
Heart Failure
TODAY
SPECIAL EDITION
WHAT YOU NEED TO KNOW ABOUT THE ACC/AHA GUIDELINES
PRIMARY DISEASE PREVENTION CLOSE AT HAND?
3 EXPERTS SPEAK UP ABOUT HF CARE
PREDICTING HEART TRANSPLANT REJECTION

ST2 is the perfect biomarker for serial testing. Levels of the biomarker ST2 change rapidly in response to changes in a heart failure patient's condition, helping you to quickly adjust care.

ST2 significantly improves the accuracy of patient prognosis over natriuretic peptide markers and is not adversely affected by confounding factors such as age, body mass index, smoking, anemia and impaired renal function.

ST2 has a single cutpoint, removing any guesswork. If your patient's ST2 level is over 35*, that's a warning sign.

ST2 can satisfy your hunger for a serial biomarker. Don't start your morning without it. To learn more about the Presage ST2 Assay, go to www. criticaldiagnostics.com or call 1-877-700-1250.

ST2 testing is available from these preferred laboratories:

ARUP LABORATORIES · MAYO CLINIC Mayo Medical Laboratories · Quest Diagnostics®

* 35ng/ml.

CRITICAL DIAGNOSTICS
ADVANCING MEDICINE. SAVING LIVES®.

THE MAGAZINE THAT **HELPS** HEALTHCARE PROFESSIONALS TO **IMPROVE** THE TREATMENT OF THEIR **HEART FAILURE** PATIENTS

CONTENTS

Heart Failure TODAY is a publication of Critical Diagnostics, makers of the Presage® ST2 Assay. This information is to educate our readers and is not intended as medical advice or a substitute for consulting a physician.

The Presage® ST2 Assay is CE Marked and has received 510(k) clearance from the US FDA for use in risk stratification of chronic heart failure patients.

What YOU NEED To KNOW

About The ACC/AHA Updated Guideline For HF Management

On June 5, 2013, the ACC Foundation (ACCF) and American Heart Association (AHA) jointly released an expanded clinical practice guideline for the management of patients with heart failure–helping standardize practice and, by doing so, removing the guesswork from treating patients.

Almost 6 million Americans are diagnosed with heart failure. More than 670,000 new cases are diagnosed annually and result in more than $30 billion of total healthcare costs.

The guideline, which puts a single reference source at clinicians' fingertips, has been published since 1980. This is the first update to the guideline since 2009.

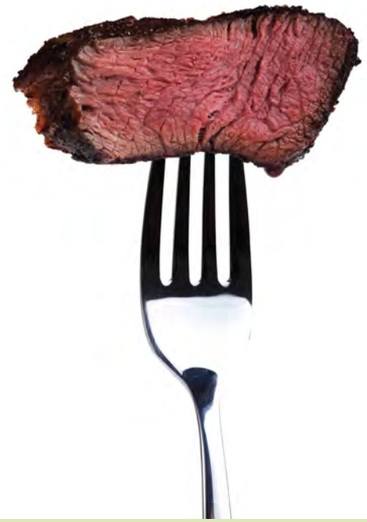
The latest guideline updates definitions and classifications for HF and provide increased emphasis on patient-centric outcomes such as quality of life, shared decision making, care coordination, transitions and palliative care. The document also discusses greater adherence to performance measures and quality measures, with timely recommendations to reduce readmissions.

The 2013 guideline classifies Critical Diagnostics' biomarker ST2 as "not only predictive of hospitalization and death in patients with HF [heart failure] but also additive to natriuretic peptide levels in [its] prognostic value."

To draft the document, the ACC and AHA selected a multidisciplinary group of experts in cardiac care and asked them to perform a comprehensive literature review and to create a series of pertinent evidence tables. Writing committee members then weighed the strength of this evidence for or against certain tests or treatments and considered patient-specific modifiers that may influence care choices.

Specifically, ST2 was included as level IIbA for additive risk stratification in acute HF as a biomarker of myocardial fibrosis. An "A" Level of Evidence is the highest classification possible, meaning that data were derived from multiple randomized clinical trials or meta-analysis, and a IIb Class of Recommendation corresponds to 'May Be Considered' for the purpose of additive risk stratification.

