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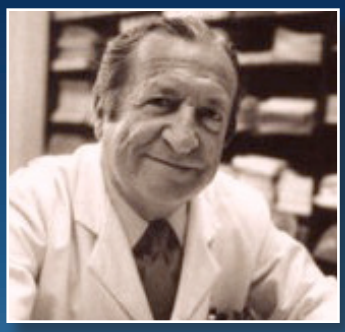

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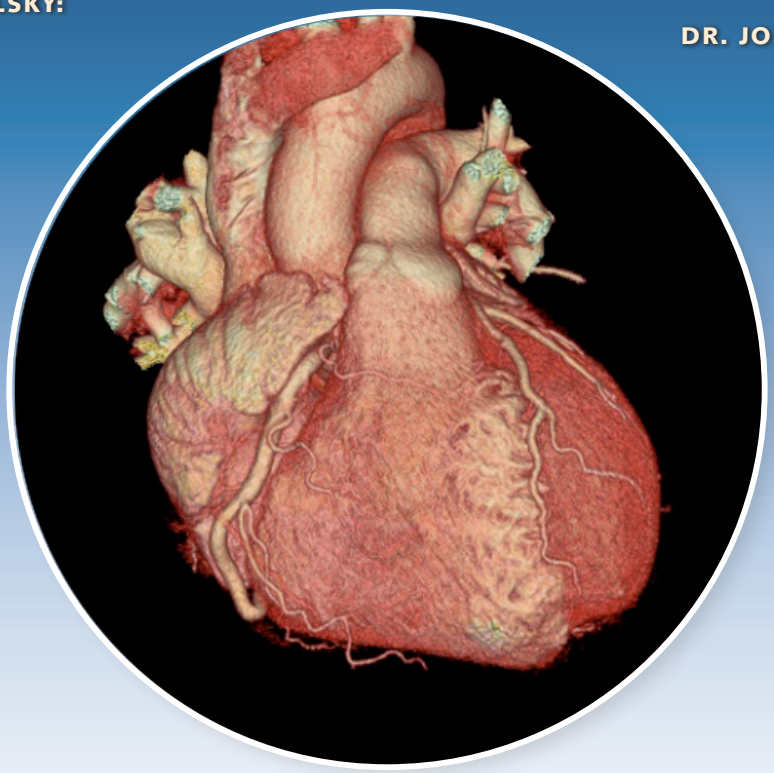

SPECIAL SECTION

ADVANCES *in* CARDIOVASCULAR DISEASE

BARBARA ROBERTS, MD, FACC, GUEST EDITOR

FEBRUARY 2014 VOLUME 97• NUMBER 2 ISSN 2327-2228

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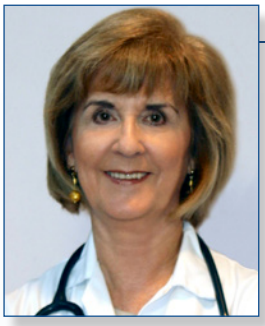

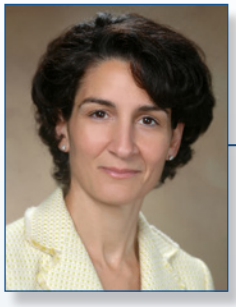

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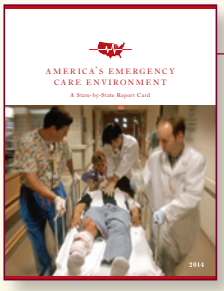
IN THE NEWS



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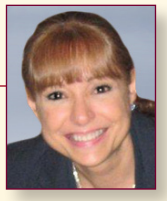

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The Hartford Hearing: Is United Listening?

ELAINE C. JONES, MD
PRESIDENT, RHODE ISLAND MEDICAL SOCIETY

United states senators Sheldon Whitehouse (D-RI) and Richard Blumenthal (D-CT) treated us all to a fascinating and valuable piece of political theater with their January 22 oversight hearing on what some are now calling "the United fiasco" – that's the decision by the UnitedHealthcare Group to disrupt hundreds of thousands of patient-doctor relationships in a dozen states by dropping thousands of doctors from their Medicare Advantage networks on short notice, without consultation and without divulging anything of the insurer's rationale or game plan.

The hearing in Hartford was a welcome diversion as we continue to wait for the Second Circuit to rule on the injunction that is currently postponing the fate of hundreds of physicians in Hartford and Fairfield Counties who received termination notices from United in October. By the way, the Rhode Island Medical Society and all of the other 49 state medical societies, in addition to the District of Columbia and the AMA itself, are represented among the *amici* whose brief urges the Second Circuit judges to uphold the injunction. We should hear soon.

Meanwhile, we all owe a great debt of gratitude to Raymond Welch, MD, the eminent dermatologist who has practiced in Providence for almost thirty years and who is without question a credit to our profession as well as a very nice guy. He took a day off from his practice right after a heavy snowstorm to travel to the Hartford state house on Wednesday, January 22. There he acquitted himself with dignity, clarity, humor and passion.

During the hearing, the interplay between the two Rhode Islanders, Dr. Welch and Senator Whitehouse, was particularly entertaining. At one point Dr. Welch made the point that insurance companies do not care for patients, only physicians do. Senator Whitehouse interjected, "In Rhode Island I have never seen an ambulance rush a patient to an insurance office."

As was to be expected, the UnitedHealthcare Group refused to send a spokesperson to the hearing, thus thumbing their corporate nose at public opinion, the people's elected representatives, and the hearing process – and squandering an opportunity to make a public case for their actions, assuming they could do so. Stephanie Kanwit, Esq., counsel to the health insurance industry's trade association (which calls itself America's Health Insurance Plans, or AHIP), had the thankless job of defending the industry's point of view in general, if not UnitedHealthcare's conduct specifically. In doing so, Ms. Kanwit predictably cited three things in the abstract: the popularity of Medicare Advantage plans; the impact of the ACA's gradual reduction in the government's payments to Medicare Advantage plans, compared with traditional fee-for-service Medicare, from +14 percent to +1 percent by 2017; and the industry's response to these phased-in funding reductions by developing "high value provider networks." The implication was that United's massive terminations this fall were but a necessary step toward consolidating "high value provider networks" in the affected markets.

At one point Dr. Welch made the point that insurance companies do not care for patients, only physicians do. Senator Whitehouse interjected, "In Rhode Island I have never seen an ambulance rush a patient to an insurance office."

Skeptical discussion of "high value networks" inspired another quip from Senator Whitehouse in support of Dr. Welch's testimony regarding the unreliability of the provider directories United makes available to subscribers who might try to find a new doctor. Dr. Welch observed that he found physicians listed there as if they were available to accept new patients, whereas in fact some of those listed had long since left the state, retired or died. Dr. Welch

even found himself listed there – with an obsolete identification number and at a street address that has not been valid for a decade. Remarked Senator Whitehouse, "You would think that a 'high value provider network' would pick up on the deadness of a doctor."

Late in the proceedings things took a new turn after Senator Whitehouse revisited one of the themes of the hearing, which was the theory, accepted by many, that United's dumping of doctors was a proxy for dumping panels of patients who suffer from costly conditions. Viewing United's action in this light, Senator Whitehouse characterized it as "cherry picking" and another example of "privatizing profits and socializing costs" – particularly since many patients would elect to stay with their doctors by switching their coverage from Medicare Advantage to traditional fee-for-service Medicare, which has the broadest, most inclusive network of all. This theory must be valid, Senator Whitehouse observed, since no one has even attempted to rebut it.

As was to be expected, the United-Healthcare Group refused to send a spokesperson to the hearing, thus thumbing their corporate nose at public opinion, the people's elected representatives, and the hearing process...

Indeed, it hadn't been rebutted, and this was by no means the first time the theory had been cited in the course of the proceedings. The hearing was almost over when Attorney Kanwit of AHIP finally responded to Senator Whitehouse's charge. She asserted that because the government's per capita payments to Medicare Advantage plans are risk-adjusted, plans have "no incentive to cherry-pick."

It is true that since 2004 Medicare has modulated its payments to Medicare Advantage plans based on patients' health status. The plans receive a higher, risk-adjusted capitation rate for a patient with diabetes or heart disease than for an otherwise similar patient without such conditions. Before 2004, the incentive for plans was simply to enroll low-cost patients; and indeed, that is what happened. One study concluded that before risk-adjustment, the government was overpaying Medicare Advantage plans by $1,800 per person on average, compared with what these relatively healthy patients would have cost under fee-for-service Medicare.

Risk-adjustment was therefore introduced in 2004 in order to correct for these overpayments by recognizing the overall lower risks of the Medicare Advantage population. But – *mirabile dictu*! – once risk adjustment was implemented, enrollment and usage patterns shifted, and Medicare Advantage spending actually increased to a differential of $3,000 per capita over traditional Medicare. It seems that somehow even enrollees with higher "risk scores" tended to be significantly below the average cost in their "risk category," and so the Medicare Advantage plans prospered even more. A study published by the National Bureau of Economic Research concluded sadly that "the Medicare Advantage program both increased total Medicare spending and transferred Medicare resources from the relatively sick to the relatively healthy, and that risk-adjustment was not able to address either of these problems."

In summing up what he learned from the hearing, Senator Whitehouse decried the human cost of what he called "Medicare gamesmanship." Senator Blumenthal said it was a case of "bait and switch" when United sold one product in bad faith and delivered another of lesser value. Both said better consumer protections are needed. We'll see how the Senators follow through. ❖

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Simplicity Isn't Always a Virtue

JOSEPH H. FRIEDMAN, MD
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In the field of neurodegenerative disorders, like Alzheimer's, Parkinson's and related diseases, there are two types of research. The more important is focused on finding the causes, which will, hopefully, result in treatments that prevent, halt progression and possibly restore function. The other type aims to treat symptoms, such as movement, cognitive and behavioral problems that occur in all of these disorders. My own work has been in the latter realm and, while I think I have contributed to better management of some of these conditions, I am quite disappointed in both myself and my colleagues for failing to accomplish more. Over the last few years I've come to believe that much of our research vision has been limited by our inability to break out of old models and become more creative. We continue to repeat our old mistakes.

A cardinal principle of research, especially clinical research, is the KISS principle: Keep It Simple, Stupid. I fully believe in it. However, it applies to designing clinical protocols. It does not apply to interpreting results or creating hypotheses. I have come to believe that much of clinical medicine has, for want of more creativity, come to cling to the KISS principle in developing new treatments. Keep it simple, or simply mimic something that works. Striking out in new directions is difficult for many reasons, if not impossible, for simple lack of funds if the funder is the marketplace.

I believe that Parkinson's disease has been like the La Brea tar pit for neuroscientists. It is the first neurological disorder for which a designed, rational therapy was instituted and found to be effective. Drugs that depleted catecholamines, a small family of chemicals in the brain, were used experimentally to treat people with schizophrenia. When these patients developed features of Parkinson's disease, which luckily was reversible, the brains of people who had died with PD were examined and were found to be deficient in catecholamines, but particularly dopamine. A gigantic simplification then was hypothesized. Increase the dopamine and perhaps people would become more normal.

Assuming that increasing dopamine in a brain that was deficient in dopamine would work similarly to giving insulin to a body that was deficient in insulin was extraordinarily naïve. After all, insulin works in the bloodstream and dopamine works in the tiny space between two brain cells called a synapse. Insulin simply has to get into the blood. Dopamine has to get into a highly targeted region. And, making the challenge more difficult, dopamine itself can't get into the brain at all because it is blocked by the blood-brain barrier. So a drug that does enter the brain and which brain cells can break down to make dopamine, L-Dopa, was given. One of my mentors, who was in training at the time L-Dopa was developed, thought that the notion that L-Dopa would be taken up by cells damaged by PD, then converted to dopamine and secreted in a normal fashion, was like expecting a car, out of gas, to start up again if gasoline was poured over it. Luckily he was wrong and L-Dopa remains our best treatment 50 years later.

We, in the clinical neurosciences, need to follow the path laid out decades ago by oncologists, and use multiple therapies simultaneously.

The problem, as I see it, is that generations of scientists have come to believe that other brain disorders are like PD and that the symptoms of disorders such as Alzheimer's, Parkinson's and related disorders may be treatable with a single drug, a "magic bullet." In PD we have the "dopamine deficit." In Alzheimer's disease it is the "cholinergic (acetylcholine) deficit." In schizophrenia there is a "dopamine excess" hypothesis. Unfortunately, even Parkinson's disease isn't like Parkinson's disease anymore. Despite learning that

improving these presumably cardinal deficits or excesses may provide some benefit, these improvements are, unfortunately, severely short of satisfying for most patients. Since almost all new medications are developed by drug companies, because of the enormous cost required they are rarely innovative, and almost always based on the notion of a single problem, to be addressed with a single drug. Unfortunately, even in PD, where dopamine replacement produces a clinically significant benefit, the results are limited and, neurologists have come to realize that most of the changes in the brain do not involve dopamine at all. Alzheimer's disease is much more than a simple memory problem. Few neurological disorders are "simple" in the sense that only one type of brain cell or one region in the brain is affected. Even in disorders in which we know the cause, a single gene abnormality, the extent of the pathological process is wide. Expecting to improve symptoms by focusing on a single chemical in the brain is destined to failure.

We, in the clinical neurosciences, need to follow the path laid out decades ago by oncologists, and use multiple therapies simultaneously. These trials will be costly and will only happen when government funds the trials or multiple pharmaceutical companies band together and patients step up to the plate and volunteer. ❖

Author

Joseph H. Friedman, MD, is Editor-in-chief of the *Rhode Island Medical Journal,* Professor and the Chief of the Division of Movement Disorders, Department of Neurology at the Alpert Medical School of Brown University, and chief of Butler Hospital's Movement Disorders Program.

Disclosures

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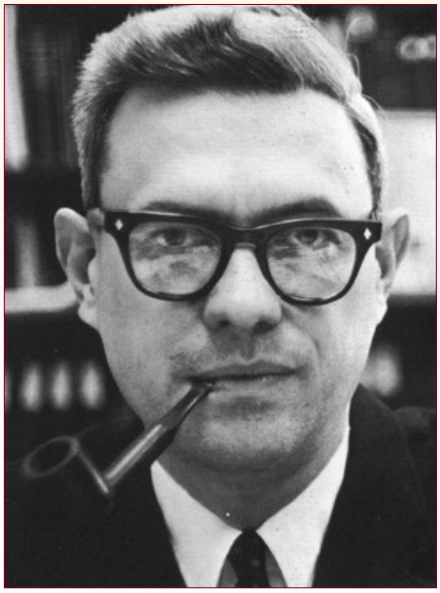
Dr. Aronson in 2007 receiving Doctor of Medical Science (DMS) at Brown in 2007.



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Stan Aronson, MD, in the early years in the 1950s at Downstate Medical Center in NYC.

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The Greek titan, Atlas, sired a daughter named Calypso, a sea nymph. Calypso, and her beguiling music, enticed Odysseus to delay his voyage (his odyssey) to home and Penelope, his wife. And for seven years Odysseus dallied on the isle of Ogygia, allegedly missing Penelope yet utterly entranced by Calypso and her music. Zeus finally declared that this sabbatical was counterproductive and Odysseus, the lone survivor of his fabled crew, went back to sea to reunite with Penelope.

The name, Calypso, from a Greek root meaning to hide, to make secret, also came to define a form of Caribbean music. And then, with the prefix, *apo-*, the Greek word, apocalypse, meaning an uncovering, a revelation. The apostle, John (6 – c.100 CE), voyaged to the Mediterranean island of Patmos to write what is now the terminal chapter of the New Testament, a book called Revelation (or The Apocalypse) which tells, in vivid metaphors, the ultimate battle between good and evil.

Two millennia ago, an apocalypse had been a revelation, neutral in its content. But the Book of Revelation changed the import of an apocalypse: it now defined a sequence of catastrophes, an eschatological view of the ultimate confrontation between the forces of divine and deadly. And the cosmic destruction that ensued was an overt expression of heavenly displeasure.

In many ancient tales, an isolated male with impeccable moral credentials lives in a deeply corrupt society. And so, when the apocalyptic event arrives, only he and his family are spared while the rest of humanity perishes. The Babylonian Epic of Gilgamesh, and its hero Utnapishtim, and the tale of Noah and his ark are early examples of apocalyptic tales. And so, the word apocalypse began life as defining a disclosure; but gradually it came to define a terrible catastrophe prompting a need for revelatory explanation.

'Another mechanism for the swift eradication of humanity is a global pandemic caused by some exotic virus originating in a primitive village in southern Madagascar.'

