CRITICAL DIAGNOSTICS

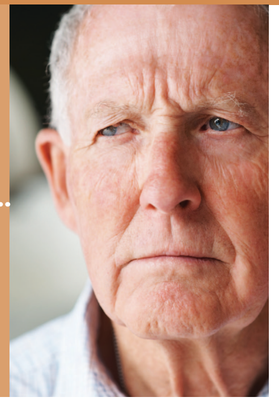
HEART FAILURE PATIENT MANAGEMENT

To The Power of 2!

Put The Power of 2 To Work For You!(sm)

THE PRESAGE® ST2 ASSAY

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



Some 14 million people in Europe have heart failure and that number is expected to jump to 30 million by 2020.[1] More than 10 percent of all Europeans over the age of 65 have heart failure.[2]

With an aging population, the prevalence of heart failure grows, as does the added burden placed on the healthcare system. The current annual economic cost to treat heart disease in the EU exceeds €200 billion,[3] 70% of which is due to hospitalization.[4]

THE VALUE OF CARDIAC BIOMARKERS

One of the ways that clinicians are improving the lives of heart failure patients while lowering overall healthcare costs is through the use of cardiac biomarkers.

Cardiac biomarkers are substances that are released into the blood when the heart is damaged or stressed. Measurement of these biomarkers is used to help risk stratify people with heart failure, to diagnose disease, assess treatment options, monitor progress, and guide in-hospital and post-discharge care.

[1] According to the Study group on Heart failure Awareness & Perception in Europe (SHAPE).
[2] Source: European Heart Journal.
[3] Source: Department of Public Health, University of Oxford.
[4] National Academy of National Biochemistry Laboratory Medical Practices Guidelines.

ST2 HELPS PHYSICIANS MAKE INFORMED DECISIONS

ST2 is expressed by the heart in response to disease or injury. Unlike many other cardiac biomarkers, ST2 levels change rapidly in response to changes in the patient's condition–thus helping physicians make informed decisions on an appropriate course of action to take and, if needed, to quickly adjust treatment.

Numerous published studies have demonstrated that the level of ST2 in blood can best predict patient outcomes. Measuring ST2 via a simple, non-invasive blood test allows for the identification of high-risk heart failure patients for re-hospitalization and mortality versus those at lower risk, as well as to provide prognostic guidance in patients at risk of developing heart failure.

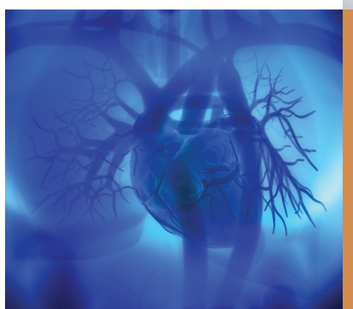
[5] Source: Ky, F. et al., High Sensitivity ST2 for Prediction of Adverse Outcomes in CHF.
[6] Source: Kohli et al., 2012, Role of ST2 in Non-ST-Elevation Acute Coronary Syndrome in the Merlin-TIMI 36 Trial.
[7] Private communication with investigators from Socrates, T., et al. Interleukin Family Member ST2 and Mortality in Acute Dyspnea.

THE NUMBERS TELL THE STORY

Heart failure patients with elevated ST2 levels are at *THREE* times greater risk of rehospitalization.[5]

MI patients with elevated ST2 levels are at *FOUR* times greater risk of developing heart failure within 30 days.[6]

Patients with acute heart failure who have elevated ST2 levels are *17x* more likely to be rehospitalized within 30 days and have *3x* greater risk of death.[7]



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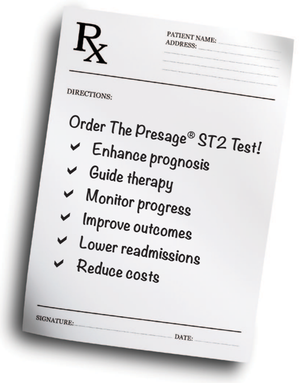
30-day rehospitalization rates for heart failure are an alarming 25%.[8] ST2 supports guided treatment and transitional care for these patients with the highest risk, in order to prevent rehospitalization and death.