"Having ST2 included in the 2013 ACC/AHA Guidelines is unprecedented," notes David Geliebter, CEO of Critical Diagnostics. "We only received FDA clearance in December of 2011. No cardiac biomarker that we know of has ever achieved this acceptance so quickly. We are honored the task force recognized the depth and breath of clinical evidence for the use of ST2."



NO BEEF HERE!

Could the culprit in heart disease go beyond meat's fat?

Researchers at the Cleveland Clinic suspected that saturated fat and cholesterol made only a minor contribution to the increased amount of heart disease seen in red-meat eaters, that the real culprit was a little-studied chemical that is "burped out" by bacteria in the intestines after people eat red meat – which is then quickly converted by the liver into yet another little-studied chemical called TMAO that gets into the blood and increases the risk of heart disease.

Steaks were fed to meat-eaters and vegans, and the meat eaters had more TMAO in their blood than the vegans, thus proving two important things: If it tastes good, it's probably not good for you; and even some vegans seemingly can't resist chowing down on a sizzling-hot, juicy steak every once in a while!

We couldn't resist:
Q: What did one vegetarian say to the other vegetarian?
A: We have to stop meating like this!

From The 2013 Guideline:

- This is the first guideline to include the new designation for optimal treatment, termed "guideline-directed medical therapy," which allows clinicians to easily determine the specific course of care deemed most important in the management of HF.
- Risk factors need to be continually addressed when managing a patient with HF, e.g., hypertension, lipid disorders, obesity, diabetes mellitus, tobacco use, and known cardiotoxic agents.
- There is a clear mortality benefit from using guideline-directed medical therapy.
- HF education, dietary restrictions, and exercise training should be provided for all patients to enhance self-care.
- A HF multidisciplinary team, including a palliative care team, should be involved when treating patients with advanced HF.

YOU CAN'T BEET IT

Emerging studies suggest that beet juice (also known as beetroot juice) is one of the richest dietary sources of antioxidants and nitrates. Drinking just one glass of beet juice could lower blood pressure, according to a study published in *Nutrition Journal*.

Fifteen women and fifteen men participated in a double-blind, randomized, placebo-controlled, crossover study. Volunteers were randomized to receive 500 grams of beetroot and apple juice or a placebo juice, on the theory that the consumption of beetroot juice on a low nitrate diet may lower blood pressure and therefore reduce the risk of cardiovascular events.

Within hours, the beet juice lowered systolic blood pressure in healthy males by four or five points compared to baseline measurements. While a relatively small change, according to the authors, based on a public health level, it could equate to a 10 percent reduction in deaths from heart disease. The results were mixed for women. Of the fifteen in the study, while beet juice lowered their blood pressure slightly, it was not significant.

Is PRIMARY DISEASE PREVENTION Close At Hand?

So much of medicine today deals with treating patients once they progress to cardiovascular disease. The results of three studies give hope that a biomarker, ST2, can change all that by helping physicians identify at-risk patients years before symptoms arise. Many experts believe this could be the future of medicine.

Determining Who Is Likely To Develop Hypertension?

In May of this year Critical Diagnostics revealed publication of a study that, for three years, followed a cohort of 1,834 otherwise healthy individuals, where those with high levels of the biomarker ST2 present in their blood were almost twice as likely to develop hypertension than those with low ST2 levels.

Hypertension affects some 67 million people in the U.S. That's 1 in every 3 adults. Hypertension costs the United States more than $100 billion in needed healthcare services, medications, and missed days of work.

Two Studies Show ST2 Predicts Development of Heart Failure

The hypertension study came out of the far-reaching Framingham Heart Study. In 1971, the Study enrolled a second generation – just over 5,000 of the original participants' adult children and their spouses - to continue its ambitious effort to identify causes of heart disease and stroke, about which little was known at the time.

Data from this second generation Framingham cohort showed that otherwise healthy individuals with the highest levels of ST2 in their blood had the greatest risk of developing heart failure years before the presence of any symptoms. In fact, ST2 was, by far, the most predictive of any biomarker tested, including such established biomarkers as the natriuretic peptides and troponin.