The revelations of St. John, in many ways, were the continuation of the prophetic responses within the Hebrew books of Jeremiah, Ezekiel and Isaiah: solitary voices predicting an apocalyptic future for an unrepentant people.

Isolated fictional works portraying worldly disaster appeared during the 19th and early 20th Centuries, particularly in the writings of Mary Shelley, Edgar Allan Poe and H. G. Wells. But the genre of apocalyptic and post-apocalyptic fiction emerged in the 20th Century only when there had been widespread apprehension of nuclear warfare and global annihilation.

The post-nuclear apocalyptic works portray, at the least, a hero and a faithful heroine undergoing an existential series of disasters, often leaving them as survivors in a world bereft of humans.

Writers of such eschatological accounts have a broad menu of destructive agents to initiate their fictional apocalypse. Nuclear warfare resulting in widespread atmospheric contamination, for example, may kill off the populace – while providentially exempting the hero/heroine from such radiologic poisoning.

Another mechanism for the swift eradication of humanity is a global pandemic caused by some exotic virus originating in a primitive village in southern Madagascar. In this variant of the apocalyptic tale, the hero may also be afflicted; but somehow he survives to contemplate a world now dominated by anthropoid creatures suddenly learning to converse in English.

Yet other themes for the apocalyptic genre include extraterrestrial invasions, genetic defects contaminating billions and ultimately, the revolt of the machines, sometimes with endearing names such as HAL, taking control of

THE HISTORY OF MEDICINE NLM COLLECTION

This poster was used in 1943 by the War Department in an Army orientation course, warning U.S. soldiers of the dangers of malaria and the pathogenicity of the Anopheles mosquito.

the world; adverse climate change; or ecological disarray caused by depletion of essential natural resources. The underlying message is best expressed in a movie advertisement: "Danger is real. Fear is a choice."

Speculation on a global apocalypse fuels such expressions as Sunday sermons, summer movies and even university commencement speeches. And whether the medium for an apocalyptic vision is the printed page, comics, radio, television or the cinema, the subtext is always twofold: first, the inevitability of human extinction; and second, except for the hero/heroine, the powerlessness of humanity to forestall the inevitable.

But amongst all of these ultimately tragic books, tales and movies, one film stands out as offering a human intervention capable of halting the disaster. In 1951, a movie appeared entitled, "The Day the Earth Stood Still." Humanity is on the brink of total extinction by alien robots. But if the heroine, played by Patricia Neal, would but remember the phrase that would nullify the robot's action, the world would then be saved. The critical words were *"Klaatu barada nikto."* At the last moment, Neal says these fateful words, and the world is saved.

Again, for your preservation, please rehearse the comforting words of salvation: *"Klaatu barada nikto."* ❖

Author

Stanley M. Aronson, MD, is Editor emeritus of the *Rhode Island Medical Journal* and dean emeritus of the Warren Alpert Medical School of Brown University.

Disclosures

The author has no financial interests to disclose.

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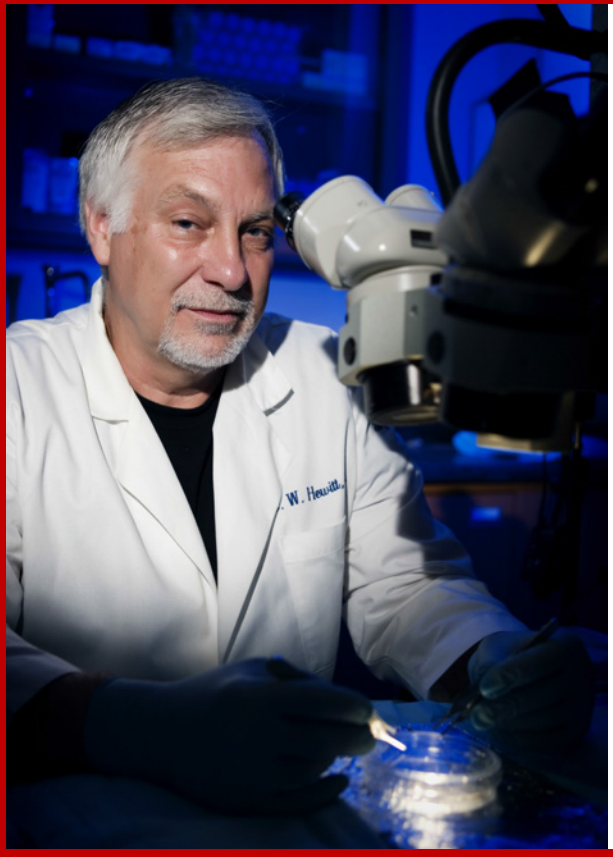

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RI Clinicians, Researchers Share Advances in Recognition and Treatment of CVD

BARBARA ROBERTS, MD, FACC
GUEST EDITOR

JOE A. AVARISTA

Barbara Roberts, MD, FACC

February is Heart Health month so it is appropriate that this issue of the *Rhode Island Medical Journal* is devoted to an update on the field of cardiology. Few specialties have seen such explosive growth in knowledge and the ability to modify disease as has cardiology over the last half century. When I was an intern in 1968–1969, coronary angiograms were new and infrequent, having been described by Cleveland Clinic physicians Drs. Sones and Shirey in 1962. Exactly one of my patients that year was referred for a cardiac catheterization. How times have changed. According to the CDC FastStats, about one million people in the United States had cardiac catheterizations/coronary angiograms in 2010 and an additional 500,000 had a coronary artery intervention. In the 1960s patients with myocardial infarction were treated with morphine and bed rest, and the first statin to be approved by the FDA was still some two decades in the future. While the mortality rate from atherosclerotic cardiovascular disease was decreasing, most of the diagnostic modalities, pharmacologic armamentarium and devices we now take for granted were not available to clinicians.

During my cardiology fellowship years in the early 1970s, echocardiography was in its infancy; a patent for the first MRI machine had just been issued; cardiac valve replacement required open heart surgery and placing the patient on cardiopulmonary bypass, diastolic heart failure was not on anyone's radar screen; Takotsubo Cardiomyopathy had not been named and percutaneous coronary interventions were still in the future – the first occurred in Switzerland in 1977. Gender-specific aspects of cardiovascular disease were not appreciated and, in fact, coronary heart disease was taught as a disease of men.

CONTRIBUTIONS

This issue of the *Rhode Island Medical Journal* features articles on various aspects of cardiovascular disease of interest to clinicians. My contribution, "Gender-Specific Aspects of Cardiovascular Disease," discusses some of the differences in symptoms, risk factors and outcomes between women and men with atherosclerotic cardiovascular disease.

In "Takotsubo Cardiomyopathy: A Clinical Review," **ATHENA POPPAS, MD, FACC, FASE** and **SADDAM ABISSE, MD**, examine this condition, which is increasingly being recognized in patients presenting with an acute coronary syndrome.

CHRISTOPHER LANG, MD, and **MICHAEL K. ATALAY, MD, PhD**, in "Cardiac Magnetic Resonance Imaging and Computed Tomography: State of the Art in Clinical Practice," review the methodologies of novel MRI and computed tomography modalities, their specific roles in the diagnosis of cardiac pathophysiology, and their utility in outcomes assessment and prognosis for various disease states.

EUY-MYOUNG JEONG, PhD, and **SAMUEL C. DUDLEY, JR., MD, PhD**, in "New Diagnostic and Therapeutic Possibilities for Diastolic Heart Failure," discuss symptoms, diagnosis, and therapeutic approaches, along with results of animal research on this condition, which is ongoing in Dr. Dudley's laboratory.

"Transcatheter Aortic Valve Replacement: A Review of Current Indications and Outcomes" by **WILLIAM PRABHU, MD**, and **PAUL GORDON, MD**, discuss this new technique for replacing stenotic aortic valves and report on the experience with the first fifty-six patients to undergo this procedure at Rhode Island Hospital.

In the last half century our understanding of cardiovascular disease has increased enormously, along with our ability to modify the course of what remains the number one killer of men and women, both in the United States and around the globe. One can only imagine what an issue of the 2054 *Rhode Island Medical Journal* on this same subject would look like. ❖

Author

Barbara H. Roberts, MD, FACC, is the Director of The Women's Cardiac Center at The Miriam Hospital and an Associate Clinical Professor of Medicine at the Warren Alpert Medical School of Brown University. She is the author of *How To Keep From Breaking Your Heart: What Every Woman Needs to Know About Cardiovascular Disease* and *The Truth About Statins: Risks and Alternatives to Cholesterol-Lowering Drugs.*

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Gender-Specific Aspects of Cardiovascular Disease

BARBARA H. ROBERTS, MD, FACC

ABSTRACT

When William Heberden gave his classic description of angina pectoris in 1768, he inadvertently described a gender-specific difference in heart disease when he noted the predominance of men with this condition. It is only in the last few decades that the medical profession has recognized that women are equally afflicted with atherosclerotic cardiovascular disease, albeit with some differences in presentation, risk factors and outcomes. This article will detail the ways in which men and women differ when it comes to the number one killer in the developed, and increasingly the developing, world.

KEYWORDS: Atherosclerotic cardiovascular disease (ASCVD), Myocardial infarction (MI), Risk factors, Coronary artery bypass graft (CABG)

INTRODUCTION

William Heberden gave an address to the Royal College of Physicians in London in 1768 in which he described a new syndrome he called "angina pectoris," a Latin term for a strangling or choking in the chest. Though he was unable to determine angina's cause, he unwittingly made the first observation of gender-specific differences in cardiovascular disease when he wrote: "I have seen nearly a hundred people under this disorder, of which number there have been three women, and one boy twelve years old. All the rest were men near, or past the fiftieth year of their age."[1]

When the epidemic of atherosclerotic cardiovascular disease (ASCVD) occurred in the twentieth century, the myth that this was a man's disease persisted. The prototypical patient with angina or myocardial infarction was described as a middle-aged male. Physicians, and women themselves, were slow to realize that atherosclerosis affected both sexes, albeit with differences that have become more apparent over the last few decades. In this article I will review gender differences in risk factors, symptoms, and outcomes in ASCVD.

RISK FACTORS

Dyslipidemia

Little was known about the etiology of ASCVD before the second half of the twentieth century. Ancel Key's Seven Countries Study in the 1950s correlated dietary saturated fat intake and serum cholesterol levels with the risk of dying of heart disease in the United States (US), Finland, Greece, Serbia, Japan, the Netherlands and Italy.[2] Unfortunately no women were included in Key's study. The Framingham Heart Study (FHS) was undertaken by the National Institutes of Health in the late 1940s in response to the epidemic of heart disease. Its objective was to identify the risk factors that contribute to the development of ASCVD.[3]

The study recruited 5,209 men and women between the ages of 29 and 62. The subjects returned every two years for detailed physical examinations, life style interviews and blood tests. FHS and other epidemiologic studies around the world led to the identification of the major modifiable risk factors for ASCVD: smoking, hypertension, hypercholesterolemia, diabetes, obesity and sedentary lifestyle. The unmodifiable risk factors include age and family history.

At that time cholesterol metabolism was poorly understood, but with the groundbreaking work of Drs. Robert Levy, Donald Fredrickson, Michael Brown and Joseph Goldstein, the roles of lipoproteins and of lipoprotein receptors in the pathogenesis of atherosclerosis were slowly unraveled.

The lipoproteins are classified according to their density, and all lipoproteins with the exception of high-density lipoprotein (HDL) are atherogenic. The first hint that low-density lipoprotein (LDL) might not be as atherogenic in women as men arose from the work of Neil Stone in the US and Joan Slack in England on kindred with Type II Familial Hypercholesterolemia.[4,5] At equivalent markedly elevated LDL-cholesterol levels, affected women in these families developed signs and symptoms of ASCVD on average 10 to 15 years later than affected men.

Cui and his colleagues followed a cohort of 2,406 healthy men and 2,056 healthy women ages 40 to 64 for an average of 19 years.[6] All had measurements of total cholesterol, LDL-cholesterol, non-HDL-cholesterol, and HDL-cholesterol. Elevations in total, LDL-cholesterol, and non-HDL cholesterol, along with low levels of HDL-cholesterol all correlated with an increased risk of cardiovascular disease (CVD) mortality in men. In women, only low levels of HDL-cholesterol and high levels of non-HDL-cholesterol predicted CVD mortality in women and the relative risk was greater in women than in men. Even at LDL-cholesterol levels of over 190 mg/dl, there was only a small and statistically insignificant increase in a woman's risk of dying of cardiovascular disease (CVD). And at equivalent LDL-cholesterol

levels ranging from under 131 mg/dl to over 160 mg/dl, women with HDL-cholesterol under 50 mg/dl had a 3 to 4 four-fold increase in the risk of dying of CVD.

Other studies have looked at triglyceride (TG) levels and the risk of CVD and found that risk in women is increased more than in men as TG increases.[7,8] With regard to lipids therefore, it appears that LDL cholesterol is less predictive of risk in women than in men, while elevations of non-HDL cholesterol (with which hypertriglyceridemia is closely linked) and low levels of HDL cholesterol are more predictive of risk.

Smoking

There is good epidemiologic evidence that smoking is a stronger risk factor in women than men. In a Danish study of smoking and age at first myocardial infarction (MI), smoking lowered the median age of first MI in women from 79 to 60, and in men from 71 to 64 years of age.[9]

Another investigation into smoking risk looked at pooled data from three studies with a total cohort of 11,472 women and 13,191 men who were followed for a mean of 12.3 years. The relative risk of MI in women who were current smokers was 2.24 compared with 1.43 in male smokers. This difference was significant and was unchanged after adjustment for other risk factors. Among women who were under 55, the relative risk of MI was increased almost 7-fold compared to almost 3-fold for same-aged men.[10]

Diabetes

Diabetes, like smoking, is a more potent risk factor in women than in men. Kannel and Wilson[11] analyzed Framingham data and found that the age-adjusted relative risk for coronary heart disease (CHD) in diabetic women compared to non-diabetic women was 3.7 (men 1.5), for peripheral arterial disease 6.4 (men 3.4) and for cardiac failure 8.0 (men 4.4). In a 40-year follow-up of the Rancho Bernardo Cohort Study, Dr. E. Barrett-Connor reported that men who had diabetes by history or fasting plasma glucose had a 2.4-fold excess risk of heart disease compared to men without diabetes, and women who had diabetes had a 3.5-fold excess risk compared to women without diabetes; these differences were independent of many covariates.[12]

In summary, while women and men have the same risk factors for ASCVD, smoking, hypertriglyceridemia, low HDL-cholesterol and diabetes impart greater risk to women than men, while elevations of LDL-cholesterol impart more risk to men than women.

SYMPTOMS

Gender disparity in the way ASCVD presents was first noted in the Framingham study.[13] In a 26-year follow-up study of the initial participants, a striking difference was found in the ways men and women presented. There were a total of 1,240 coronary events among the initial cohort; these included MI's, sudden death, angina pectoris and unstable angina. Despite roughly equal numbers of men and women, 60% of these events occurred in men and 40% occurred in women. Among men, acute MI was the most frequent presentation, comprising 43% of men's initial coronary events; an additional 10% of first events in men were episodes of sudden death. Among women however, angina was the presenting complaint in 53% of women and MI was the initial event in only 29% of women. The authors also noted that once ASCVD was manifest in women they had a greater risk

HISTORY OF MEDICINE (NLM) COLLECTION

This portrait of English physician William Heberden, MD, (1710–1801) was painted by Sir William Beechey.

The following is from an address called "Some Account of a Disorder of the Breast" given by William Heberden, MD, in 1768, to the Royal College of Physicians in London, in which he coined the term *angina pectoris.*

… But there is a disorder of the breast marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, which deserves to be mentioned more at length. The seat of it and sense of strangling, and anxiety with which it is attended, may make it not improperly be called angina pectoris. They who are afflicted with it are seized while they are walking (more especially if it be up hill, and soon after eating) with a painful and most disagreeable sensation in the breast, which seems as if it would extinguish life, if it were to increase or continue; but the moment they stand still this uneasiness vanishes…

of mortality with an MI than did men. This finding has been found in other studies as well.[14,15] FHS was first to report on the greater likelihood of silent or unrecognized MI's in women compared to men (34% vs 27% respectively).[13]

The Coronary Artery Surgery Study revealed gender discrepancies in anginal prognosis. Among the study population of 20,391 patients, all of whom had coronary angiograms for the evaluation of chest pain (CP), 50% of women compared to 17% of men were found to have minimal or no atherosclerosis.[16]

Because women with angina were less likely than men to have obstructive coronary artery disease (CAD) the Women's Ischemia Syndrome Evaluation (WISE) investigations were undertaken to optimize symptom evaluation and testing, to explore the mechanisms for symptoms and ischemia in the absence of angiographic coronary stenosis and to investigate the role of reproductive hormones on symptoms.[17] A total of 159 women (out of 323) who had coronary angiograms for chest pain were found to have minimal or no luminal irregularities. Intracoronary adenosine was used to determine the presence or absence of coronary microvascular dysfunction. Seventy-four (47%) had sub-normal coronary flow velocity reserve suggestive of microvascular dysfunction. The authors concluded that this abnormality was present in about half of women who had chest pain in the absence of obstructive CAD.