[8] Based on U.S. statistics.

ST2 And You. That's The Power of 2!

In an era of cost reduction, quick and accurate risk assessment of patients is of utmost importance.

HELPING PHYSICIANS REALIZE THE VISION OF PATIENT CENTRIC MEDICINE

By utilizing Critical Diagnostic's Presage® ST2 Assay as part of a patient management program, clinicians can be more precise in caring for people with heart failure by halting or slowing down the progression of the disease.

ST2 OFFERS SUPERIOR PROGNOSIS OVER PEPTIDE MARKERS

While natriuretic peptide markers like BNP and NT-proBNP may help a physician diagnose heart failure in a symptomatic patient, in study after study, ST2 has consistently demonstrated improved accuracy of patient prognosis over peptides markers alone. ST2 also has twice the predictive value of galectin-3.[9]

Moreover, ST2 levels are not adversely affected by such confounding factors as age, gender, body mass index, atrial fibrillation, anemia, history of heart failure and impaired renal function.

USING ST2 REDUCES REHOSPITALIZATION AND DEATH

In spite of all the advancements in medicine, over one million Europeans a year end up hospitalized for heart failure; half of all heart failure patients will die within four years; and of those diagnosed with severe heart failure, more than half will die within a year of diagnosis.[10]

PATIENTS WITH ACUTE HEART FAILURE who have elevated ST2 levels are *17x* more likely to be rehospitalized within 30 days and have *3x* greater risk of death.

Heart failure is a serious and costly public health problem. But there are solutions.

For instance, intensive disease management programs have been demonstrated to reduce 30-day rehospitalization and mortality rates, and therefore improve outcomes while driving down costs.

ST2 ALLOWS ACCURATE PROGNOSIS AND STRATIFIES RISK

The Presage ST2 Assay from Critical Diagnostics, allows accurate prognosis and risk stratification of these heart failure patients, which, in turn, provides an essential element to disease management programs that provides physicians with a means of selecting those patients who are identified as requiring focused care.

By way of example, acute heart failure patients with ST2 levels above the standard cutpoint[11] are an alarming 17 times more likely to be rehospitalized and have a three times greater risk of death. Measuring ST2 levels in these patients provides clinically useful information with which to evaluate treatment options.

Using ST2 as part of a patient management program can reduce 30-day rehospitalization rates by 17.3% and also reduce 30-day mortality rates by 17.6%.[12]

USING ST2 TO PREDICT HEART FAILURE IN THE FUTURE

ST2 can also be used to predict the development of heart failure and other adverse outcomes in the general population.

The Framingham Heart Study Cohort evaluated over 3,400 "healthy" individuals to determine the prognostic utility of ST2. Study participants were followed for approximately 11 years. ST2 was the most predictive of all biomarkers studied for heart failure or death.

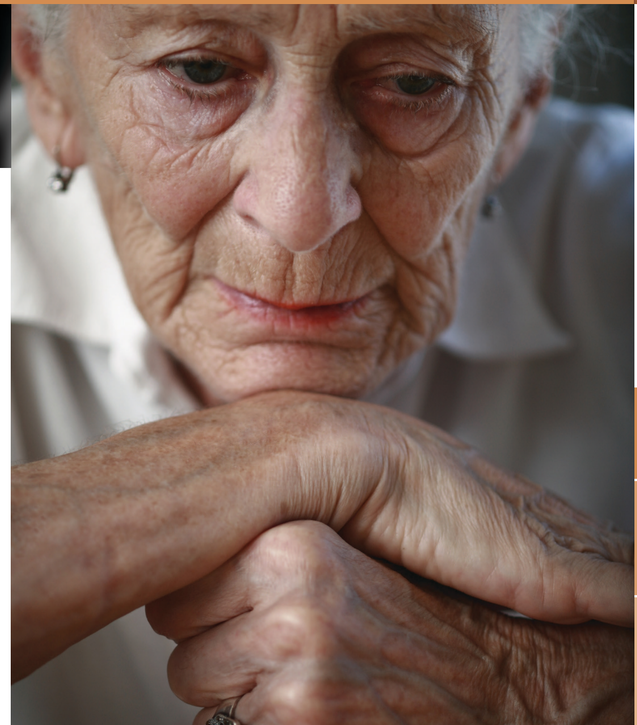
As the study authors note, "higher levels of circulating sST2[13] (comparable to those found in hospitalized patients) can be detected in apparently healthy individuals and precede adverse outcomes."