"the onset of hypertension or heart failure are not a certainty . . . risk can be attenuated."

It was late last year that another study, this one conducted through the Mayo Clinic and Foundation, once again proved the remarkable accuracy of ST2 in predicting the risk of heart failure and mortality in the general population. The study of 1,831 healthy individuals from Olmsted County, Minnesota, who were followed for approximately a decade, showed that those with the highest ST2 concentrations were at the most risk of heart failure or death over this same period of time.

HYPERTENSION FACTS & FIGURES

- Nearly one billion people worldwide have high blood pressure
- Hypertension is one of the most important causes of premature death
- Hypertension is the leading cause of cardiovascular disease
- People with hypertension are more likely to develop complications of diabetes

Taking A Preventative Approach

"The implications of these findings from both Framingham and Olmsted are enormous," notes David Geliebter, CEO of Critical Diagnostics. "They mean that the onset of hypertension or heart failure are not a certainty, that risk can be attenuated, and with this knowledge in hand, physicians may be able to offer their patients tailored treatment options as part of a preventative approach to medicine that can postpone or even prevent such life-threatening disorders."

FIVE STEPS To Prevent Hypertension

- **Maintain a healthy weight:** Being overweight makes you two to six times more likely to develop high blood pressure than if you are at your desirable weight.
- **Get regular exercise:** People who are physically active have a 20% to 50% lower risk of getting high blood pressure.
- **Lower salt intake:** Cutting back on salt also prevents blood pressure from rising.
- **Drinking alcohol in moderation:** Drinking too much alcohol can raise your blood pressure.
- **Reduce stress:** Stress can make blood pressure go up, and over time may contribute to the cause of high blood pressure.

THE BUZZ ABOUT COFFEE AND HEART FAILURE

Drinking about two cups of coffee a day may have reduced the risk of heart failure by as much as 11 percent over the decade that the subjects were followed, according to a study published in *Circulation: Heart Failure*.

The effects of coffee have been the subject of numerous studies. Coffee contains several compounds that are known to affect human body chemistry. In the past, the consumption of coffee was generally regarded as being detrimental to heart health. Coffee was said to increase blood pressure, increase cholesterol levels, and increase the risk of heart attack and cardiac arrhythmias.

In this case, scientists did a meta-analysis of five prospective studies—which included more than 140,000 men and women—that related to coffee consumption and heart risk.

"Beyond that (two eight-ounce cups), any potential benefits seem to decrease and eventually go away," says Dr. Murray Mittleman, senior study author and Director of Cardiovascular Epidemiology at Beth Israel Deaconess Medical Center, adding that the study found a link, but not cause and effect.

In case you were wondering, no analysis was done of the effects of eating two donuts a day with those coffees – so dunk away!

THE EXPERTS SPEAK OUT

Key Opinion Leaders Talk About The Latest Advancements in Heart Failure Care

The treatment of patients with heart failure is constantly changing and evolving, as witnessed by the latest update to the ACC/AHA guidelines. Heart Failure TODAY spoke with three noted experts in the field to learn what changes they've seen over the past several years, specifically how the use of biomarkers has affected their practice, the potential role of ST2 in treating patients, and other insights into heart failure care.

Our distinguished panel includes (in alphabetical order), Doctors Lori Daniels, James Januzzi and Peter McCullough.

Lori Daniels, MD, MAS, FACC, is an Associate Professor of Medicine at UC San Diego, where she is also the Director for the hospital's Coronary Care Unit at UCSD's Sulpizio Cardiovascular Center. Dr. Daniels has been named one of U.S. News & World Report Top Doctors, as well as a Top Doctor in the 2012 San Diego Magazine "Physicians of Exceptional Excellence" survey. She has several publications on cardiac biomarkers and is a frequent lecturer.

James Januzzi, Jr, MD, FACC, FESC, in addition to being an Associate Professor of Medicine at Harvard Medical School, is a member of the Massachusetts General Hospital Cardiology Division and Director of its Cardiac Intensive Care Unit. He was the PI on the PRIDE study, which was instrumental in establishing NT-proBNP as a diagnostic biomarker. Dr. Januzzi has more than 300 publications to his name, has edited 3 textbooks, and speaks widely on the topic of cardiac biomarkers.