Despite the absence of coronary obstruction, the WISE investigators observed a high rate of adverse outcomes in these women. They subsequently undertook an intravascular ultrasound (IVUS) study of 100 women with suspected ischemia without obstructive CAD ($\geq$50% stenosis).[18]

The study showed 69.6% of patients had no ($\leq$20% stenosis) and 30.4% had minimal CAD. IVUS investigation in 92 women showed that 21% had no atherosclerosis while in the remaining 79% per cent atheroma volume was 27$\pm$8%. The number of risk factors correlated with the percent of atheroma volume and percent of vessel involvement. Seventy-three percent of the women in whom remodeling was assessed had evidence of positive remodeling. These findings were felt to help explain the increased risk of adverse outcomes.

A recent study of sex differences in symptoms in acute coronary syndrome (ACS) among 1,015 patients (30% women) under 55 found that women were significantly more likely than men to have non-ST-segment elevation MI (37.5% vs 30.7%) and to present without chest pain (19.0% vs 13.7%).[19] Although CP was the most common presenting symptom of ACS, patients without CP were not different from those with CP in type of ACS, troponin level, or coronary stenosis.

Multiple studies have looked at gender differences in symptom presentation with acute MI. In addition to the FHS finding mentioned above, a study from Canada found that women with MI were more likely than men to have atypical symptoms, had a higher prevalence of diabetes and hypertension, and were older.[20] McSweeney and her colleagues administered questionnaires to 515 female survivors of documented MI. Among prodromal symptoms the most common was unusual fatigue, occurring in almost 71% of women. Only 29.7% of women had prodromal chest pain. Acutely, at presentation with MI, the most common symptom was shortness of breath (57.9%). Forty-three percent of women experienced no chest pain and of those who experienced discomfort the most frequent locations were the back (37%) and high chest (27.7%).[21]

Disparate findings were reported from the Myocardial Infarction Triage and Intervention Registry which found no gender differences in symptoms of MI with 99% of 841 men and 99.6% of women presenting with chest pain.[22]

OUTCOMES

Women have a higher mortality than men from MI. Vaccarino and her colleagues abstracted data on over 155,000 women and over 229,000 men entered into the National Registry of Myocardial Infarctions 2.[23] Overall in-hospital mortality was 16.7% for women and 11.5% for men. Among patients under age 50, women's mortality was 6.1% compared to 2.9% for same-aged men. The difference in mortality between men and women was no longer significant after age 74. More recent data was reported from 78,254 patients with acute MI in 420 United States hospitals from 2001-2006.[24] In the overall cohort, mortality was 8.2% in women and 5.7% in men. This difference was not statistically significant, but in the ST segment elevation MI cohort, there was a significant difference in mortality, 10.2% in women vs 5.5% in men. In this study, women were less likely to receive early medical and acute reperfusion therapies, timely pharmacological and mechanical reperfusion, and invasive procedures. Women were older than men and had more co-morbidities.

Other studies have found that women have higher operative mortality from coronary artery bypass surgery (CABG).[25] In this retrospective analysis of 15,440 patients who had CABG at 31 Midwestern hospitals, operative mortality (OM) was 4.24% in women and 2.23% in men, $p<0.0001$. After adjustment for all co-morbidities, even body surface area, female gender remained an independent predictor of increased mortality (risk adjusted OM 3.81% in women and 2.43% in men). Another review of CABG and percutaneous coronary interventions (PCI)[26] in 2007 examined 23 studies reporting outcomes by gender for CABG and 48 reporting outcomes for PCI. The authors found that the majority of studies noted greater in-hospital mortality in women than men, with mortality differences resolving with longer follow-up.

SUMMARY

Gender differences in ASCVD exist for presenting symptoms, risk factor weighting, and outcomes. More research will hopefully elucidate mechanisms and improve the treatment of women with this disease.

References

1. Heberden W. Some account of a disorder of the breast. *Medical Transactions 2*, 59-67 (1772) London: Royal College of Physicians.
2. Keys A, Menotti A, Karvonen MJ et al. The diet and 15-year death rate in the seven countries study. *Am J Epidemiol*. 1986;124:903-915.
3. http://www.framinghamheartstudy.org/about/history.html. Accessed September 2013.
4. Stone NJ, Levy RI, Fredrickson DS, Verter J. Coronary artery disease in 116 kindred with familial type II hyperlipoproteinemia. *Circulation*. 1974;49:476-488.
5. Slack J. Risks of ischaemic heart disease in familial hyperlipoproteinaemic states. *Lancet*. 1969;2:1380-1382.
6. Cui Y, Blumenthal RS, Flaws JA et al. Non-High-Density-Cholesterol Level as a Predictor of Cardiovascular Disease Mortality. *Arch Intern Med.* 2001;161:1413-1419.
7. Castelli WP. Epidemiology of triglyercerides: a view from Framingham. *Am J Cardiol*. 1992;70:3H-9H.
8. Austen MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. *Am J Cardiol.* 1998;81:7B-12B.
9. Hansen EF, Andersen LT, Von Eyben FE. Cigarette smoking and age at first myocardial infarction, and influence of gender and extent of smoking. *Am J Cardiol*. 1993;71:1439-1442.
10. Prescott E, Hippe M, Schnohr P et al. Smoking and risk of myocardial infarction in women and men: longitudinal population study. *BMJ*. 1998;316:1043-47.
11. Kannel WB, Wilson PW. Comparison of risk profiles for cardiovascular events: implications for prevention**.** *Adv Intern Med.* 1997;42:39-66.
12. Barrett-Connor E. Why Women Have Less Heart Disease Than Men and How Diabetes Modifies Women's Usual Cardiac Protection. A 40-Year Rancho Bernardo Cohort Study. Global Heart http://dx.doi.org/10.1016/j.gheart.2012.12.002. Accessed Sept. 20, 2013.
13. Lerner DJ, Kannel WB. Patterns of coronary heart disease morbidity and mortality in the sexes: A 26-year follow-up of the Framingham population. *Am Heart J*. 1986;111:383-390.
14. Vaccarino V, Parsons L, Every NR et al. Sex-based differences in early mortality after myocardial infarction. *N Engl J Med*. 1999;341:217-225.
15. Hanratty B, Lawlor D, Robinson M et al. Sex differences in risk factors, treatment and mortality after acute myocardial infarction: an observational study. *J Epidemiol Community Health*. 2000;54(12): 912-916.
16. Chaitman BR, Bourassa MG, Davis K et al. Angiographic prevalence of high-risk coronary artery disease in patient subsets (CASS). *Circulation*. 1981;64:360-367.
17. Rogers WJ, Bairey Merz CN, Sopko F, Pepine CJ for the WISE Study Group. Coronary microvascular dysfunction is highly prevalent in women with chest pain in the absence of coronary artery disease: Results from the NHLBI WISE study. *Am Heart J*. 2001;141:735-741.
18. Khuddus MA, Pepine CJ, Handberg EM et al. An intravascular ultrasound analysis in women experiencing chest pain in the absence of obstructive coronary artery disease: a substudy from the National Heart, Lung and Blood Institute-Sponsored Women's Ischemia Syndrome Evaluation (WISE). *J Interv Cardiol*. 2010 Dec;23(6):511-9. doi: 10.1111/j.1540-8183.2010.00598.x. Epub 2010 Oct 4. Accessed Sept. 27, 2013.
19. Khan NA, Daskalopoulou SS, Karp I et al. Sex Differences in Acute Coronary Syndrome Symptom Presentation in Young Patients. *JAMA Intern Med*. 2013. DOI: 10.1001/jamainternmed.2013.10149. Accessed Sept. 24, 2013.
20. Gregor RD, Bata IR, Eastwood BJ et al. Gender differences in the presentation, treatment and short-term mortality of acute chest pain. *Clin Invest Med.* 1994;17(6):551-562.
21. McSweeney JC, Cody M, O'Sullivan P et al. Women's Early Warning Symptoms of Acute Myocardial Infarction. *Circulation*. 2003;108:2619-2623.
22. Kudenchuk PJ, Maynard C, Martin JS et al. for the MITI Project Investigators. Comparison of presentation, treatment, and outcome of acute myocardial infarction in men versus women. *Am J Cardiol*. 1996;78:9-14.
23. Vaccarino V, Parsons L, Every R et al. Sex-Based Differences in Early Mortality after Myocardial Infarction. *N Engl J Med*. 1999;341:217-225.
24. Jneid H, Fonarow GC, Cannon CP et al. Sex Differences in Medical Care and Early Death After Acute Myocardial Infarction. *Circulation*. 2008;118:2803-2810.
25. Blankstein R, Parker Ward R, Arnsdorf M et al. Female Gender Is an Independent Predictor of Operative Mortality After Coronary Artery Bypass Graft Surgery. *Circulation*. 2005;112: I-323-I-327.
26. Kim C, Redberg R, Pavlic T and Eagle KA. A Systematic Review of Gender Differences in Mortality after Coronary Artery Bypass Graft Surgery and Percutaneous Coronary Interventions. *Clin. Cardiol*. 2007;30(10):491-495.

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Takotsubo Cardiomyopathy: A Clinical Review

SADDAM S. ABISSE, MD; ATHENA POPPAS, MD, FACC, FASE

ABSTRACT

Takotsubo cardiomyopathy is a reversible cardiomyopathy which has increasingly been recognized in the differential diagnosis of patients presenting with acute coronary syndrome. It is characterized by transient systolic ventricular dysfunction with regional wall motion abnormalities beyond a single vascular territory and in the absence of significant epicardial coronary artery obstruction. Often, there is an acute emotional or physical stressor immediately preceding the presentation. Classical apical ballooning is seen on ventriculography or echocardiography but variants with isolated basal or mid wall akinesis have been described. Catecholamine excess and cardiotoxicity is the most compelling putative mechanism. The long-term prognosis is excellent but serious complications including cardiogenic shock and arrhythmias may occur acutely. Supportive treatment is the mainstay of therapy.

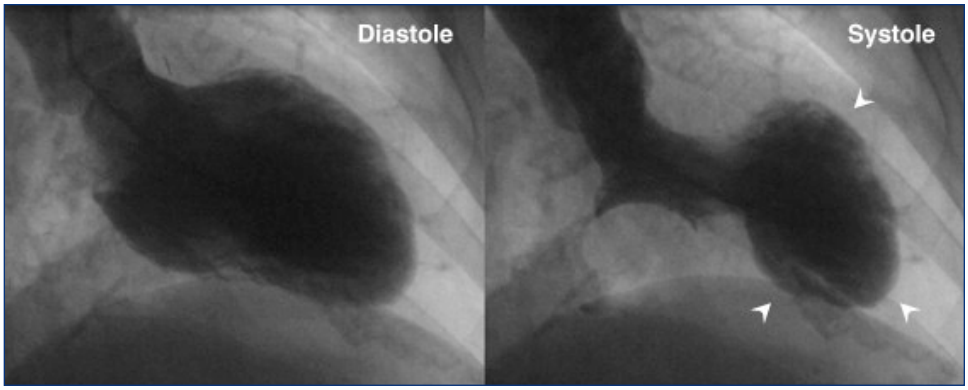
KEYWORDS: Takotsubo cardiomyopathy (TTC), Apical ballooning syndrome (ABS), Stress Cardiomyopathy

INTRODUCTION

Takotsubo cardiomyopathy (TTC) is also known as broken-heart syndrome, apical ballooning syndrome and stress-induced cardiomyopathy. It is a reversible cardiomyopathy characterized by transient systolic ventricular dysfunction with a clinical presentation indistinguishable from acute myocardial infarction but in the absence of significant coronary artery obstruction.[1,2] It is frequently precipitated by sudden, stressful emotional events, but there are also reports of TTC following physiologic stress such as sepsis, non-cardiac surgery, and subarachnoid hemorrhage.[2,3,4] This syndrome was reported as early as 1967 in patients under intense emotional stress such as bereavement or after homicidal assault.[5,6] In the 1990s, Sato and colleagues coined the term takotsubo cardiomyopathy to describe the unusual shape of the left ventricular during systole.[7,8] Typically, the mid to apical segments of the left ventricle are akinetic and the spared, basal walls exhibit compensatory hypercontractility. Takotsubo is a pot with round base and narrow neck used in Japan for trapping octopuses and has a similar appearance to this apical ballooning. TTC occurs most commonly in post-menopausal women and has a very good prognosis. Acutely, patients are often critically ill with heart failure and secondary complications such as left ventricular outflow tract obstruction, and arrhythmias but ventricular dysfunction and symptoms resolve quickly and death is very rare. In this systemic review we will describe the clinical presentation, pathophysiology, prognosis and treatment of this syndrome.

Epidemiology and clinical presentation

Because of increasing awareness of this condition, in 2006 the American Heart Association incorporated TTC into the classification of cardiomyopathies as a primary acquired cardiomyopathy.[9] The lack of consensus on a diagnostic criteria and the under-recognition of the disease makes it challenging to estimate the true prevalence of TTC. The best estimates come from several studies looking at consecutive patients presenting to the hospital with suspected acute coronary syndrome or myocardial infarction. Here, it has been reported to account for 1-3% of all acute coronary cases.[10,11] Retrospective and prospective reports have noted a marked gender discrepancy in this condition.[12,13] A recent review of published case series reveals that 90% of cases reported are in post-menopausal women



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ages 58-75 years old, with only < 3% of cases being found in those under 50 years old. [1,14,15]

The clinical presentation of TTC is often identical to acute myocardial infarction (AMI). Most patients with takotsubo cardiomyopathy present with typical anginal chest pain, dyspnea, ischemic changes on electrocardiogram (ECG), and elevated cardiac markers, where as syncope and out-of-hospital cardiac arrest are rare.[16] Emotional stress, such as news of the death of a family member, divorce, or public speaking, is implicated as the trigger in approximately two-thirds of patients.[3,5,6,11] However, other physical stressors such as non-cardiac surgery, sepsis, or critical illness have been reported.[2,3,4] In one provocative prospective study, consecutive critically ill patients with no prior cardiac history who were admitted to a medical ICU underwent serial echocardiograms; 28% were noted to have transient reduced ejection fraction with imaging features consistent with takotsubo cardiomyopathy.[17] Interestingly, there is a gender disparity in precipitants of TTC. In a recent TTC registry, Scheinder et al[12] observed that physical stress was a more frequent trigger in men compared to women, 57% vs 30%; these result confirm previous reports in gender difference among hospitalized patients.[13]

Table 1. Mayo clinical Criteria for Takotsubo Cardiomyopathy

(1) transient hypokinesis, akinesis, or dyskinesis of the left ventricular mid segments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution; a stressful trigger is often, but not always present
(2) absence of obstructive CAD or angiographic evidence of acute plaque rupture
(3) new electrocardiographic abnormalities (either ST-segment elevation and/or T wave inversion) or modest elevation in cardiac troponin
(4) absence of pheochromocytoma and myocarditis

Electrocardiographic changes and cardiac biomarkers

The most common abnormality on the ECG is ST elevation and T-wave inversion in the precordial leads.[18] However there is significant variability in the frequency of these abnormalities in the literature. Prasad et al[1] proposed two possible explanations for the variability. First, ST elevations are transient, thus the time from symptom onset to presentation might determine whether or not ST elevation is found. Secondly, there may be selection bias towards those patients with ST elevation, where early invasive coronary angiography and ventriculography are usually performed. Several investigators have proposed ECG criteria to differentiate TTC from acute myocardial infarction.[18] The absence of q waves, reciprocal changes, ST segment elevation in V1 with sum of ST elevation in V4-6 greater than that in V1-V3 as well as ST depressions in a VR have been shown to discriminate between the two diseases with high sensitivity and specificity.[18,19] Also, more extensive ST elevation in inferior leads were seen more frequently in TTC compared with anterior myocardial infarction.[20] However, these findings were described in an Asian population and in a subsequent, larger study in Caucasian population, the discriminatory ability of these findings could not be validated. [21] Hence, there may be some population differences in presenting signs and specific ECG changes should be considered suggestive but not diagnostic of TTC.