PARTNERING WITH YOU TO BRING PATIENTS HOPE FOR A BETTER LIFE

Critical Diagnostics, through its Presage ST2 Assay, is partnering with healthcare professionals to offer heart failure patients hope for a better life. That's the power of *2*.

To learn more about the benefits of ST2, go to: www.criticaldiagnostics.com.

Find out how you can put the power of *2* to work for you!



ST2 enables assessment of a patient's heart failure severity to properly guide in-hospital patient care, help determine the timing of discharge, and facilitate focused disease management to drive effective transition to outpatient care.

ST2 levels change rapidly—decreasing—in response to specific therapies that improve outcomes, thus helping guide therapy.

In several independent studies, ST2 has been shown to be a stronger prognostic indicator than the peptide markers. ST2 also has twice the predictive value of galectin-3.

Clinicians that use ST2 as part of a patient management program can dramatically reduce 30-day rehospitalization and mortality rates.

[9] Framingham Heart Study. Moreover, when galectin-3 values were adjusted for kidney function, the association with incident heart failure was not statistically relevant.
[10] Source: Department of Public Health, University of Oxford.
[11] 35 ng/ml
[12] White Paper report, *The Presage ST2 Assay is an Effective Tool to Reduce 30-Day Heart Failure Hospital Readmissions*, available through Critical Diagnostics: www.criticaldiagnostics.com.
[13] Soluble ST2, as measured by the Presage ST2 Assay.

The Impact of ST2 On Patient Management

WHAT LEADING CLINICIANS ARE SAYING ABOUT ST2

"ST2 gives prognostic information above and beyond natriuretic peptide measurements."
Alan Maisel, MD, VA Hospital, San Diego

"We continue to find that ST2 is a valuable prognostic tool in assessing patients across various stages of cardiovascular disease."
James Januzzi, Jr., MD., Mass. General Hospital

"ST2 is a very important advance in our ability to provide accurate prognostic information for patients diagnosed with chronic heart failure."
G. Michael Felker, MD., Duke University