Peter McCullough M.D., M.P.H., F.A.C.P., F.C.C.P., F.A.H.A., F.N.K.F., Chief Academic and Scientific Officer at the St. John Providence Health System in Warren, Michigan, is an internationally recognized authority on the role of chronic kidney disease as a cardiovascular risk state with over 800 published, scientific communications, including a section in Braunwald's Heart Disease Handbook. Dr. McCullough is the co-editor of *Reviews in Cardiovascular Medicine* and serves on the editorial boards of multiple specialty journals.

Q. *What are the biggest challenges you face in treating your HF patients, particularly as it relates to risk stratification, treatment selection and monitoring?*

(Januzzi) In many cases, the evaluation and management of patients with HF is extremely challenging. Part of that is identifying the presence of things that are not as easily detected at the bedside, such as persistent congestion as well as ongoing ventricular remodeling. Both of these deleterious processes can be treated, but knowledge of their presence is crucial before such therapies can be started or intensified.

(Daniels) As a cardiologist who treats a number of acute and chronic heart failure patients, a big challenge for me is identifying which patients need the closest attention and quickest follow-up. Sometimes this is obvious, but there are other times when a patient who appears to be doing well can be at higher risk than is apparent despite a careful history and physical exam. Knowing when to step up therapy, and knowing this in a timely fashion, is not always straightforward.

(McCullough) While echocardiography is the mainstay to establish a diagnosis of left ventricular dysfunction, it does not change much over the course of care. Novel biomarkers such as ST2 have a clear role in the prognosis of patients with left ventricular dysfunction. In all outpatients, I am sure to have ST2 as part of the office consultation much like an oncologist has molecular pathology results of tumor marker or a rheumatologist as serologies to guide the case.

Q. *Now that you mention it, how has the introduction of cardiac biomarkers changed your practice?*

(Daniels) Cardiac biomarkers have provided me with an objective measure of how my heart failure patients are doing. I use this in conjunction with what the patients themselves tell me about how they are doing, and with what I see on examination. Together, these three components (biomarkers, history, physical exam) provide a more complete picture; and if any one of the these components is not in sync with the others, it prompts me to investigate a bit more. Existing biomarkers like the natriuretic peptides have proven tremendously useful for aiding in diagnosis and prognosis, but they do have some shortcomings. They are more difficult to interpret in the setting of renal dysfunction; they have fairly high

DO YOU KNOW THE WARNING SIGNS FOR HEART FAILURE?

IT COULD SAVE YOUR LIFE.

Here are some common early warning signs that may indicate the presence of heart failure.

- Shortness of breath
- Swelling of the legs or ankles
- Sudden weight gain
- Swelling or pain in the abdomen
- Frequent dry, hacking cough
- Increase fatigue
- Trouble sleeping, waking up with shortness of breath
- Nausea

Just because you may experience one or more of these symptoms, doesn't mean you have heart failure. It could be caused by something else, but, regardless, you should consult your physician or healthcare professional.

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CRITICAL DIAGNOSTICS

MAKERS OF THE ST2 ASSAY

The Presage® ST2 Assay is CE Marked and has received 510(k) clearance from the US FDA for use in risk stratification of chronic heart failure patients.

intra-individual variability; and they do not always respond as expected after titration of guideline-based therapy.

(Januzzi) Biomarkers add information that supplements my history taking and physical exam ... [but] ... there are important things to still learn and improve upon. For example, while the natriuretic peptides are the foundation of biomarker-based evaluation of risk in heart failure, it would be overly simplistic to assume that BNP or NT-proBNP tell the entire story. There are many examples where natriuretic peptides either overestimate or underestimate the severity of HF. Part of the reason why this is relates to the fact that BNP and NT-proBNP reflect a broad range of clinical correlates, which may make their elevation non-specific. BNP and NT-proBNP may be modestly confounded by renal dysfunction, age, body-mass index or ejection fraction. Thus, multimarker testing has been shown to provide incremental information and value.

(McCullough) Probably the greatest value of novel markers is their negative predictive value. It is so reassuring to tell a patient that things are going to be fine when now multiple markers of cardiac function are normal.

