

Impedance Beats Weight in Predicting HF Events

BY DIANA MAHONEY

BOSTON — Monitoring fluid buildup in the chest by intrathoracic impedance is more predictive of events in heart failure patients than is daily weight monitoring, a multicenter, prospective, double-blind investigation has found.

Dr. William T. Abraham of Ohio State University, Columbus, and colleagues conducted the Fluid Accumulation Status Trial (FAST), comparing results of intrathoracic impedance monitoring with those of daily weight monitoring—the current standard of care—in 156 heart failure (HF) patients. The investigators used a drop in intrathoracic impedance as a surrogate to identify presymptomatic, treatable fluid buildup. Impedance changes were detected with software downloaded onto the patients' implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy-defibrillator (CRT-D) devices.

All participants had HF symptoms for a mean of 18 months. At baseline, 85% were in New York Heart Association

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(NYHA) class II or III and most of the rest were in NYHA class I, Dr. Abraham reported in a late-breaking abstract presented at the annual meeting of the Heart Failure Society of America.

The investigators compared data collected by the impedance monitoring software and the patient-completed daily weight diaries. Impedance data were available nearly every day of the trial, but only 76% of the patients complied with daily weight monitoring, said Dr. Abraham.

Of the 65 HF events that occurred in 31 patients, intrathoracic impedance monitoring accurately predicted 48 of them; daily weight monitoring predicted 13. "The adjusted sensitivity for [impedance monitoring] was more than three times higher than with daily weight monitoring," at 76% and 23%, respectively, he reported. Of the predicted events, 40 of those detected by impedance monitoring were not detected by weight monitoring and 5 of those detected by weight monitoring were not detected by fluid monitoring, Dr. Abraham said.

Both impedance and weight monitoring set off many false alarms. The impedance monitoring system identified 417 "impedance crossings," which are the signals predicting an HF event, while there were 890 changes in weight that met the warning level criteria (at least three pounds gained in 1 day or at least five pounds gained over 3 days), Dr. Abraham said.

"With daily weight [monitoring], you

have less sensitivity and more false alarms to respond to [compared with impedance monitoring]," suggesting that impedance status monitoring may be the better option and should be used in addition to the daily weight monitoring in patients with implanted devices that have this capability, he said.

The findings should not be considered in a vacuum, said Dr. Lynne Warner Stevenson of Brigham and Women's

Hospital, Boston. "It's crucial that 88% of impedance crossings in this study were not associated with a following event. Responding to these could worsen renal function and lead to electrolyte derangements."

Frequent such nonevents could blunt the system's responsiveness, she added. "If you keep seeing things go up, and nothing is happening, it would be like crying 'wolf.' It will be difficult to decide

when we actually do need to intervene."

FAST was sponsored by Medtronic Inc., maker of the OptiVol Fluid Status Monitoring System used in the study. Dr. Abraham has received research grants and/or consulting fees from Medtronic, Biotronik Inc., Boston Scientific Corp., and St. Jude Medical Inc. Dr. Stevenson has received funding and/or consulting fees from CardioMEMS Inc. and Medtronic. ■

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RAAS: Knowledge is power

RAAS: an evolution in knowledge is occurring

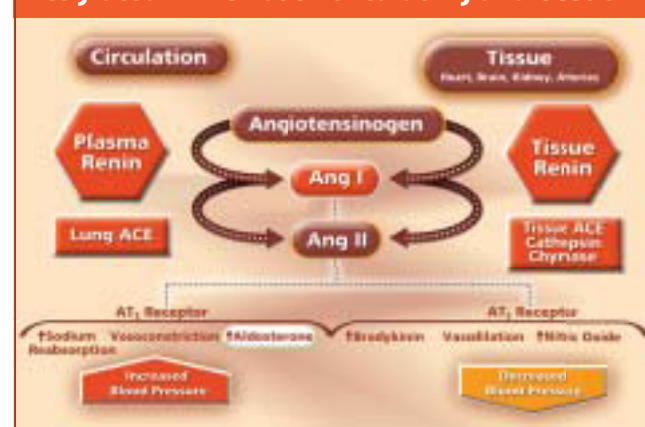
Of all the pathophysiologic pathways involved in hypertension, the renin-angiotensin-aldosterone system (RAAS) has emerged as one of the most important.¹ Although first identified more than 100 years ago, our understanding of renin and the RAAS continues to evolve.²

