁹<u>Cardiovascular Diseases</u>. *World Health Organization*. Last reviewed June 11, 2021.

¹⁰Comedian Brad Upton has 'significant' heart attack despite normal cardiac stress test: What to know. Fox News. June 6, 2022.

¹¹National Study Finds Americans Don't Know the Facts or Their Risk for Heart Disease. *MDVIP*. Jan. 31, 2019.

¹² <u>The 2021 Chest Pain Guideline: A Revolutionary New Paradigm for Cardiac</u> <u>Testing</u>. *JACC: Cardiovascular Imaging*. Last updated January 15, 2022.

¹³<u>Association of High-Density Calcified 1K Plaque With Risk of Acute Coronary</u> <u>Syndrome</u>. JAMA Cardiology. Released January 22, 2022.

¹⁴ <u>Coronary Atherosclerotic Precursors of Acute Coronary Syndromes</u>. Journal of the American College of Cardiology. Released June, 2018.

¹⁵ Al Evaluation of Stenosis on Coronary CT Angiography, Comparison with Quantitative Coronary Angiography and Fractional Flow Reserve: A CREDENCE <u>Trial SubStudy</u>. *JACC: Cardiovascular Imaging*. Published Feb. 16, 2022.

¹⁶ When It's Good to Find Something Bad. Cleerly. May 19, 2022.

¹⁷ <u>CT Evaluation by Artificial Intelligence for Atherosclerosis, Stenosis and</u> <u>Vascular Morphology (CLARIFY): A Multi-center, international study</u>. *Journal of Cardiovascular Computed Tomography*. June 3, 2021.

¹⁸ Al Evaluation of Coronary Stenosis on CT Coronary Angiography, Comparison with Quantitative Coronary Angiography and Fractional Flow Reserve; A <u>CREDENCE Trial Sub-study</u>. Journal of the American College of Cardiology: Cardiovascular Imaging. Feb. 16, 2022.

¹⁹ Coronary CT angiography versus intravascular ultrasound for estimation of coronary stenosis and atherosclerotic plaque burden: a meta-analysis. Journal of Cardiovascular Computed Tomography. Aug. 23, 2013.

²¹ A CREDENCE Trial Sub-study.

²² <u>CCTA versus IVUS: a meta-analysis</u>.

²³ Health Literacy and Outcomes Among Patients With Heart Failure: A Systematic Review and Meta-Analysis. Journal of the American College of Cardiology: Heart Failure. June 2020.

²⁴Health Literacy and Cardiovascular Disease: Fundamental Relevance to Primary and Secondary Prevention. *Circulation.* June 4, 2018.

²⁵ Patient education in the management of coronary heart disease. Cochrane Database of Systematic Reviews. June 28, 2017.

²⁶ <u>Cleerly Analysis Offers Critical Insight on Heart Health</u>. *Cleerly.* June 8, 2022.

²⁷ <u>Cleerly Analysis Offers Critical Insight on Heart Health</u>. *Cleerly*. June 8, 2022.

²⁸ Coronary CTA plaque volume severity stages according to invasive coronary angiography and FFR. Journal of Cardiovascular Computed Tomography. March 28, 2022.

²⁹ Coronary Atherosclerosis Burden and Progression to Guide Clinical Decision Making: A Report from the American College of Cardiology (ACC) Innovations in Prevention Working Group. Paper in development.

³⁰ <u>CCTA receives Multiple Class 1, Level A recommendations in the 2021 New</u> <u>Chest Pain Guideline</u>. Society of Cardiovascular Computer Tomography. Oct. 28, 2021.

³¹ Cardiac CT angiography in current practice: An American society for preventive cardiology clinical practice statement. *American Journal of Preventive Cardiology*. March 9, 2022.

³² <u>SCOT-HEART Trial: Reshuffling Our Approach to Stable Ischemic Heart Disease</u>. *British Journal of Radiology*. September 1, 2020.

³³ <u>Coronary CT Angiography and 5-Year Risk of Myocardial Infarction</u>. *The New England Journal of Medicine*. Sept. 6, 2018.

³⁴ CT Evaluation by Artificial Intelligence, JCCT.

³⁵ Atherosclerosis Imaging and Quantitative Computed Tomography to Guide Referral to Invasive Coronary Angiography in the Randomized Controlled CONSERVE Trial. Resubmission in progress to *European Heart Journal Imaging*.

³⁶ Al Evaluation of Stenosis on Coronary CT Angiography, Comparison With Quantitative Coronary Angiography and Fractional Flow Reserve: A CREDENCE <u>Trial Substudy</u>. Journal of the American College of Cardiology: Cardiovascular Imaging. February 16, 2022.

³⁷Temporal trends in the frequency of inducible myocardial ischemia during cardiac stress testing: 1991 to 2009. Journal of the American College of Cardiology: Cardiovascular Imaging. March 12, 2013.



Page

26