Evolutionary changes on ECG often occur two to three days after initial symptoms and presentation, with resolution of ST elevation, followed by diffuse and deep T-wave inversion, prolongation of QT interval. Pathologic q waves may be observed initially but rarely persist. T-wave inversion and QT-prolongation may persist for three to four months.[22]

Modest elevation of cardiac biomarkers is often observed in TTC.[3,23] In the systematic review of 14 studies which included 286 patients, 14% of patients had no measured troponin release.[11] Also, cardiac troponin levels in TTC are much less than that typically observed in acute ST elevation myocardial infarction and are out of proportions to the extensive wall motion abnormalities and hemodynamic compromise.[25] Troponin T levels are typically < 5ng/ml.[4]

Diagnosis

Due to the dramatic clinical presentation and high suspicion for acute myocardial infarction, most patients undergo emergent coronary angiography. Typical findings in TTC are normal epicardial coronaries, mild non-obstructive atherosclerosis, or rarely coexistent coronary artery disease.[1,2] Therefore, TTC is a diagnosis of exclusion which can only be made after coronary angiography. It should be on the differential diagnosis in any post-menopausal women over 50 years old presenting with chest pain and ischemic ECG changes particularly in the setting of emotional stress. Furthermore it should also be considered in critically ill patients with sudden hemodynamic compromise and/or heart failure. Researchers at Mayo Clinic proposed diagnostic criteria in 2004 (modified in 2008) for TTC which includes four components. (**See Table 1**).[1]

Cardiac imaging

Ventriculography reveals apical ballooning, with characteristic sparing of the basal segments and akinesis of the mid and apical left ventricle. However, variants of this pattern have been described including midventricular ballooning or basal and midventricular akinesis with apical sparing (inverted Takotsubo).[24] In patients with typical TTC, the wall motion abnormality usually extends beyond the distribution of a single coronary artery.

Other imaging modalities are complementary in diagnosis of the condition, eliciting potential complications and in directing management. Echocardiography can detect and measure the degree of left ventricular outflow (LVOT) obstruction and associated systolic motion of the anterior mitral valve

and significant mitral regurgitation. LVOT obstruction is reported to occur in 25% patients[3,15] and can have a major impact on acute management. In patients with hemodynamic compromise and shock, inotropes would worsen this situation and betablockers and pure vasopressor pharmacologic or mechanical support may be needed. The typical findings on cardiac MRI include the absence of delayed gadolinium hyperenhancement. This is specific to TTC and can help differentiate it from myocarditis and acute myocardial infarction in which delayed hyperenhancement is present.[25]

Pathophysiology

The pathophysiologic basis of TTC has not been conclusively determined but several mechanisms have been proposed. The underlying histopathological findings on myocardial biopsy include interstitial infiltrates of mononuclear lymphocytes and macrophages with fibrosis and contraction band necrosis; these findings are distinctly different than those of coagulation necrosis seen in typical atherosclerotic epicardial artery occlusion and myocardial infarction. Potential pathophysiologic mechanisms include: multivessel coronary artery spasm with resultant ischemia and stunning of the myocardium; aborted myocardial infarction of a long wrap around left anterior descending artery (LAD); microvascular dysfunction and myocarditis; and most prominently, catecholamine overload.

In the early Japanese literature, Dote et al,[8] in the review of their 5 cases, suggested that multivessel coronary spasm was the cause of the reversible cardiomyopathy. However, the inability of intracoronary ergometrine or acetylcholine to induce vasospasm in a majority of patients with TTC (28% of patients),[11] and the lack of coronary spasm during cardiac catheterization in the majority of patients presenting with TTC, makes multivessel coronary spasm unlikely. A possibility of a spontaneously aborted myocardial infarction has been put forth in patients with a long wrap around left anterior descending[21]; however, later studies using intravascular ultrasound have failed to show typical plaque rupture of a culprit lesion.[26] Studies showing absence of delayed hyperenhancement on cardiac MRI make myocarditis extremely unlikely.[25] Diminished coronary flow reserve and increased TIMI frame counts, which are markers of microvascular dysfunction, have been found in some patients with TTC.[23,27] However, in many cases of TTC, angiography failed to show slow flow.[28] Though impaired microcirculation may occur in the acute phase, it is not direct evidence of causation; microcirculatory impairment can be the result of primary myocardial injury and increased wall stress.[28]

Enhanced sympathetic activity appears to play a central role in the pathophysiology of takotsubo cardiomyopathy. The last and most plausible mechanism is a catecholamine-induced stunning of the myocardium and local cardiac sympathetic disruption. Similarly, increased sympathetic activity is also observed during acute cerebrovascular accidents and during the catecholamine-induced cardiomyopathy in patients with pheochromocytoma.[29] Excessive levels of catecholamines have been observed in patients with takotsubo cardiomyopathy.[30] Catecholamines have been shown to induce myocardial damage,[31,] and excessive stimulation of cardiac adrenergic receptors has led to transient LV dysfunction in animal models.[32] Furthermore, a recent hypothesis favors local cardiac sympathetic disruption. Y-Hassan[28] argues that the emerging evidence in animal models, showing local cardiac sympathetic nerve endings with local norepinephrine (NE) release and spill over to the myocardium; as well as the circular ventricular wall motion abnormality that follows the nerve end distribution rather than vascular distribution support the hypothesis of local sympathetic disruption as the pathologic mechanism underlying TTC.

Prognosis and Treatment

Takotsubo cardiomyopathy has an excellent prognosis, with full and early recovery in virtually all patients**.** The majority of patients have normalization of LVEF within a week and all patients by 4-8 weeks. The reported in-hospital mortality is low (0-8%) with the largest case series reporting 3% mortality; it may be increased in those with underlying conditions.[14-16] Long-term survival is similar to the general population .[12-14] In published data, the reported 4-year recurrence rate is approximately 4-10%.[13,14,33] The mechanisms underlying recurrence or risk factors predisposing an individual patient to recurrence are not understood.

Although TTC has a favorable prognosis, several acute complications have been reported and should be anticipated. Congestive heart failure is documented in 3-46% of published cases, but hypotension and shock are rare in 4%.[14] Systemic thromboembolism is reported in 5%.[34] LVOT obstruction has been seen in 20-25% of patients[3] but symptomatic obstruction is uncommon.[1] Recent data suggest the arrhythmias, including atrial fibrillation, are presents in 10-26% of cases, but fatal arrhythmias such as ventricular fibrillation are rare.[35]

Takotsubo cardiomyopathy is a temporary condition and hence the goals of treatment are usually conservative, supportive care. The therapy is guided by the patient's clinical presentation and hemodynamic status. Despite the putative causal role of catecholamines in the disorder, patients who present in cardiogenic shock, and in the absence of LVOT obstruction, may be treated with inotropes. Alternatively patients may derive further benefit from mechanical hemodynamic support with intra-aortic balloon pump or rarely, left ventricular assist devices. If LVOT obstruction is present with cardiogenic shock, inotropes should be avoided and phenylphrine is the pressor agent of choice often combined with betablockade. Most experts advocate guideline-directed medical therapy for patients with left ventricular dysfunction. This includes cardioselective beta-blockers and ACE inhibitor for a short period of time (3-6 months).[10] Full anticoagulation is usually reserved for those with documented ventricular thrombus or evidence of embolic events.

CONCLUSION

Takotsubo cardiomyopathy is an acquired, transient cardiomyopathy with an excellent prognosis. Patients present after an acute emotional or physical stressor with signs and symptoms similar to acute coronary syndrome but on coronary angiography do not have obstructive coronary artery disease. Catecholamine cardiotoxicity is the most likely causative mechanism. Typically, TTC has acute left ventricular systolic dysfunction sparing only the base of the heart and may be complicated by heart failure. Supportive treatment is the mainstay of therapy.

References

1. Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. *Am Heart J*. 2008 Mar;155(3):408-1.
2. Kono T, Morita H, Kuroiwa T, Onaka H, Takatsuka H, Fujiwara A. Ventricular wall motion abnormalities in patients with subarachnoid hemorrhage: neurogenic stunned myocardium. *J Am Coll Cardiol*. 1994;24:636–640.
3. Sharkey SW, Lesser JR, Zenovich AG, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation*. 2005;111:472–47.
4. Rivera JM, Locketz AJ, Fritz KD, et al. "Broken Heart syndrome" after separation (from OxyContin). *Mayo Clin Proc*. 2006;81:825–828.
5. Rees WD, Lutkins SG. Mortality of bereavement. *Br Med J*. 1967;4:13–16.
6. Cebelin MS, Hirsch CS. Human stress cardiomyopathy. Myocardial lesions in victims of homicidal assaults without internal injuries. *Hum Pathol*. 1980;11:123–132
7. Sato HTH, Tateishi H, Uchida T, et al. (1990) Takotsubo type cardiomyopathy due to multivessel spasm. In: Kodama, K., Haze, K. and Hon, M., Eds., Clinical Aspect of Myocardial Injury: From Ischemia to Heart Failure (in Japanese). *Kagakuhyouronsya Co*., Tokyo, 56-64.
8. Dote K, Sato H, Tateishi H, Uchida T, Ishihara M. Myocardial stunning due to multivessel coronary spasm: a review of 5 cases. *J Cardiol*. 1991;21:203–214. [in Japanese]
9. Maron BJ, Towbin JA, Thiene G, Antzelevitch C, Corrado D, Arnett D, Moss AJ, Seidman CE, Young JB. American Heart Association; Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; Council on Epidemiology and Prevention. Contemporary definitions and classification of the cardiomyopathies: an American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention. *Circulation*. 2006 Apr 11;113(14):1807-16.
10. Parodi G, Del Pace S, Carrabba N, Salvadori C, Memisha G, Simonetti I, Antoniucci D, Gensini GF. Incidence, clinical findings, and outcome of women with left ventricular apical ballooning syndrome. *Am J Cardiol*. 2007 Jan 15;99(2):182-5.
11. Azzarelli S, Galassi AR, Amico F, Giacoppo M, Argentino V, Tomasello SD, Tamburino C, Fiscella A. Clinical features of transient left ventricular apical ballooning. *Am J Cardiol*. 2006 Nov 1;98(9):1273-6.
12. Schneider B, Athanasiadis A, Stöllberger C, Pistner W, Schwab J, Gottwald U, Schoeller R, Gerecke B, Hoffmann E, Wegner C, Sechtem U. Gender differences in the manifestation of tako-tsubo cardiomyopathy. *Int J Cardiol*. 2013 Jul 1;166(3):584-8.
13. Kurisu S, Inoue I, Kawagoe T, Ishihara M, Shimatani Y, Nakama Y, Kagawa E, Dai K, Ikenaga H. Presentation of Tako-tsubo cardiomyopathy in men and women. *Clin Cardiol*. 2010 Jan;33(1):42-5.
14. Kurisu S, Sato H, Kawagoe T, Ishihara M, Shimatani Y, Nishioka K, Kono Y, Umemura T, Nakamura S. Tako-tsubo-like left ventricular dysfunction with ST-segment elevation: a novel cardiac syndrome mimicking acute myocardial infarction. *Am Heart J*. 2002 Mar;143(3):448-55.
15. Tsuchihashi K, Ueshima K, Uchida T, Oh-mura N, Kimura K, Owa M, Yoshiyama M, Miyazaki S, Haze K, Ogawa H, Honda T, Hase M, Kai R, Morii I. Angina Pectoris-Myocardial Infarction Investigations in Japan. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. Angina Pectoris-Myocardial Infarction Investigations in Japan. *J Am Coll Cardiol*. 2001 Jul;38(1):11-8.
16. Bybee KA, Kara T, Prasad A, Lerman A, Barsness GW, Wright RS, Rihal CS. Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. *Ann Intern Med*. 2004 Dec 7;141(11):858-65.
17. Park JH, Kang SJ, Song JK, Kim HK, Lim CM, Kang DH, Koh Y. Left ventricular apical ballooning due to severe physical stress in patients admitted to the medical ICU. *Chest*. 2005;128(1):296.
18. Ogura R, Hiasa Y, Takahashi T, Yamaguchi K, Fujiwara K, Ohara Y, Nada T, Ogata T, Kusunoki K, Yuba K, Hosokawa S, Kishi K, Ohtani R. Specific findings of the standard 12-lead ECG in patients with 'Takotsubo' cardiomyopathy: comparison with the findings of acute anterior myocardial infarction. *Circ J*. 2003 Aug;67(8):687-90.
19. Kosuge M, Ebina T, Hibi K, Morita S, Okuda J, Iwahashi N, Tsukahara K, Nakachi T, Kiyokuni M, Ishikawa T, Umemura S, Kimura K. Simple and accurate electrocardiographic criteria to differentiate takotsubo cardiomyopathy from anterior acute myocardial infarction. *J Am Coll Cardiol*. 2010 Jun 1;55(22):2514-6.
20. Jim MH, Chan AO, Tsui PT, Lau ST, Siu CW, Chow WH, Lau CP. A new ECG criterion to identify takotsubo cardiomyopathy from anterior myocardial infarction: role of inferior leads. *Heart Vessels*. 2009 Mar;24(2):124-30.
21. Núñez-Gil IJ, Luaces M, Garcia-Rubira JC, Zamorano J. Electrocardiographic criteria in Takotsubo cardiomyopathy and race differences: Asians versus Caucasians. *J Am Coll Cardiol*. 2010 Oct 19;56(17):1433-4.
22. Kurisu S, Inoue I, Kawagoe T, Ishihara M, Shimatani Y, Nakamura S, Yoshida M, Mitsuba N, Hata T, Sato H. Time course of electrocardiographic changes in patients with tako-tsubo syndrome: comparison with acute myocardial infarction with minimal enzymatic release. *Circ J*. 2004 Jan;68(1):77-81.
23. Bybee KA, Prasad A, Barsness GW, Lerman A, Jaffe AS, Murphy JG, Wright RS, Rihal CS. Clinical characteristics and thrombolysis in myocardial infarction frame counts in women with transient left ventricular apical ballooning syndrome. *Am J Cardiol*. 2004 Aug 1;94(3):343-6.
24. Van de Walle SO, Gevaert SA, Gheeraert PJ, De Pauw M, Gillebert TC. Transient stress-induced cardiomyopathy with an "inverted takotsubo" contractile pattern. *Mayo Clin Proc*. 2006 Nov;81(11):1499-502.
25. Haghi D, Fluechter S, Suselbeck T, Kaden JJ, Borggrefe M, Papavassiliu T. Cardiovascular magnetic resonance findings in typical versus atypical forms of the acute apical ballooning syndrome (Takotsubo cardiomyopathy). *Int J Cardiol*. 2007 Aug 21;120(2):205-11.
26. Haghi D, Roehm S, Hamm K, Harder N, Suselbeck T, Borggrefe M, Papavassiliu T. Takotsubo cardiomyopathy is not due to plaque rupture: an intravascular ultrasound study. *Clin Cardiol*. 2010 May;33(5):307-10.

27. Sadamatsu K, Tashiro H, Maehira N, Yamamoto K. Coronary microvascular abnormality in the reversible systolic dysfunction observed after noncardiac disease. *Jpn Circ J*. 2000 Oct;64(10):789-92.
28. Y-Hassan S. Acute cardiac sympathetic disruption in the pathogenesis of the takotsubo syndrome: A systematic review of the literature to date. *Cardiovasc Revasc Med*. 2013 Oct 17.
29. Yamanaka O, Yasumasa F, Nakamura T, Ohno A, Endo Y, Yoshimi K, et al. "Myocardial stunning"-like phenomenon during a crisis of pheochromocytoma. *Jpn Circ J*. 1994;58: 737–42.
30. Akashi YJ, Nakazawa K, Sakakibara M, Miyake F, Koike H, Sasaka K. The clinical features of takotsubo cardiomyopathy. *QJM*. 2003;96:563–73.
31. Mann DL, Kent RL, Parsons B, Cooper G 4th. Adrenergic effects on the biology of the adult mammalian cardiocyte. *Circulation*. 1992;85:790–804.
32. Ueyama T, Kasamatsu K, Hano T, Yamamoto K, Tsuruo Y, Nishio I. Emotional stress induces transient left ventricular hypocontraction in the rat via activation of cardiac adrenoceptors: a possible animal model of 'tako-tsubo' cardiomyopathy. *Circ J*. 2002;66:712–3.
33. Elesber AA, Prasad A, Lennon RJ, Wright RS, Lerman A, Rihal CS. Four-year recurrence rate and prognosis of the apical ballooning syndrome. *J Am Coll Cardiol*. 2007 Jul 31;50(5):448-52.
34. Kurisu S, Inoue I, Kawagoe T, Ishihara M, Shimatani Y, Nakama Y, Maruhashi T, Kagawa E, Dai K. Incidence and treatment of left ventricular apical thrombosis in Tako-tsubo cardiomyopathy. *Int J Cardiol*. 2011 Feb 3;146(3):e58-60.
35. Pant S, Deshmukh A, Mehta K, Badheka AO, Tuliani T, Patel NJ, Dabhadkar K, Prasad A, Paydak H. Burden of arrhythmias in patients with Takotsubo Cardiomyopathy (Apical Ballooning Syndrome). Int J Cardiol. 2013 Dec 5;170(1):64-8.