Q. *How do you see the biomarker ST2 fitting into HF patient care?*

(McCullough) ST2 offers excellent objective confirmation that we are on the right treatment path with the up titration and sometimes down titration of complicated drug regimens.

(Januzzi) ST2 is not only additive to, but possibly superior to the gold standard biomarker class, the natriuretic peptides. I foresee a number of valuable roles for ST2 in the care of our patients with HF. Firstly, we test ST2 in the Massachusetts General Hospital Heart Center when evaluating chronic HF patients in the office. We find unique additive value beyond NT-proBNP for predicting risk, which allows for a more refined assessment of our patient, and informs decisions about treatment adjustment. Secondly, the patient with acutely decompensated HF represents an important population at very high risk for readmission or death. A good understanding of risk in such patients would be expected to reduce adverse outcomes. We and others have found great value from measurement of ST2 at the beginning and at the end of a hospitalization, in order to monitor response to therapy; those without a significant reduction in ST2 by hospital discharge are at highest risk for an adverse outcome, and merit the most aggressive treatment decisions.

> "ST2 is not only additive to, but possibly superior to the gold standard biomarker class, the natriuretic peptides."

(Daniels) I am hopeful that ST2 can help me to further refine my care of HF patients, and help me target those patients who really need extra attention to ensure they are taking their aldosterone blockers and other guideline-based therapies. In addition, I think using ST2 serially will help give positive reinforcement to patients taking multiple HF medications, since levels tend to drop nicely with therapy titration.

Q. *Can you provide a case study example of how you used ST2 to treat a patient(s)?*

(Januzzi) A good example of how ST2 measurement has helped me in practice is the case of an elderly man with asymptomatic left ventricular dysfunction, who had a low NT-proBNP but a very high ST2 value. He had a history of sensitivity to medications, which had left his prior physician uncomfortable about up titration of his medications. Given the ST2 value of 78 ng/mL, together with the patient, the decision was made to adjust his medications, given the extremely high likelihood for progression to symptomatic HF. We up titrated his beta blocker, with a smooth response in ST2 concentration, falling from 78 ng/mL to 24 ng/mL over a period of 6 months *[Editor's note: The standard cutpoint for ST2 is 35 ng/ml.]*

(Daniels) Here is one example. A woman showed up in my clinic at the UCSD Sulpizio Cardiovascular Center in florid heart failure; her legs were so edematous that they were weeping onto the floor and literally creating puddles. She had not seen a doctor in many years; her son finally drove the 20 hours to her home out of state, picked her up, and showed up unannounced in my clinic. We admitted her to the Cardiovascular Center, diuresed her, controlled her rapid atrial fibrillation, and began slowly titrating up her beta blockade and ACE inhibition. Prior to discharge, we checked an ST2 level and it was significantly above 35 ng/ml. We got her a home health RN who visited her daily, and she kept a careful log of daily blood pressure and weights. We also kept close tabs on her with labs and clinic visits. After about three months of this, a repeat ST2 level was down to the low 20's. She was able to maintain euvolemia and an independent lifestyle, and we then felt comfortable discontinuing her home health RN. We were also able to stretch out the amount of time between clinic visits.

(McCullough) I have a complicated patient with rheumatic aortic and mitral valve disease with heart failure and I struggled to figure out how much real left ventricular dysfunction was present. During an exacerbation, his ST2 was above100 ng/ml, thus a strong signal that there was clear dysfunction related to immune system and myocyte interactions as ST2 blocks the interleukin-33 receptors on cardiomyocytes. As the patient has been treated with standard drugs for heart failure, levels have come down to the 30-40 ng/ml range.

Q. *ST2 has a single cutpoint; it changes rapidly with the patient's condition. How important is that to you?*

(Januzzi) Extremely attractive. It opens up the opportunity to serial assessment, dynamic risk stratification, and easy interpretability.