Classically, the RAAS has been thought of as a circulating neuro-endocrine system, whose components are produced by different organs: renin by the kidney, angiotensinogen by the liver, and angiotensin-converting enzyme by the lung. The principal biologic effector of the RAAS is angiotensin II, a potent vasoconstrictor.³ Through its actions on the AT₁ receptor, angiotensin II causes vasoconstriction and stimulates the release of aldosterone, which increases sodium reabsorption and water retention. Both of these effects increase arterial pressure.⁴

RAAS, angiotensin II, and aldosterone: state of the science

Newer research has supplemented our understanding of the RAAS and where it is located. According to a recent model, components of the RAAS have also been found in a number of different tissues throughout the body, including the heart, brain, kidneys, and vasculature. This local, or "tissue," RAAS may have autocrine and paracrine influences on local tissue function.⁵

Integrated RAAS: both circulating and tissue^{3,5-7}



Regardless of whether angiotensin II or aldosterone are found in the plasma or tissue, they are still associated with potential pathophysiological effects. For example, angiotensin II, in addition to being a potent vasoconstrictor, is also associated with direct tissue effects and has been linked to abnormalities in vascular structure and function.⁸ Similar phenomena have also been linked to aldosterone.⁹ Note that the clinical significance of tissue RAAS is unknown, as is the clinical significance of tissue vs circulating RAAS.

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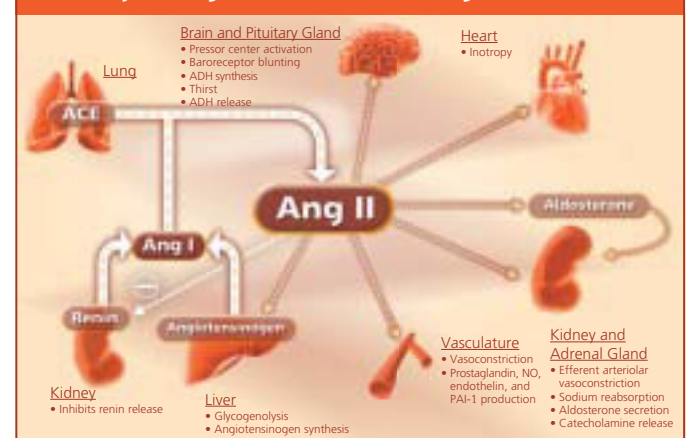
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Physiologic influence of angiotensin II⁷



Tissue vs circulating RAAS

Plasma renin activity (PRA) is a traditional measure of circulating RAAS activity: the higher the PRA, the more active the RAAS in the bloodstream.¹⁰ However, PRA doesn't tell the whole story. It has been proposed that in some patients, tissue RAAS activity may be high despite low plasma renin activity.¹¹ Although research is ongoing, there is currently no validated measure of tissue RAAS activity.

Overactive RAAS

Renin catalyzes the rate-limiting step in the RAAS. In fact, various feedback mechanisms in the RAAS target renin production as a way to regulate the system. In normotensive subjects, for example, an increase in blood pressure triggers a negative feedback loop in the RAAS that reduces RAAS activity. However, in many patients with hypertension, this response is impaired. These patients have a chronic overactive RAAS, despite the presence of elevated blood pressure.¹² In hypertensive patients, numerous comorbid conditions have been associated with an overactive RAAS, including obesity³ and diabetes.^{11,12}

In one observational study, 70% of patients with untreated hypertension had medium to high plasma renin activity.¹² This included many hypertensive patients traditionally believed to have low renin activity, such as African Americans and diabetics.¹²

New directions, exciting possibilities

We, at Novartis, are continuing to advance the understanding of the RAAS to help better manage hypertension.