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Cardiac Magnetic Resonance Imaging and Computed Tomography: State of the Art in Clinical Practice

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ABSTRACT

Recent technological innovations in CT and MR imaging of the heart have vastly expanded the clinical utility of these modalities allowing them to complement and in some ways surpass the capabilities of more traditional methods. Cardiac MR (CMR) has an unrivaled ability to assess contractile function, characterize tissue, and detect minute areas of scar. In turn, CMR can reliably risk stratify ischemic heart disease and has emerged as a non-invasive gold standard technique for imaging non-ischemic cardiomyopathies.[1] Cardiac CT (CCT) by comparison reveals cardiac structure and, in particular, coronary anatomy with remarkable sub-millimeter detail. For the first time, coronary stenoses can be directly and reliably visualized non-invasively. Owing to its very high negative predictive value for the detection of significant coronary obstruction, CCT can accurately exclude coronary disease as a cause of chest pain in low- to intermediate-risk populations. This article describes these modalities and their recent clinical advances.

KEYWORDS: Cardiac CT (CCT), Cardiac MR (CMR)

INTRODUCTION

This article briefly reviews the methodologies of CCT and CMR, their specific roles in the diagnosis of cardiac pathophysiology, and their utility in outcomes assessment and prognosis with various disease states.

Cardiac MR: The Basics

Magnetic resonance imaging is based on the absorption and subsequent emission of radiofrequency (RF) energy by water protons in various tissues of the body while immersed in a strong magnetic field. The RF emission is tissue dependent and leads to the unparalleled ability of MRI to distinguish subtle regional tissue differences within a single organ of the body, for example scar or edema within myocardium (Figures 1 and 2). With intravenous gadolinium-based contrast agents, MRI can further distinguish tissues based on their blood flow and blood volume differences. Using ECG-gating for stop-action imaging and novel acquisition methods, MRI can readily demonstrate regional myocardial differences in tissue perfusion and in the same examination detect areas of acute myocyte necrosis or scar – sometimes 1 cm^3 or less. Myocardial fibrosis is a common endpoint of many cardiomyopathies, but the geographic patterns of fibrosis vary between disease states. As will be seen, with CMR these patterns commonly point towards a limited differential diagnosis, or in some cases the specific diagnosis. In the setting of ischemic heart disease, scar delineation has important prognostic utility. It has been shown that CMR with contrast accurately predicts viability – that is whether or not underperfused tissue will recover function after revascularization – and is probably the best method for determining this.[2] Moreover, the presence of even a small amount of scar,

Figure 1. Short axis (a) bright-blood and (b) post-contrast CMR images from a patient with occlusion of the right coronary artery. A small (bright) inferior scar is demonstrated (arrows) consistent with an infarction. LV/RV: Left/Right ventricle.

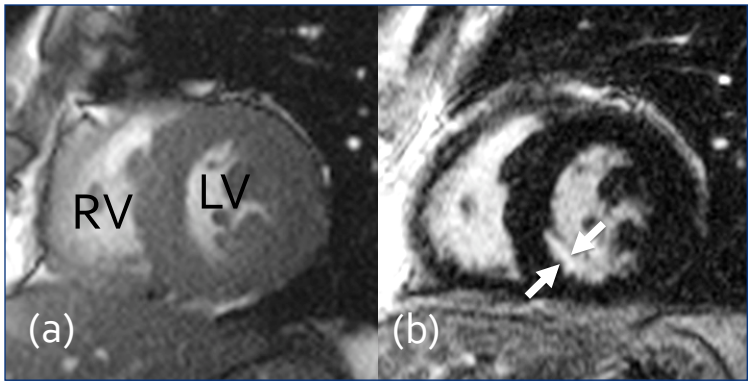
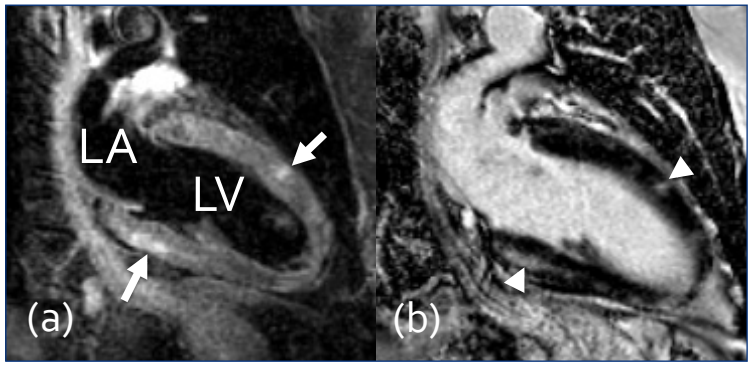


Figure 2. Vertical long axis (a) dark blood and (b) post-contrast CMR images from a patient with acute myocarditis. Bright areas of myocardial edema in image (a) (arrows) overlap spatially with areas of acute myonecrosis in image (b) (arrowheads). LA/LV: Left atrium/ventricle.



much smaller than can be detected with nuclear methods, confers a substantial increase in the risk of major adverse cardiovascular events compared with no scar.[3]

Combining techniques for tissue characterization with cine movie loops having high spatial and high temporal resolution yields a robust evaluation of myocardial tissue and contractile function. Moreover, dynamic MR imaging during contrast infusion under conditions of induced coronary vasodilation (with intravenous adenosine for example) delineates regions of underperfusion due to upstream coronary artery stenosis. In its ability to detect significant coronary obstruction, CMR stress perfusion is superior to nuclear pharmacologic stress perfusion.[4]

Another powerful tool in the CMR arsenal is so-called phase-contrast MRI where image brightness is proportional to tissue velocity. Importantly, this technique permits dynamic *quantification* of blood flow (in cc/min) through large vessels enabling calculation of regurgitant valve severity and shunt fraction. As with echo, CMR can also characterize the severity of valvular stenosis.

The typical CMR study can be completed within 45 to 60 minutes. The patient is required to undergo a series of breath-holds while lying flat, which are generally well tolerated. The duration of the breath-holds is variable and can be adjusted based on the patient's capability. Generally, the imaging of patients with arrhythmias is non-problematic, and MR imaging, like CT, is not significantly hampered by body habitus.

Advantages, disadvantages, and appropriate indications of CMR are listed in Tables 1 and 2.[5]

Cardiac CT: The Basics

CT is an x-ray based modality in which a ring, or gantry, containing an x-ray tube diametrically opposite a series of detectors rotates around a patient as the patient is moved through the ring. With modern scanners, volumetric data with submillimeter spatial resolution is collected over the scanned area of interest allowing images to be reconstructed in any orientation with equal clarity. Early CT systems lacked the spatial and temporal resolution to adequately visualize cardiac structures. The advent of very rapid gantry rotation, ECG-gating, and sub-mm resolution now permits stop-action imaging of very small rapidly moving structures such as the coronary arteries (Figure 3). With intravenous iodinated contrast, CT readily depicts cardiac morphology and vascular anatomy and can be useful for

Table 1. Advantages and Disadvantages of cardiac MR (CMR) and cardiac CT (CCT)

	CMR	CCT
Advantages	No ionizing radiation	Short scan times
	Image anatomy, function & physiology	Image anatomy/function
	Can scan patients with arrhythmias	Convenient for patient
	High temporal resolution	High spatial resolution
	Moderate spatial resolution	Moderate temporal resolution
	Tissue characterization (e.g. scar)	
Disadvantages	Longer scan times	Ionizing radiation
	Contrast carries risk of NSF	Requires heart rate control
	Claustrophobia	Risks of iodinated contrast
	Artifacts from foreign matter	
	MRI contraindications (e.g. pacemaker)	

Table 2. Appropriate indications for CMR.(Modified from Table 19 in Hendel et al[5]).

Stress CMR (e.g. Adenosine perfusion)
- Chest pain syndrome
  - Intermediate PTP of CAD & either ECG uninterpretable or unable to exercise
- Stenosis of unclear significance on coronary angiography

Detection of Myocardial Scar and Viability
- Location & extent of myonecrosis after acute MI
- Viability prior to revascularization or medical therapy
- Viability after "equivocal or indeterminate" results on SPECT or dobutamine echo

Ventricular and valvular function
- Congenital heart disease
- LV function after MI or in heart failure patients when echo is limited
- Quantification of LV function when prior tests give discordant data
- Evaluation of specific CMs (infiltrative [amyloid/sarcoid], HCM, or due to cardiotoxic therapies)
- Native & prosthetic valves, with planimetry & quantification, when echo is limited
- Evaluation for ARVC in patients with syncope or ventricular arrhythmia
- Myocarditis or MI with positive cardiac enzymes & no obstructive coronary lesions

Cardiac masses using contrast to assess vascularity

Pericardial disease (e.g. mass, constrictive pericarditis)

Suspected coronary anomalies (CT is preferred)

Pulmonary vein mapping pre- and post-RF ablation for atrial fibrillation

PTP: pre-test probability.
CAD: coronary artery disease.
LV: left ventricle. MI: myocardial infarction.
CM: cardiomyopathy.
HCM: Hypertrophic cardiomyopathy.
ARVC: Arrhythmogenic right ventricular cardiomyopathy.
SPECT: Single-photon emission computed tomography.
RF: Radiofrequency.

unraveling congenital and acquired cardiovascular anomalies. While cardiac masses and thrombi are generally evident with CT, MRI is usually preferred for mass characterization because of its superior tissue contrast resolution.

Cardiac CT scans can be performed rapidly, with typical table times of ~10 minutes and actual scan times of less than 10 seconds. With current CT technology lower heart rates generally provide better scan quality, and patients are often given intravenous beta-blocker prior to the scan. Contrast and radiation are necessary elements of the study. The newest scanners and imaging protocols have decreased average patient radiation exposure, and doses are usually at or below those of nuclear myocardial perfusion imaging using ^{99m} Tc-sestamibi. In contrast to CMR, only a few breath holds are necessary with CCT.

Advantages, disadvantages, and appropriate indications of cardiac CT are listed in Tables 1 and 3.[6]

Roles of CMR and CCT in Specific Cardiac Diseases

Evaluation of Ischemic Heart disease

As the number one cause of death in the US, identification and qualification of coronary artery disease is a critical area for diagnostic evaluation.[7] Diagnosis of acute plaque rupture in a coronary artery is typically made using a combination of history, electrocardiogram, and cardiac biomarkers, and risk-scoring systems help to predict which of these patients require urgent coronary angiography. In patients with acute coronary syndromes not indicated for emergent angiography, and those patients with progressive luminal narrowing, non-invasive imaging techniques are important tools for accurate diagnosis and further management decisions. Ideally, a comprehensive non-invasive diagnostic test is able to assess coronary anatomy and lumen defects, plaque composition, tissue perfusion, cardiac function as a result of stenosis, and viability of myocardium.

Most of these items can be met when patients with ischemic heart disease are evaluated using CMR. A large prospective study compared adenosine stress CMR with adenosine stress nuclear imaging (Single Photon Emission Computed Tomography, SPECT) in suspected ischemic coronary disease and found similar specificity for both modalities but a superiority in sensitivity, negative predictive value, and overall diagnostic accuracy for CMR.[4] Cardiac function assessment using CMR is highly accurate and CMR is considered the reference standard for non-invasive assessment of chamber volumes and ventricular

Figure 3. In (a), a widely patent mid-right coronary artery (RCA) stent (double arrow) is depicted on 3-D (left) and reformatted (right) CCT images. Image (b) demonstrates a severe stenosis (arrowhead) of the proximal left anterior descending coronary artery in another patient. Note the extensive soft plaque (arrows) in the coronary artery wall. RV/LV: Right/left ventricle. RA: Right atrium.

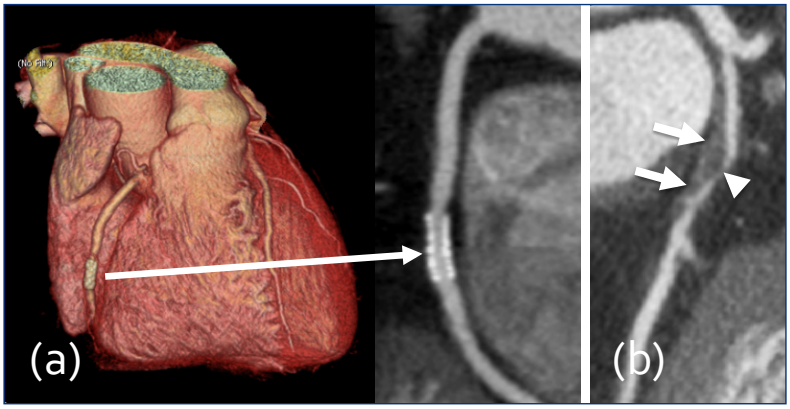


Table 3. Appropriate indications for CCT (Modified from Table 8 in Taylor *et al.*[6] CHD: Coronary heart disease. Other abbreviations are in Table 2.)

Coronary angiography

- Nonacute symptoms, possibly an ischemic equivalent
  - Intermediate PTP of CAD and ECG interpretable and able to exercise
  - Low/Intermediate PTP of CAD and either ECG uninterpretable or unable to exercise
- Acute chest pain
  - Normal ECG and cardiac biomarkers and low/intermediate PTP of CAD
  - Low/Intermediate PTP of CAD and ECG uninterpretable
  - Low/Intermediate PTP of CAD and either nondiagnostic ECG or equivocal biomarkers
- New onset or newly diagnosed clinical heart failure to assess etiology
  - Low/Intermediate PTP of CAD and reduced LV ejection fraction
- Intermediate preoperative coronary assessment prior to noncoronary cardiac surgery
- Continued symptoms after normal ECG exercise test
- Intermediate risk findings on Duke Treadmill Score
- Discordant ECG exercise and imaging results or equivocal stress imaging results
- Evaluation of graft patency after coronary bypass in symptomatic patient
- Evaluation of left main stent patency in asymptomatic patient
- Calcium Score: Family history or premature CHD and low global CHD risk estimate OR asymptomatic with no known CAD and intermediate CHD risk estimate

Congenital heart disease

Evaluation of LV function after acute MI or in HF patients in the setting of inadequate images from other noninvasive methods

Quantitative evaluation of right ventricular function/morphology (ARVC)

Evaluation of suspected dysfunctional native or prosthetic valves or of a cardiac mass in the setting of inadequate images from other noninvasive methods

Pericardial anatomy

Pulmonary vein mapping prior to ablation for atrial fibrillation

Coronary vein mapping prior to biventricular pacemaker placement

Localization of coronary bypass grafts and other retrosternal anatomy prior to reoperative chest or cardiac surgery

ejection fraction.[8] As mentioned earlier, necrotic tissue and the corresponding wall-motion abnormalities can be accurately distinguished from viable tissue, despite regional functional defects, with contrast CMR.

The use of cardiac CT (CCT) in the detection of significant coronary artery disease relies on its excellent spatial resolution.[9] CCT can accurately diagnose coronary stenoses >50%.[10,11] Further, the high negative predictive value of this technique for detecting significant obstructive disease has permitted chest pain units to safely, efficiently, and cost-effectively 'rule out' coronary disease in low-intermediate risk populations.[12-14] The spatial resolution of CT also lends itself to an assessment of coronary bypass grafts, large coronary stents (Figure 3), and congenital coronary anomalies.[15,16] Registry data suggest that the presence of even non-obstructive atherosclerotic plaque confers increased risk of major adverse cardiovascular events.[17]

While efforts to evaluate artherosclerotic plaque composition to determine likelihood of plaque rupture are not yet mature, coronary artery calcification is a definite marker of atherosclerosis. Coronary artery calcium (CAC) scoring using non-contrast CT technology is a well-established tool for risk assessment in asymptomatic patients, particularly those with intermediate pretest risk for coronary disease.[18,19]

Non-ischemic cardiomyopathies

Diagnosis and characterization of non-ischemic cardiomyopathies has historically been difficult, sometimes requiring biopsy to make a definitive diagnosis. In most patients with new onset cardiomyopathy, it is important to first exclude ischemic heart disease, which both CCT and CMR can confidently do owing to their high negative predictive values.[5,6] Further, cardiac MR can help delineate between the heterogeneous group of NICMs, and potentially give important information regarding prognosis.[1,20] Select cardiomyopathies are discussed below.