(Daniels) These are the main factors that set ST2 apart from natriuretic peptides, and are a principle reason that I have started using ST2. Furthermore, ST2 shows excellent prognostic capability especially for short-term events. This is a major strength of ST2, since it can help clinicians focus on those HF patients who are most at risk for decompensating. In our own study of 588 outpatients undergoing echocardiograms, no patients with an ST2 level below the median (in this case, 20 ng/mL) died within the ensuing 6 months, whereas patients with higher levels of ST2 were at significantly greater risk. This same impressive risk stratification has been replicated in a number of other studies and patient settings. In this era where we are being scrutinized for HF readmissions, using ST2 to focus attention on patients at risk for readmission or other adverse events can help us allocate our resources more wisely.

> "ST2 shows excellent prognostic capability especially for short-term events. This is a major strength of ST2, since it can help clinicians focus on those HF patients who are most at risk for decompensating."

(McCullough) The single cutpoint gives physicians a teachable algorithm for use of the test. This never existed for some markers like NT-proBNP; hence their adoption has been slow.

Q. *Given the strength of ST2 in predicting hypertension and HF (i.e., the Framingham and Olmsted studies), what do you think about the future of biomarkers in primary disease prevention and ST2 in particular?*

(Januzzi) I envision a day when ST2 could very feasibly be part of a standard "risk" work up for the apparently well patient. Beyond this application, it's very clear that ST2 has powerful prognostic ability in patients with acute coronary syndrome, forecasting the onset of HF before patients have symptoms. As shown by Weir and colleagues, concentrations of ST2 may predict remodeling after acute myocardial infarction, and also identify those likely to respond to antiremodeling therapies, such as eplerenone. This is important. Additionally, we at the Massachusetts General Hospital Intensive Care Unit showed that concentrations of ST2 are powerfully prognostic for death in patients with critical illness states, such as ARDS. Thus, it's likely that ST2 testing will expand in "both directions" from HF, to encompass lower acuity patients as well as those with more severe illness.

(McCullough) The ability to have ST2 work upstream in Stage A heart failure to provide important risk prediction for the development of hypertension and myocardial disease is truly extraordinary. As we move towards prevention of chronic diseases and novel interventions in at-risk groups, undoubtedly ST2 will play a role.

(Daniels) I am hopeful that ST2, either alone or more likely as a key component of a panel of multiple biomarkers, will be able to help improve risk stratification in individuals at intermediate risk for future cardiovascular disease. Since the pathophysiology leading to elevated ST2 levels is different from that of other currently available cardiovascular biomarkers (e.g., natriuretic peptides and troponin), it makes sense that looking at these markers together will give us a better picture of an individual's risk profile.

Q. *Laboratorian Alan Wu's (of UCSF) study on biological variability shows ST2 to have the lowest RCV (Reference Change Value) of any of the commercially available cardiac markers. How important is that to you?*

(McCullough) Large variation in natriuretic peptide levels have been a cause of concern among physicians who are wondering what is a meaningful change in the lab value. Low variability and a stable analyte is a huge advance in molecular cardiology.

(Januzzi) RCV is the combination of analytical and biological variation. A low RCV therefore indicates that the assay is extremely precise, which is something of great value, and allows for a good understanding of how much change in ST2 must be seen before we know that a clinically relevant change has occurred. Most important is a good understanding of "how much change is important" and good knowledge of the ST2 RCV is thus a great advance. (continued on page 14)

ST2 PREDICTS Rejection & Death in Heart Transplant Patients

Results of a Utah Transplantation Affiliated Hospitals Cardiac Transplant Program study involving the use of ST2 to monitor heart transplant patients for rejection showed subjects with the highest levels of ST2 had a more than 3-fold increase in the risk for death than those with the lowest ST2 levels.

Worldwide, about 3,500 heart transplants are performed annually. The vast majority of these are performed in the United States (2,000 - 2,300 annually). Post-operative complications include infection, sepsis, organ rejection, as well as the side effects of the immunosuppressive medication. The prognosis for heart transplant patients following the orthotopic procedure has increased over the past 20 years. Survival after one year was 88% for males and 86.2% for females, and after five years, it was 73.2% for males and 69% for females.

Currently, biopsy-driven diagnoses are used to predict transplant organ rejection, but this type of procedure is costly, involves risk, and offers little consideration of the underlying biological processes that predict the presence or severity of rejection and/or likelihood of adverse consequences.