Low — **ST2 Level** — **High**

STANDARD CUTPOINT

HEALTH STATUS	PATIENT TYPE	TREATMENT STRATEGY
HEALTHY No cardiac disease	Asymptomatic patients; ST2 median 20 ng/ml[1]	**Prevention:** Lifestyle, i.e., exercise **ST2 Testing:** Annual
PRIMARY DISEASE PREVENTION No known cardiac disease	Ambulatory patients that fall below the top quartile[2]	**Prevention:** Lifestyle, i.e., exercise **ST2 Testing:** Annual
SECONDARY DISEASE PREVENTION Treated for a recent MI	Patients who had an MI but are responding to treatment and are below the ST2 cutpoint	**Treatment:** Standard of Care (SOC) **ST2 Testing:** Regularly scheduled follow up visits
DIAGNOSED HEART FAILURE Previously diagnosed with HF	Ambulatory patients who have been diagnosed with heart failure, are responding to treatment and have ST2 levels below the cutpoint	**Treatment:** Standard of Care (SOC) **ST2 Testing:** Regularly scheduled follow up visits
PRIMARY DISEASE PREVENTION No known cardiac disease	Ambulatory patients who appear healthy but test in the top quartile[2] • 45% great risk for HF • 32% greater risk for death	**Treatment:** Lifestyle change, better hypertension management, consider prophylactic ACEi **ST2 Testing:** Quarterly
SECONDARY DISEASE PREVENTION Treated for a recent MI	MI patients with ST2 levels above the cutpoint • 4X more likely to develop HF within 30 days[3] • Predict risk of HF or CV death[4]	**Treatment:** In addition SOC, consider aldosterone antagonist to reduce fibrosis[5] **ST2 Testing:** Monthly or at each follow up visit
ACUTE HF Previously diagnosed HF, admitted to hospital	Admitted to hospital with SOB and Dx with decompensated heart failure, plus ST2 levels above the cutpoint • 17X more likely to be rehospitalized[6] • 3X greater risk of death[7]	**Treatment:** In addition to SOC, consider up titration of current therapy, add or increase dosage of beta blocker[6] **ST2 Testing:** Admission, day 3, discharge, each follow up visit
CHRONIC HF Previously diagnosed with HF, ambulatory	CHF patients currently receiving treatment, with ST2 levels above the cutpoint • 3X more likely to be rehospitalized[8] • 3X greater risk for adverse event[9]	**Treatment:** In addition to SOC, consider up titration of current therapy, add or increase beta blocker, consider inotrope and/or aldosterone antagonist[10] **ST2 Testing:** Monthly or each follow up visit

[1] Framingham Heart Study: 1136 ambulatory patients excluding patients with any cardiac disease characteristics. Publication pending 2012.
[2] Based on the Framingham Heart Study of 3,300 ambulatory patients followed for 11 years. Wang, et al. 2012 epub Circ.
Olmsted County Study: 1,831 ambulatory patients followed for over 9 years. AbouEzzeddine, et al. 2012 AHA Conference.
[3] 400 Patients: Eggers, KM., et al. ST2 and Mortality in Non-ST segment Elevation ACS.
[4] 4513 Patients: Bonaca, M., et al. ST2 and the Risk of CV Death or Heart Failure in Patients with Non-ST elevation ACS. Observations from MERLIN-TIMI-36.
[5] 100 Patients: Weir, RA., et al. Serum Soluble ST2: A Potential Novel Mediator in Left Ventricular and Infarct Remodeling After Infarct Myocardial Infarction.
[6] 1091 Patients: Socrates, T., et al. Interleukin Family Member ST2 and Mortality in Acute Dyspnea.
[7] 517 Patients: Januzzi, J., et al. Importance of Biomarkers for Long-Term Mortality Prediction in Acutely Dyspneic Patients.
[8] 1141 Patients: Ky, F., et al. High Sensitivity ST2 for Prediction of Adverse Outcomes in CHF. (PHFS)
[9] 1449 Patients: Broch K, et al. Soluble ST2 is associated with adverse outcomes in patients with heart failure of ischaemic aetiology (CORONA).
[10] HF ACTION, publication pending 2012.

"Clearly there is a need for a biomarker whose change during therapy predicts outcome . . . ST2 is the first to show changes predict 90 day mortality."
Robert L. Fitzgerald, Ph.D., UCSD

"We concluded that measurement of ST2 may help us determine which patients are at highest risk, which should allow us to treat them more appropriately."
Dr. Antoni Bayes-Genis, Hospital Universitari Germans Trias i Pujol

"Presage ST2 allows me to predict which heart failure and dyspneic patients are at highest risk of hospital readmission and serious adverse events, including death."
Dr. Christian Mueller, University Hospital Basel, Switzerland

The Presage® ST2 Assay is CE Marked and has received 510(k) clearance from the US FDA.

PRESAGE® ST2 ASSAY*

A PRODUCT OF

CRITICAL DIAGNOSTICS

*The Presage ST2 Assay is CE Marked and has received 510(k) clearance from the US FDA for use as an aid in assessing prognosis of patients with chronic heart failure.

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