Hypertrophic cardiomyopathy (HCM)

In HCM, CMR like echo can identify regions of abnormal myocardial thickening. However, because CMR is a true 3-D modality with no 'blind spots' it occasionally reveals abnormalities not seen on echo. CMR has been able to detect an additional 6-12% of patients with HCM that were not found on echocardiogram.[21] Moreover, CMR with contrast delineates fibrosis in a few typical patterns, further supporting and usually – with the support of morphologic data – cinching the diagnosis. Extent and severity of fibrosis may correlate with an increased risk of sudden cardiac death and in turn modify clinical management.[21]

Cardiac sarcoidosis (CS)

Cardiac sarcoidosis is a challenging diagnosis that has traditionally relied on complex criteria issue by the Japanese Ministry of Health.[22] Knowledge of cardiac involvement may prompt changes in clinical management. While cardiac involvement is clinically evident in only 5% of patients with sarcoidosis,[23] post-mortem evaluation indicates that the prevalence is far greater.[24] CMR has recently been shown to be superior to conventional criteria in identifying areas of myocardial damage due to sarcoid manifested as patchy enhancement in affected areas, typically in the subepicardial basal septum, in patients with the appropriate clinical context (Figure 4).[25]

Myocarditis

Viral myocarditis can often have patchy midwall or subepicardial enhancement – typically in the inferolateral left ventricle or the septum – with extent and distribution of the enhancement associated with prognosis and probable viral pathogen (Figure 2).[26,27]

Figure 4. (a) Short axis and (b) vertical long axis post-contrast CMR images of a patient with cardiac sarcoid demonstrate anterior and anteroseptal enhancement (arrows) consistent with myocardial damage.

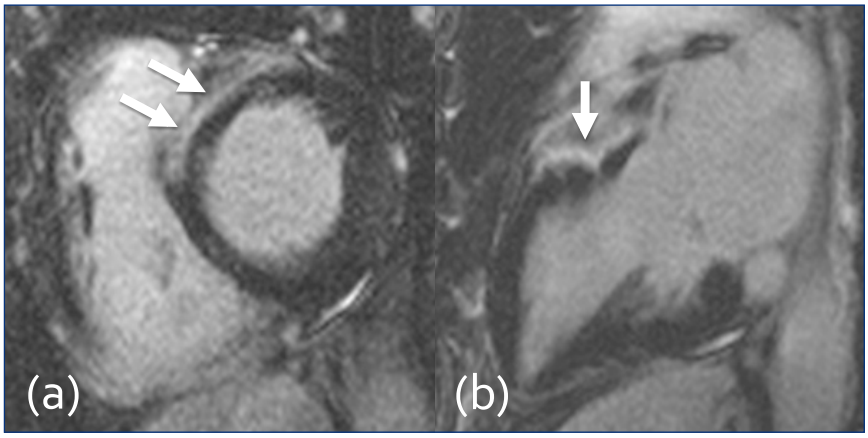
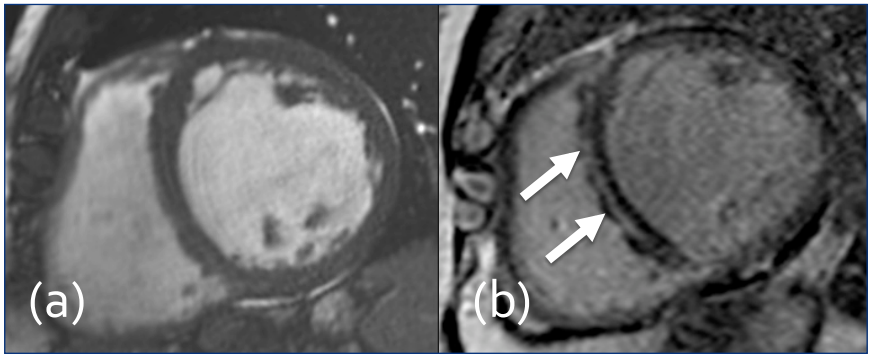


Figure 5. Short axis (a) bright-blood and (b) post-contrast CMR images from a patient with dilated non-ischemic cardiomyopathy (DCM). (Coronary arteries were normal at catheterization.) Note the midwall stripe of enhancement in the septum typical for DCM.



Dilated Cardiomyopathy (DCM)

The vast majority of patients with DCM demonstrate no enhancement at CMR or a characteristic midwall stripe of enhancement in the septum (Figure 5).[28] In patients presenting with heart failure, these findings aid in the distinction of DCM from ischemic heart disease where virtually all subjects demonstrate subendocardial or transmural scar when scar is present.

Cardiac Amyloidosis

Cardiac amyloidosis is an uncommon cardiomyopathy resulting from the deposition of amyloid protein in myocardial interstitium (as well as other tissues of the body). Myocardial thickness is usually increased, and over time left ventricular function deteriorates. Diagnosis relies on endomyocardial biopsy, but may be inferred from positive fat pad biopsy in the appropriate clinical context. The CMR enhancement pattern for this condition is unique and very suggestive in unclear cases.[29]

Iron overload syndromes

In iron overload syndromes such as Thalessemia and sickle cell disease, CMR has the unique ablility to detect myocardial iron deposition and quantify its severity.[30] This advance has led to optimal detection of patients for chelation therapy prior to developing irreversible cardiomyopathy, significantly impacting mortality.

Valvular heart disease

The visual assessment of valvular heart disease by echo is generally superior to that of CMR and CCT. While CMR estimates of stenosis severity are reliable, CMR offers a unique advantage in its ability to *quantify* regurgitant fraction.[31] Also, CMR is emerging as a useful tool for characterization of pulmonic valvular lesions often difficult to assess with echocardiography.

Pericardial disease

Although CT is able to demonstrate pericardial effusions, thickening, calcification and masses, CMR is generally regarded as the preferred modality for imaging the pericardium.[32] A particular strength of CMR is its ability to distinguish constrictive pericarditis from restrictive cardiomyopathy, two entities with overlapping clinical presentations. In this regard, CMR is the gold standard.

Masses

Both intracardiac and extracardiac masses can be visualized using CMR and CCT, but again CMR is the preferred imaging modality. CMR assessment of a mass can be useful in evaluating its size, location, tissue characteristics including enhancement pattern, and functional significance. Recent studies have indicated that increased T2 signal, gadolinium enhancement, and lack of mobility all are suggestive of malignant neoplasm with reasonably high sensitivity and specificity compared with pathological correlates.[33] CMR is accurate in the detection of intracardiac thrombus and is more sensitive than echo.[34,35]

Congenital Heart Disease

Evaluation of adult congenital heart disease by echocardiography can be hampered by limited views due to body habitus and low pre-test suspicion of a congenital anomaly. Both CCT and MRI are able to detect and characterize congenital cardiovascular lesions. Patients that have had previous surgeries can have a comprehensive anatomic evaluation using either of these techniques. In general, CCT is preferred when anatomy is the principle concern, for example in the detection and evaluation of congenital coronary anomalies.[36] Cardiac MR offers the additional ability to quantify blood flow — for estimating shunt and valve lesion severity — and cardiac chamber volumes and ejection fraction, and characterize wall-motion abnormalities. Patients with stable congenital heart disease can be followed periodically using these non-invasive techniques to detect progression of pathology and support management decisions.

SUMMARY

Cardiac MR and CT have both become mature tools for the clinical evaluation of a vast array of cardiac diseases. These 'new' modalities are in many ways complementary to one another and to other tools in the traditional clinical armamentarium and offer unique and powerful insights into cardiac pathology and pathophysiology. Their uses for diagnosing disease, predicting prognoses and outcomes, and modifying clinical management continue to emerge and evolve. CMR offers a dynamic range of capabilities for assessment of the cardiovascular system, allowing for a single, radiation-free imaging study to answer a multitude of clinical questions, especially with regards to cardiomopathy. CCT has become an excellent non-invasive technique for anatomic assessment of the heart, and is a quick and useful tool for rapid evaluation of low-intermediate risk chest pain syndromes. The future is bright for CCT and CMR and for the physicians and patients who benefit from their use.

References

1. Parsai C, O'Hanlon R, Prasad SK, Mohiaddin RH. Diagnostic and prognostic value of cardiovascular magnetic resonance in non-ischaemic cardiomyopathies. *J Cardiovasc Magn Reson*. 2012;14:54.
2. Kim RJ, Wu E, Rafael A, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. *The New England Journal of Medicine*. 2000;343:1445-53.
3. Kwong RY, Chan AK, Brown KA, et al. Impact of unrecognized myocardial scar detected by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease. *Circulation*. 2006;113:2733-43.

4. Greenwood JP, Maredia N, Younger JF, et al. Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. *Lancet*. 2012;379:453-60.
5. Hendel RC, Patel MR, Kramer CM, et al. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. *Journal of the American College of Cardiology*. 2006;48:1475-97.
6. Taylor AJ, Cerqueira M, Hodgson JM, et al. ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 appropriate use criteria for cardiac computed tomography. A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the Society of Cardiovascular Computed Tomography, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of Nuclear Cardiology, the North American Society for Cardiovascular Imaging, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance. *Journal of the American College of Cardiology*. 2010;56:1864-94.
7. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics--2013 update: a report from the American Heart Association. *Circulation*. 2013;127:e6-e245.
8. Schuster A, Morton G, Chiribiri A, Perera D, Vanoverschelde JL, Nagel E. Imaging in the management of ischemic cardiomyopathy: special focus on magnetic resonance. *Journal of the American College of Cardiology*. 2012;59:359-70.
9. Fayad ZA, Fuster V, Nikolaou K, Becker C. Computed tomography and magnetic resonance imaging for noninvasive coronary angiography and plaque imaging: current and potential future concepts. *Circulation*. 2002;106:2026-34.
10. Achenbach S, Friedrich MG, Nagel E, et al. CV imaging: what was new in 2012? *JACC Cardiovasc Imaging*. 2013;6:714-34.
11. Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. *Journal of the American College of Cardiology*. 2008;52:1724-32.
12. Ladapo JA, Jaffer FA, Hoffmann U, et al. Clinical outcomes and cost-effectiveness of coronary computed tomography angiography in the evaluation of patients with chest pain. *Journal of the American College of Cardiology*. 2009;54:2409-22.
13. Hoffmann U, Bamberg F, Chae CU, et al. Coronary computed tomography angiography for early triage of patients with acute chest pain: the ROMICAT (Rule Out Myocardial Infarction using Computer Assisted Tomography) trial. *Journal of the American College of Cardiology*. 2009;53:1642-50.
14. Litt HI, Gatsonis C, Snyder B, et al. CT angiography for safe discharge of patients with possible acute coronary syndromes. *The New England Journal of Medicine*. 2012;366:1393-403.
15. Pache G, Saueressig U, Frydrychowicz A, et al. Initial experience with 64-slice cardiac CT: non-invasive visualization of coronary artery bypass grafts. *European Heart Journal*. 2006;27:976-80.
16. Carrabba N, Schuijf JD, de Graaf FR, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography for the detection of in-stent restenosis: a meta-analysis. *Journal of Nuclear Cardiology* : official publication of the American Society of Nuclear Cardiology. 2010;17:470-8.
17. Min JK, Dunning A, Lin FY, et al. Age- and sex-related differences in all-cause mortality risk based on coronary computed tomography angiography findings results from the International Multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) of 23,854 patients without known coronary artery disease. *Journal of the American College of Cardiology*. 2011;58:849-60.
18. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. *JAMA* : the journal of the American Medical Association. 2004;291:210-5.
19. Budoff MJ, Shaw LJ, Liu ST, et al. Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. *Journal of the American College of Cardiology*. 2007;49:1860-70.
20. Karamitsos TD, Neubauer S. The prognostic value of late gadolinium enhancement CMR in nonischemic cardiomyopathies. *Current Cardiology Reports*. 2013;15:326.
21. Maron MS. Clinical utility of cardiovascular magnetic resonance in hypertrophic cardiomyopathy. *J Cardiovasc Magn Reson*. 2012;14:13.
22. Tahara N, Tahara A, Nitta Y, et al. Heterogeneous myocardial FDG uptake and the disease activity in cardiac sarcoidosis. *JACC Cardiovasc Imaging*. 2010;3:1219-28.
23. Hunninghake GW, Costabel U, Ando M, et al. ATS/ERS/WASOG statement on sarcoidosis. American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and other Granulomatous Disorders. Sarcoidosis, vasculitis, and diffuse lung diseases : official journal of WASOG / World Association of Sarcoidosis and Other Granulomatous Disorders. 1999;16:149-73.
24. Silverman KJ, Hutchins GM, Bulkley BH. Cardiac sarcoid: a clinicopathologic study of 84 unselected patients with systemic sarcoidosis. *Circulation*. 1978;58:1204-11.
25. Patel MR, Cawley PJ, Heitner JF, et al. Detection of myocardial damage in patients with sarcoidosis. *Circulation*. 2009;120:1969-77.
26. Grun S, Schumm J, Greulich S, et al. Long-term follow-up of biopsy-proven viral myocarditis: predictors of mortality and incomplete recovery. *Journal of the American College of Cardiology*. 2012;59:1604-15.
27. Mahrholdt H, Wagner A, Deluigi CC, et al. Presentation, patterns of myocardial damage, and clinical course of viral myocarditis. *Circulation*. 2006;114:1581-90.
28. McCrohon JA, Moon JC, Prasad SK, et al. Differentiation of heart failure related to dilated cardiomyopathy and coronary artery disease using gadolinium-enhanced cardiovascular magnetic resonance. *Circulation*. 2003;108:54-9.
29. Vogelsberg H, Mahrholdt H, Deluigi CC, et al. Cardiovascular magnetic resonance in clinically suspected cardiac amyloidosis: noninvasive imaging compared to endomyocardial biopsy. *Journal of the American College of Cardiology*. 2008;51:1022-30.
30. Kirk P, Roughton M, Porter JB, et al. Cardiac T2* magnetic resonance for prediction of cardiac complications in thalassemia major. *Circulation*. 2009;120:1961-8.
31. Didier D, Ratib O, Lerch R, Friedli B. Detection and quantification of valvular heart disease with dynamic cardiac MR imaging. *Radiographics*: a review publication of the Radiological Society of North America, Inc. 2000;20:1279-99; discussion 99-301.
32. Misselt AJ, Harris SR, Glockner J, Feng D, Syed IS, Araoz PA. MR imaging of the pericardium. *Magn Reson Imaging Clin N Am*. 2008;16:185-99, vii.
33. Altbach MI, Squire SW, Kudithipudi V, Castellano L, Sorrell VL. Cardiac MRI is complementary to echocardiography in the assessment of cardiac masses. *Echocardiography*. 2007;24:286-300.
34. Weinsaft JW, Kim HW, Crowley AL, et al. LV thrombus detection by routine echocardiography: insights into performance characteristics using delayed enhancement CMR. *JACC Cardiovasc Imaging*. 2011;4:702-12.

35. Weinsaft JW, Kim HW, Shah DJ, et al. Detection of left ventricular thrombus by delayed-enhancement cardiovascular magnetic resonance prevalence and markers in patients with systolic dysfunction. *Journal of the American College of Cardiology*. 2008;52:148-57.
36. Datta J, White CS, Gilkeson RC, et al. Anomalous coronary arteries in adults: depiction at multi-detector row CT angiography. *Radiology*. 2005;235:812-8.

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New Diagnostic and Therapeutic Possibilities For Diastolic Heart Failure

EUY-MYOUNG JEONG, PhD; SAMUEL C. DUDLEY, JR., MD, PhD

ABSTRACT

Despite the fact that up to half of all heart failure occurs in patients without evidence of systolic cardiac dysfunction, there are no universally accepted diagnostic markers and no approved therapies for heart failure with preserved ejection fraction (HFpEF). HFpEF, otherwise known as diastolic heart failure, has nearly the same grim prognosis as systolic heart failure, and diastolic heart failure is increasing in incidence and prevalence. Major trials have shown that many of the treatments that are salutary in systolic heart failure have no beneficial effects in diastolic heart failure, suggesting different underlying mechanisms for these two disorders. Even criteria for diagnosis of HFpEF are still debated, and there is still no gold standard marker to detect diastolic dysfunction. Here, we will review some promising new insights into the pathogenesis of diastolic dysfunction that may lead to new diagnostic and therapeutic tools.