In the ST2 study, a total of 241 transplant patients were followed for a period of just over 7 years, during which time there were 62 deaths. The prognostic ability of ST2 was examined for both rejection and death. ST2 concentrations were measured approximately a month after transplantation and found to be highly predictive of short-, intermediate-, and longer-term outcomes.

He was NO DUMMY. He INVENTED the ARTIFICIAL HEART

If you're one of the millions of U.S. post-war baby boomers, you probably know Paul Winchell as the talented ventriloquist who hosted a children's show on Saturday mornings with his two dummies named Jerry Mahoney (millions of kids had their very own Jerry Mahoney doll with the pull string in the back) and Knucklehead Smiff (the name came from Snuffy Smiff comics).

What few know, however, is that Winchell, who had studied pre-med at Columbia, was no dummy. In fact, he was a very successful inventor with over 30 patents to his name, including one for the first artificial heart. That's right, the artificial heart (some of his other inventions include a disposable razor, a retractable fountain pen and an idea he had to farm raise tilapia fish to help feed starving people in under-developed nations).

This invention was developed in collaboration with Dr. Henry Heimlich, creator of the Heimlich Maneuver – whom Winchell met at a cast party while competing on the TV show, "Arthur Murray Dance Party" (he won a Buick). Later, Heimlich invited Winchell to observe him in the operating room, which led to Winchell coming up with the idea for an artificial heart.

"I got to wondering if an artificial heart with its own power source were available, could it keep a patient alive during a crucial period?" thought Winchell. "I went right to work constructing a model."

Though Dr. Robert Jarvik has been referred to as "the inventor of the artificial heart," it would be over two decades after Winchell filed his patent, in 1982, before Javik would successfully implant the first artificial heart, the Jarvik-7, in Barney Clarke, a Seattle dentist who volunteered to undergo the pioneering procedure because he wanted to make a contribution to medical science.

As Winchell told it, "I heard rumblings that the FDA was considering trying the technology on a human being. I met a young man there who had been hired to adapt the invention for human physiology. His name was Robert Jarvik, a brilliant biomedical engineer who had begun to modify the heart for a human being. Until then my patent had been used primarily for animal studies and was much too large for the human chest. By the time Jarvik had reduced the unit, a brave dentist named Barney Clark volunteered to be the first recipient of an artificial heart."

Winchell, who died in 2005, had a knack for bringing life to his wooden characters, but it was his gift for bringing life to so many people that makes him special. Jerry Mahoney and Knucklehead live on, too, at the Smithsonian Institution.

Ready For A Ha, Ha, HEARTY Laugh?

A heart surgeon took his car to his local garage for maintenance, where he exchanged a little friendly banter with the mechanic he had known for years.

"So tell me," says the mechanic, "I've been wondering about what we both do for a living, and how much more you get paid than me…"

"Yes?…" says the surgeon.

"Well look at this," says the mechanic, as he worked on the complicated engine, "I work on the heart of the car, check how it's running, open it up, if needed, fix the valves, and put it all back together so it works good as new. So we basically do the same job, don't we? Yet, you get ten times what I am paid. How do you explain that?"

The surgeon thought for a moment, smiled gently, and replied, "Try it with the engine running."

(continued from page 11)

(Daniels) The low RCV of ST2 shows that there is less variability in the assay due to the combination of both analytic characteristics inherent in the assay as well as biologic characteristics. With the low RCV of ST2, I can trust that when a patient's level of ST2 rises or falls over time, it is more likely to be due to their disease process than to a spurious finding. That is the reason that measuring serial levels of ST2 is turning out to be a very useful strategy, and it means that I am more likely to guide therapy based upon changes in ST2 levels.

Q. *ST2 was included in the new 2013 ACC/AHA update to the guidelines for heart failure identifying It as, "not only predictive of hospitalization and death in patients with HF [heart failure] but also additive to natriuretic peptide levels in [its] prognostic value." How, then, should clinicians think of including ST2 into their practice?*

> "measuring serial levels of ST2 is turning out to be a very useful strategy, and it means that I am more likely to guide therapy based upon changes in ST2 levels."

(Januzzi) Having written that sentence, I can concur with it. I think that the present strategy for ST2 measurement is to include it together with clinical judgment and natriuretic peptide testing in a comprehensive risk assessment package.