[Abbreviations: tetrahydrobiopterin, **BH_4** ;cardiac magnetic resonance, **CMR**; diabetes mellitus, **DM**; heart failure with preserved ejection fraction, **HFpEF;** cardiac myosin binding protein C, **MyBP-C;** nitric oxide synthase, **NOS]**

KEYWORDS: heart failure, diastolic dysfunction, hypertension, diabetes, oxidative stress

INTRODUCTION

Heart failure is a major and growing public health problem in the United States affecting ~5 million patients in this country. Up to half of the 550,000 patients newly diagnosed with heart failure in each year have diastolic heart failure or heart failure with preserved ejection fraction (HFpEF). The disorder is the primary reason for 12 to 15 million office visits and 6.5 million hospital days each year.[1] HFpEF is increasing in prevalence and incidence. Both systolic and diastolic heart failure has similar grim prognoses,[2] and there are no approved therapies for diastolic heart failure.

What is diastolic dysfunction or diastolic heart failure?

Diastolic heart failure is a diagnosis of exclusion applied when a patient has heart failure symptoms, no evidence of other causes, and diastolic dysfunction. The disorder is thought to arise from impaired cardiac relaxation. While a considerable number of patients may have demonstrated diastolic dysfunction, a much smaller number suffer from heart failure. The determinants of progression from asymptomatic dysfunction to overt heart failure are unknown, and many people remain without clinical symptoms of heart failure. Another area of investigation is the role of diastolic dysfunction in right heart failure syndromes.

Symptoms

The major signs and symptoms of diastolic heart failure are lung congestion accompanied with breathlessness, coughing, tachypnea, dyspnea on exertion, or paroxysmal nocturnal dyspnea. Dyspnea on exertion is the sensation of difficult or uncomfortable breathing after a level of activity. Paroxysmal nocturnal dyspnea is a sensation of shortness of breath that awakens the patient, often after one or two hours of sleep and is usually relieved in the upright position.

Diagnosis

The incidence of diastolic dysfunction is increasing, affecting 15% percent of patients less than 50 years old and 50% of patients older than 70. Furthermore, there appears to be a gender bias towards women with approximately 75% patients with diastolic dysfunction being women. There are no specific blood markers of diastolic dysfunction, but there are some useful diagnostic tests.

Echocardiography

The fundamental requirements of the diagnosis are heart failure with a normal left ventricular ejection fraction (i.e. >50%). Suggestive of the diagnosis is the presence of left ventricular diastolic dysfunction. While the gold standard for diastolic dysfunction is thought to be derived from ventricular pressure volume loops, this is generally an impractical measure. Commonly, echocardiography can be used to evaluate the characteristics of diastolic left ventricular relaxation, filling, and distensibility. Echocardiography has been used to assess the dimensional changes and abnormal diastolic function by E/A ratio (i.e. early to late left ventricular blood filling velocity as measured by Doppler flow across the mitral value in diastole). In early, mild diastolic dysfunction, impaired relaxation results in an inversion of the normal E/A ratio, increased mitral flow deceleration time, and increased isovolumic relaxation time, the time interval from closure of the aortic valve to onset of left ventricular filling.

In a second stage of diastolic dysfunction thought to be more severe, the pseudo-normal stage, the E/A ratio normalizes to E>A. Finally, patients can show a restrictive filling pattern with the E/A ratio >2. Aside from blood flow velocity across the mitral valve during diastole, direct assessment of mitral annular displacement can be used as a marker of diastolic function. Diastolic dysfunction is accompanied by significant reductions in tissue mitral annulus early longitudinal (E′) velocities and the ratio of early annulus to late annulus (E′/A′) velocities. Also, the ratio of early diastolic filling velocity to the early diastolic mitral annulus velocity (E/E′) has been reported to have the highest correlation with invasive hemodynamic measures of diastolic dysfunction and can predict LV filling pressures (E/E′ >15 suggests increased filling pressures).[3] Color Doppler echocardiography can be used to estimate the rapidity of movement of a wave of blood across the mitral valve, and slow flow velocity is an indication for diastolic dysfunction.

Echocardiographic speckle tracking

Developing methods for diagnosis of diastolic dysfunction include assessing left ventricular relaxation directly. Speckle-tracking echocardiography is a new method that evaluates myocardial deformation. In this technique distinct echocardiography patterns, speckles, are followed to assess wall motion. Speckle analysis can be used to assess radial, longitudinal, and circumferential displacement and strain. Decreased strain rate in diastole is consistent with diastolic dysfunction.

Cardiac magnetic resonance (CMR) imaging

Recently, CMR imaging has been used to evaluate diastolic dysfunction. This technology provides the excellent spatial resolution, visualization of mitral valve inflow velocity, and pulmonary veins blood flows. With myocardial tagging (a pulse sequence that amounts to marking specific locations on the myocardium that can be followed in time), diastolic myocardial strain rate can be calculated. Delay and prolonged strain rates are related to relaxation impairment.

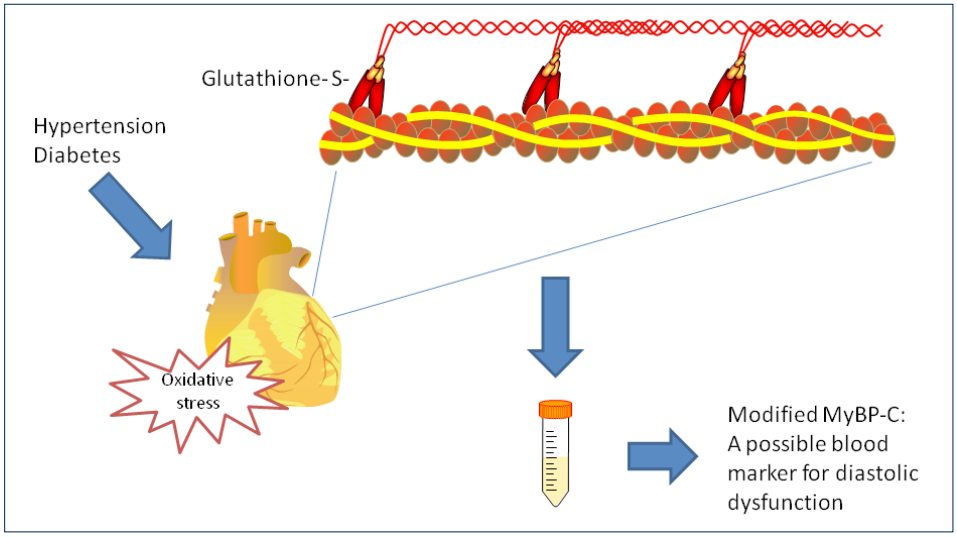
MECHANISM AND THERAPEUTIC APPROACHES

Research is shedding new light on the mechanism of diastolic dysfunction, and these new insights might lead to improved diagnostics and specific therapies. American Heart Association/American College of Cardiology guidelines recommend treatment of hypertension, maintenance of sinus rhythm, prevention of tachycardia, venous pressure reduction, and prevention of myocardial ischemia.[4]

Epidemiological risk factors for diastolic dysfunction include age, hypertension, atrial fibrillation, and diabetes mellitus. Of note, diastolic dysfunction is observed in about 40% of patients with diabetes.[5] These risk factors have considerable overlap with atherosclerosis, which suggested that these two conditions might have similar pathology. This idea was reinforced by the observation that β-blockers, angiotensin converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers (ARBs), and aldosterone antagonists, all salutary in systolic heart failure, have no beneficial effect in diastolic heart failure. These observations suggested that systolic and diastolic heart failure represent fundamentally different pathologies.

To begin to address the underlying pathology, we developed two unique mouse models of isolated diastolic dysfunction by inducing hypertension or glucose intolerance in the mice. Just like in blood vessels, nitric oxide made by nitric oxide synthase (NOS) is thought to contribute to cardiac relaxation. Hypertension-induced diastolic dysfunction was accompanied by cardiac tetrahydrobiopterin (BH_4; a co-factor in NOS) depletion, NOS dysfunction, a depression in myofilament cross-bridge kinetics, and S-glutathionylation of cardiac myosin binding protein C (MyBP-C).(6, 7) BH_4 supplementation was able to ameliorate diastolic dysfunction by preventing glutathionylation of MyBP-C and by reversing changes of myofilament properties that occurred during diastolic dysfunction. MyBP-C glutathionylation correlated with the presence of diastolic dysfunction. Our results suggest that by depressing S-glutathionylation of MyBP-C, BH_4

Figure 1. A possible mechanism and marker for diastolic dysfunction.
Hypertension and diabetes lead to cardiac oxidation and S-glutathionylation of cardiac myosin binding protein-C (MyBP-C), a cardiac contractile protein. This leads to impaired relaxation, and modified MyBP-C in the blood may represent a biomarker for diastolic dysfunction.



ameliorates diastolic dysfunction by reversing a decrease in cross-bridge turnover kinetics. These data provide evidence for modulation of cardiac relaxation by post-translational modification of myofilament proteins. In the same model, we found that ranolazine, a drug used now for angina, was able to ameliorate diastolic dysfunction. This effect was a result of ranolazine acting directly on the myofilaments.[6] Recently, we have demonstrated a similar pathology occurs in a mouse model of type II diabetes mellitus, and a mitochondria-target anti-oxidant is useful in reversing diastolic dysfunction.[8] In this same study, glucose control alone was ineffective in reversing diastolic dysfunction. In preliminary studies, we have found that modified MyBP-C can be measured in blood and is elevated in patients with diastolic dysfunction (**Figure 1**).

Despite these promising observations, it appears that age-associated diastolic dysfunction may be a distinct pathology involving myocardial fibrosis. In a senescence-accelerated mouse model, diastolic dysfunction was accompanied by fibrosis that arose in conjunction with an increase in pro-fibrotic cytokines.[9] This model suggests that there may be more than one form of diastolic dysfunction and that age-associated dysfunction would have distinctly different biological markers and treatments than hypertension or diabetes-associated diastolic dysfunction.

SUMMARY

In summary, diastolic heart failure occurs in approximately half of all heart failure cases. This type of heart failure is caused by a failure of the myocardium to relax properly. Cardiac diastolic dysfunction and subsequent heart failure appear to be distinct pathological entities from systolic heart failure. Diastolic dysfunction is accompanied by cardiac oxidation and oxidative modification of a cardiac contractile protein, MyBP-C (**Figure 1**). Oxidation of this protein appears to result in increased sensitivity to calcium and delayed and incomplete relaxation. Treatments that inhibit oxidation such as BH_4 and mitochondria-target antioxidants can treat diastolic dysfunction caused by hypertension or diabetes mellitus. Levels of modified MyBP-C may represent a new blood test for the presence of diastolic dysfunction and a marker of therapy. These observations suggest that physicians may be able to diagnose diastolic heart failure more accurately and dispense specific therapies in the future.

References

1. Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society. *Circulation.* 2005;112:e154-e235.
2. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med.* 2006;355:251-9.
3. Jeong EM, Monasky MM, Gu L, et al. Tetrahydrobiopterin improves diastolic dysfunction by reversing changes in myofilament properties. *J Mol Cell Cardiol.* 2013;56:44-54.
4. Hunt SA, Abraham WT, Chin MH, et al. 2009 Focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Developed in Collaboration With the International Society for Heart and Lung Transplantation. *J Am Coll Cardiol.* 2009;53:e1-e90.
5. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med.* 2006;355:251-9.
6. Lovelock JD, Monasky MM, Jeong EM, et al. Ranolazine improves cardiac diastolic dysfunction through modulation of myofilament calcium sensitivity. *Circ Res.* 2012;110:841-50.
7. Silberman GA, Fan TH, Liu H, et al. Uncoupled cardiac nitric oxide synthase mediates diastolic dysfunction. *Circulation.* 2010;121:519-28.
8. Chung J, Jeong EM, Go Y, et al. Mitochondria-Targeted Antioxidant Ameliorates Diet-Induced Diabetes and Diastolic Dysfunction (abstr). *J Am Coll Cardiol.* 2013;61:E597.
9. Reed AL, Tanaka A, Sorescu D, et al. Diastolic dysfunction is associated with cardiac fibrosis in the senescence-accelerated mouse. *Am J Physiol Heart Circ Physiol.* 2011;301:H824-H831.

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Disclosures

Samuel C. Dudley, MD, PhD is the inventor on patent applications: 1) 11/895,883 Methods and Compositions for Treating Diastolic Dysfunction, 2) 13/503,812 Methods of Diagnosing Diastolic Dysfunction, 3) 13/397,622 Methods for Treating Diastolic Dysfunction and Related Conditions, 4) 13/658,943 Method of Improving Diastolic Dysfunction, 5) 13/841,843 Myosin Binding Protein-C for Use in Methods Relating to Diastolic Heart Failure, and 6) 61/728,302 Mitochondrial Antioxidants and Diabetes.

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Transcatheter Aortic Valve Replacement: A Review of Current Indications and Outcomes

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ABSTRACT

In patients with symptomatic severe aortic stenosis, surgical aortic valve replacement (SAVR) improves survival, quality of life, and functional status compared with medical therapy. Based on the results of the randomized PARTNER Trial, Transcatheter Aortic Valve Replacement (TAVR) using the Edwards Sapien balloon expandable valve is now available in the United States for patients who are either inoperable due to anatomic concerns or severe medical co-morbidities, or as an alternative in patients considered high risk for SAVR. Fifty-six patients have been treated with TAVR at Rhode Island Hospital from March 2012 through October 2013 with similar outcomes to The PARTNER Trial and several large European registries. Second- generation valves and lower profile delivery systems designed to reduce the incidence of vascular complications, stroke, and perivalvular leak; and extension of TAVR to intermediate risk surgical patients, are under investigation.

KEYWORDS: Aortic Stenosis, Transcather Aortic Valve Replacement

INTRODUCTION

When patients with severe calcific aortic stenosis (AS) develop symptoms, survival at 2 years is less than 50%, and by five years less than 10% of these patients are alive.[1,2] Surgical aortic valve replacement (SAVR) improves symptoms, quality of life, and mortality.[3] However, there are patients with severe AS with coexisting morbidities or anatomical concerns who have a prohibitive operative risk for SAVR. In the late 1980s, balloon aortic valvuloplasty was developed as an alternative to surgery, but this procedure did not improve mortality; it suffered from high restenosis rates, and thus remained a palliative treatment for inoperable patients.[4] TAVR has been shown to improve mortality and relieve symptoms in patients deemed to have a prohibitive operative risk for SAVR compared to medical management.[5] Since the first TAVR was performed in 2002, over 60,000 patients have been treated worldwide, either with a balloon expandable Edwards Sapien valve (Edwards Lifesciences Corp., Irvine, CA) or the self-expanding Medtronic CoreValve (Medtronic, Inc., Minneapolis, MN). Increased operator and institutional experience along with improved technology has led to procedural success rates greater than 95% with reduction in early mortality, vascular complications and stroke rates.

The PARTNER Trial

The PARTNER (Placement of Transcatheter Aortic Valves) Trial was the first, and to date, only randomized controlled trial of TAVR in patients with aortic stenosis. It thus remains a pivotal study guiding current practice. This was a two-armed trial in which patients with severe symptomatic aortic stenosis considered high risk for SAVR were randomized to either TAVR or SAVR (cohort A). If they were deemed inoperable (cohort B) by two cardiac surgeons and had adequate access for transfemoral TAVR, patients were randomized to TAVR or medical therapy.

Three hundred and fifty-eight patients were randomized in the inoperable arm of the trial (cohort B). Among those cohort B patients treated with TAVR, there was a 20.0% absolute reduction in mortality at 1 year compared with patients treated medically (30.7% vs. 50.7%, $p<0.001$), despite 85% of the medically treated patients receiving at least one balloon aortic valvuloplasty. Mortality continued to diverge with a 24.7% (43.3% vs. 68.0%) and 26.8% (54.1% vs. 80.9%) absolute reduction for the TAVR treated patients at years 2 and 3 ($p<0.001$), respectively. The number needed to treat was less than 4 patients to save one life. There were also significantly lower readmission rates for recurrent congestive heart failure (CHF), improved New York Heart Association functional class (75% vs. 42% NYHA class 1 or 2), and improved quality of life in TAVR treated patients.[5,6] The very high mortality at 2 and 3 years in the medically treated patients in this contemporary trial confirms the poor prognosis for patients with symptomatic aortic stenosis, with no long-term symptomatic or mortality benefit from palliative balloon valvuloplasty.