(Daniels) ST2 is not meant as a replacement to natriuretic peptides; rather, it can be helpful in situations where the clinical picture is still cloudy despite the use of NP's. For example, ST2 can help with patients whose natriuretic peptide levels are jumping all around; and conversely, in those whose natriuretic peptide levels are not moving despite significant treatment changes or apparent status changes. Clinicians might also think of including ST2 in their practice for those patients whose NP levels are difficult to interpret due to comorbidities (e.g., obesity, renal dysfunction).

(McCullough) ST2 and natriuretic peptide levels are clearly complementary and the tests should be used in tandem, much like the components of biochemistry or rheumatology, or endocrinology panel.

Q. *Any other thoughts to add?*

(McCullough) Clinicians will learn to respect very high ST2 levels. These patients are in for rocky courses and we should be very vigilant with patients with marked elevations of this protein.

> "I can think of no other biomarker candidate since the natriuretic peptides that has as much promise as ST2."

(Daniels) As physicians get more comfortable with using ST2 and interpreting levels, I think they will see that it can be a very useful marker for helping manage patients with HF. Biomarkers will never replace clinical judgment, and need to be taken in context of the whole clinical picture; however, for the more challenging patients, especially those patients with a mixed clinical picture, a tenuous balance, or even those in need of quantitative feedback, ST2 can be a helpful tool to have at our disposal.

(Januzzi) I can think of no other biomarker candidate since the natriuretic peptides that has as much promise as ST2. I think its analytical and clinical value is superb. I expect to see it used in both acute and chronic settings, and its value may expand to other indications, including primary care, as well as in the evaluation and management of patients with critical illness in the ICU, as we have examined here at the Massachusetts General Hospital.

EDITOR'S NOTE: The Presage ST2 is FDA cleared for use in risk stratification with chronic heart failure patients.

You don't need a crystal ball to see that ST2 is the most prognostic of all cardiac biomarkers. The clinical evidence proves it.

ST2 is included in the 2013 ACC/AHA Guideline For The Management of Heart Failure, which calls ST2 "*not only predictive of hospitalization and death in patients with HF [heart failure] but also additive to natriuretic peptide levels in [its] prognostic value.*" And the guideline gives ST2 its highest classification ("A") for the body of evidence supporting its recommendation.

Wait, something is coming to us . . . it's a message from the other side. It says you're a wonderful person and using ST2 to improve patient care is in your future!

To learn more about the Presage ST2 Assay, go to www. criticaldiagnostics.com or call 1-877-700-1250.

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Perception Versus Reality

Data from the Study on Heart failure Awareness and Perception in Europe (SHAPE) found that:

67% of people wrongly believe that HF patients have a better prognosis than cancer patients.

70% of people do not consider HF to be a serious condition.

86% of people have heard of HF, but only **3%** can identify its signs and symptoms.

I Want My MUMMY!

The ancient Egyptians were the first to discover heart disease, according to a papyrus discovered in 1873.

Half an onion and the froth of beer was considered "a delightful remedy against death."

The 110-page scroll described various types of diseases along with about 700 magical remedies and formulas including many incantations meant to turn away disease-causing demons. Half an onion and the froth of beer was considered "a delightful remedy against death."

The papyrus also defined the heart as the center of the body's blood supply system, with vessels attached for every member of the body, and recommended basil as a heart medicine.

CRITICAL DIAGNOSTICS

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THE PRESAGE® ST2 ASSAY is a simple blood test that aids physicians in risk assessment of chronic heart failure patients. Elevated ST2 levels are indicative of increased risk of an adverse event, hospitalization or death.

FROM THE 2013 ACC/AHA GUIDELINE FOR HEART FAILURE MANAGEMENT:

ST2 is "not only predictive of hospitalization and death in patients with HF [heart failure] but also additive to natriuretic peptide levels in [its] prognostic value."

THE PRESAGE ST2 ASSAY IS AVAILABLE FROM THESE PREFERRED LABORATORIES:

ARUP® LABORATORIES

MAYO CLINIC
Mayo Medical Laboratories

Quest Diagnostics®

AW 201079 Rev. 1