Complications from TAVR included an increased risk of stroke in the TAVR-treated patients at 30 days (6.7% vs. 1.7%) and 2 years (13.8% vs. 5.5%), with the majority of early strokes occurring during the procedure from aortic atheroembolic or valvular particulate embolization. Due to the large diameter delivery sheaths (22 or 24 French requiring iliac artery diameter ≥ 7 or 8mm), major vascular complications were higher with TAVR (16.2% vs. 1.1%) as compared with medical therapy with or without balloon valvuloplasty.[5,6]

Figure 1. [L] Edwards Sapien Valve, [R} Sapien Valve on balloon and Delivery System

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In cohort A of the trial, 688 high-risk operable patients were randomized 1:1 to either TAVR (transfemoral or transapical from a left thoracotomy if iliofemoral access was not adequate) or SAVR. Mortality was similar in each group at 30 days (TAVR 3.4% vs. SAVR 6.5%), 1 year (TAVR 24.2% vs. SAVR 26.8%), 2 years (TAVR 33.9% vs. SAVR 35%) and 3 years (TAVR 44.2% vs. SAVR 44.8%). Combined stroke or transient ischemic attacks were more frequent after TAVR than SAVR at 30 days (5.5% vs. 2.4%), 1 year (8.7% vs. 4.3%) and 2 years (11.2% vs. 6.5%). At 30 days, TAVR was associated with more frequent vascular complications (11.0% vs. 3.2%), but SAVR was associated with more frequent major bleeding (19.5% vs. 9.3%) and new onset atrial fibrillation (16.0% vs. 8.6%). More TAVR patients experienced early symptomatic improvement at 30 days, but by 1 year, symptoms and exercise tolerance were similar in both groups.[7,8]

Based largely on the results of the PARTNER Trial, the United States FDA first approved TAVR from a transfemoral approach using the Edwards balloon expandable Sapien Valve (**Figure 1)** in late November 2011 for patients deemed inoperable for SAVR, followed by approval of transfemoral or transapical TAVR as an alternative to SAVR in high-risk patients in October 2012. Since FDA approval of the Edwards Sapien heart valve two years ago, more than 13,500 patients in the United States have undergone TAVR. All patients treated with TAVR are enrolled in the Transcatheter Valve Registry. In a report of the first 7,710 patients (20% inoperable and 80% high risk, with 64% treated transfemorally), device success was 92% with a 30-day mortality of 5.5% and stroke rate of 2.0%.[9]

PATIENT SCREENING

The Valve Academic Research Consortium (VARC) has produced guidelines for effective implementation of TAVR across the United States.[10,11] Patients with symptomatic aortic stenosis who are considered high risk for SAVR or inoperable are seen by a multidisciplinary team including at least two cardiac surgeons and an interventional cardiologist. The Society of Thoracic Surgery (STS) score is used to risk stratify patients for AVR; however, there are some comorbidities not accounted for in the STS score that prohibit SAVR. These include severe lung disease, severe liver disease with Child-Pugh B or greater cirrhosis, severe pulmonary hypertension with right ventricular dysfunction, and prior mediastinal radiation. Some frail and elderly patients may fail to pass a surgeon's "eyeball test." Anatomic considerations that carry a prohibitive surgical risk include severe kyphoscoliosis, a heavily calcified or "porcelain" ascending aorta, and one or more prior median sternotomies with dense adhesions, prior sternal wound infection, or bypass graft anatomy such as a left internal mammary graft coursing anteriorly under the sternum.

Complications

There are several serious procedural complications that may occur during TAVR. Patients may transiently develop shock and low cardiac output states following rapid pacing, required to prevent movement during valve deployment. This may require temporary hemodynamic support. Rarely, coronary artery obstruction may occur (1%-2%) – especially with low coronary ostia heights < 10mm, small coronary sinuses, or with bulky displaced native leaflet calcification.[12] Annular rupture, aortic dissection, or valve embolization (< 1%) are rare, but may require pericardiocentesis or emergency median sternotomy with open surgical repair. Complete heart block requiring permanent pacemaker placement (especially with a preexisting right bundle branch block) occurred in 5-10% of patients.[13]

Vascular complications occur in approximately 10% of patients, including iliac artery dissection, perforation or avulsion.[5,7,13] Most can be treated percutaneously with stents or stent grafts, but with proper procedural planning and vessel sizing, many vascular complications can be avoided. Major vascular complications are associated with an increase in late mortality.[6,8]

Perivalvular regurgitation occurs in nearly 85% of TAVR patients as a result of incomplete apposition of the valve prosthesis within the aortic annulus due to inadequate inflation and expansion of the prosthesis or calcific deposits that prevent proper seating. In the PARTNERS Trial, moderate or severe perivalvular aortic regurgitation was more frequent after TAVR compared with SAVR at 30 days and out to 2 years (6.9% vs. 0.9%). Any more than trivial perivalvular regurgitation is associated with an increased late mortality at 2 years (hazard ratio 2.11, 95% CI 1.43-3.10), but it is uncertain if the aortic insufficiency itself is a cause of late mortality or just a marker of increased risk.[6,8]

Stroke occurs in 4%-8% of patients, with the majority occurring early due to aortic or valvular atheroemboli. The rate of stroke has fallen over time with improved procedural technique, improved delivery systems, and more aggressive

anticoagulation. MRI-detected "silent" embolic events occur in nearly 85% of TAVR procedures.[14] Embolic protection filter devices delivered from the radial artery to shield the aortic arch vessels are being tested in clinical trials.

RHODE ISLAND HOSPITAL OUTCOMES

From March 2012 through October 2013, 56 patients have undergone TAVR using the Edwards Sapien balloon expandable valve, 30 from a transfemoral approach and 26 from a transapical approach. During the same time period, 157 patients underwent SAVR and 89 patients underwent combined CABG and AVR for aortic stenosis (TAVR performed in 23% of the total AVR procedures). Procedural success has been 100%, with one annular perforation from displacement of bulky calcification that resulted in tamponade treated with pericardiocentesis. There have been 3 vascular complications in transfemoral TAVR patients (10%) from iliac artery dissections managed with stenting. We have had 2 major periprocedural strokes resulting in death at 34 and 60 days, and one minor stroke without residual neurologic deficit – an overall 5.4% stroke rate. Four patients died within 30 days (7.1% mortality), with 7 more deaths after 30 days for a total mortality of 20%. Of the first 14 patients with more than 1-year follow-up, 2 patients have died (14% mortality).

FUTURE DIRECTIONS

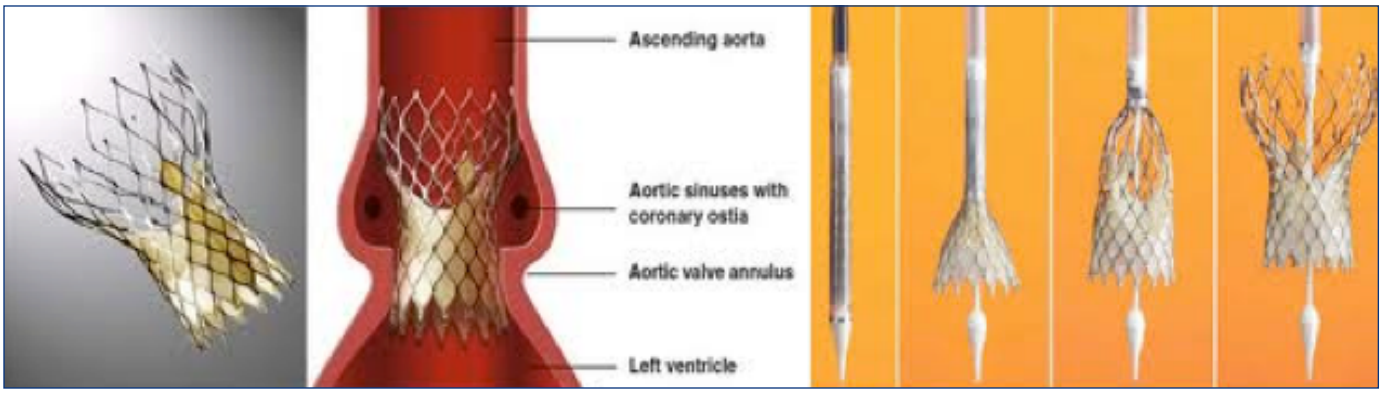
Next-generation lower profile valve and delivery systems are available and have replaced the first-generation Edwards Sapien valve outside of the United States.[15,16] The Edwards Sapien XT balloon expandable valve (Edwards Lifesciences Corp., Irvine, CA) made of cobalt-chromium is delivered through an 18 or 19 French delivery system. In the PARTNER 2 Trial, 560 inoperable or extreme-risk patients with adequate iliofemoral access for TAVR were randomized to either the current FDA-approved Edwards Sapien valve or the lower profile Sapien XT valve. There was no difference in 1-year mortality (23.7% vs. 22.5%) or stroke (4.6% vs. 4.5%) between the devices. However, procedural times were shorter with Sapien XT, and major vascular complications were significantly reduced at 30 days (15.5% vs. 9.6%).[17]

The Medtronic CoreValve is a self-expanding valve with bovine pericardial leaflets sewn to a nitinol cage that extends from the left ventricular outflow tract to the proximal ascending aorta (**Figure 2**). Four valve sizes range from 23-31 mm in diameter. This valve is used in approximately 50% of the TAVR procedures outside of the United States. The 18 French delivery system allows for transfemoral access through a minimum 6mm iliac artery. Multiple large registries using both the Edwards Sapien XT and Medtronic valves show procedural success is greater than 95%, with stroke rates reduced to 4-5% and vascular complications reduced to 5%.[15,16] The need for permanent pacemaker is higher with the Corevalve (25.8%) compared with the Sapien XT valve (6.5%) due to extension of the self-expanding nitinol cage within the left ventricular outflow track.[18]

The 1-year outcomes for the CoreValve SURTAVI Trial (Surgical Placement and Transcatheter Aortic Valve Implantation) were recently released in October 2013. This was a non-randomized registry of extreme-risk patients with aortic stenosis (Society of Thoracic Surgery predicted combined morbidity and mortality > 50%). Four hundred and seventy-one patients were enrolled and treated with transfemoral TAVR using the CoreValve; 30-day mortality was 7.9%, with all cause mortality at 1 year of 24%. The 30-day stroke rate was 4.1%. While perivalvular leak was common, 80% of patients with a moderate or less perivalvular leak post procedure improved by 1 year.[19] This was likely due to the self-expanding nature of this valve conforming to the aortic annulus over time.

TAVR has been extended to intermediate-risk patients in Europe with similar late 1- and 3-year mortality to SAVR in propensity-matched cohorts.[20] Extension to intermediate-risk patients is being tested in the randomized PARTNER 2 and SURTAVI Trials. In PARTNER 2, operable patients are randomized to TAVR with the second-generation Sapien XT valve or SAVR. Patients with significant obstructive CAD are included in this trial (percutaneous intervention with TAVR vs. CABG and AVR). In the SURTAVI trial, intermediate-risk

Figure 2. [L] Medtronic CoreValve, [R} Self-Expanding CoreValve and Delivery System



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patients are randomized to TAVR with the CoreValve (femoral or direct aortic approach) or SAVR.

The direct transaortic retrograde approach from a small incision to the right of the upper sternum with a sheath placed in the ascending aorta is being developed as an alternative to the transapical approach in patients who are not candidates for transfemoral TAVR. In small-matched series, there were fewer bleeding complications compared with the transapical approach,[21] and it may be a better alternative in patients with severe lung disease who may not tolerate a left thoracotomy. Within the PARTNER 2 trial, the direct aortic approach is being compared to transapical TAVR in a subset of patients.

With lower profile second-generation valves, some centers have been performing TAVR procedures in catheterization laboratories under conscious sedation without transesophageal echocardiography using percutaneous suture closure devices with excellent outcomes.[22] This approach significantly lowers ancillary costs and hospital lengths of stay, with many patients being discharged 1 day post procedure. The PARTNER 3 trial is about to begin enrollment testing an even smaller diameter 14F delivery system with a third-generation balloon expandable valve with a self-sealing cuff to reduce the incidence of perivalvular leak.

SAVR remains the treatment of choice in most patients with severe symptomatic aortic stenosis. At present, TAVR remains an alternative to surgery in high-risk or inoperable patients. As technology improves to lower stroke rates, vascular complications, and perivalvular leak, TAVR likely will be extended to lower-risk patients with comparable outcomes to SAVR.

References

1. Chizner MA, Pearle DL, deLeon AC Jr. The natural history of aortic stenosis in adults. *Am Heart J.* 1980;99:419.
2. Ross J Jr, Braunwald E. Aortic stenosis. *Circulation.* 1968;38:61.
3. Schwarz F, Baumann P, Manthey J, et al. The effect of aortic valve replacement on survival. *Circulation.* 1982;66:1105.
4. Safian RD, Berman AD, Diver DJ, McKay LL, Come PC, Riley MF, Warren SE, Cunningham MJ, Wyman RM, Weinstein JS, et al. Balloon aortic valvuloplasty in 170 consecutive patients. *N Engl J Med.* 1988 Jul 21;319(3):125–130.
5. Leon MB, Smith CR, Mack M, et al., for the PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* .2010;363:1597–607.
6. Makkar RR, Fontana GP, Jilaihawi H, et al., for the PARTNER Trial Investigators. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. *N Engl J Med.* 2012;366:1696–704.
7. Smith CR, Leon MB, Mack MJ, et al., for the PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med.* 2011;364:2187–98.
8. Kodali SK, Williams MR, Smith CR, et al., for the PARTNER Trial Investigators. Two-year outcomes after transcatheter or surgical aortic- valve replacement. *N Engl J Med*. 2012;366:1686–95.
9. Mack MJ, Brennan MJ, Brindis R, et al., Outcomes Following Transcatheter Aortic Valve Replacement in the United States *JAMA.* 2013;310(19):2069-2077.
10. Leon MB, Piazza N, Nikolsky E, et al. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. *J Am Coll Cardiol*. 2011;57:253–69.
11. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Am Coll Cardiol.* 2012;60:1438–54.
12. Ribeiro HB, Nombela-Franco L, Urena M, et al. Coronary Obstruction following Transcatheter Aortic Valve Implantation: A Systematic Review. *JACC Interv.* 2013; 6:452.
13. Thomas M, Schymik G, Walther T, et al. Thirty-day results of the SAPIEN aortic Bioprosthesis European Outcome (SOURCE) Registry: A European registry of transcatheter aortic valve implantation using the Edwards SAPIEN valve. *Circulation.* 2010;122:62.
14. Kahlert P, Knipp SC, Schlamann M, et al. Silent and apparent cerebral ischemia after percutaneous transfemoral aortic valve implantation: a diffusion-weighted magnetic resonance imaging study. *Circulation.* 2010;121:870.
15. Mylotte D, Osnabrugge RL, Windecker S, et al. Transcatheter aortic valve implantation in Europe: adoption trends and factors influencing device utilization. *J Am Coll Cardiol.* 2013;62:210–9.
16. Moat NE, Ludman P, de Belder MA, et al. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. *J Am Coll Cardiol.* 2011;58:2130.
17. Leon MB. A randomized evaluation of the SAPIEN XT transcatheter valve system in patients with aortic stenosis who are not candidates for surgery: PARTNER 2, inoperable cohort. *J Am Coll Cardiol*. 2013;61(10_S).
18. Jilaihawi H, Chakravarty T, Weiss RE, Fontana GP, Forrester J, Makkar RR. Meta-analysis of complications in aortic valve replacement: comparison of Medtronic-CoreValve, Edwards-Sapien and surgical aortic valve replacement in 8,536 patients. *Catheter Cardiovasc Interv*. 2012;80:128–38.
19. Popma J. CoreValve US Pivotal Trial Extreme Risk Iliofemoral Study Results. *J Am Coll Cardiol*. 2013;62(18_S1).
20. Piazza N, Kalesan B, van Mieghem N, et al. A 3-center comparison of 1-year mortality outcomes between transcatheter aortic valve implantation and surgical aortic valve replacement on the basis of propensity score matching among intermediate-risk surgical patients. *JACC Cardiovasc Interv.* 2013;6:443.
21. Lardizabal JA, O'Neill BP, Desai HV, et al. The transaortic approach for transcatheter aortic valve replacement: initial clinical experience in the United States. *J Am Coll Cardiol*. 2013;61:2341.
22. Durand E, Bogdan B, Godin M, et al. Transfemoral Aortic Valve Replacement with the Edwards Sapien and Edwards Sapien XT Prosthesis using Exclusively Local Anesthesia and Flouroscopic Guidance: Feasibility and 30 day Outcomes. *JACC Interv*. 2012;5:461-7.

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Using the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) to Determine Substance Abuse Prevalence in the RI Trauma Population

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ABSTRACT

BACKGROUND: Level I trauma centers are required to provide screening and brief interventions for alcohol abuse. The World Health Organization (WHO) Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) is a validated screening measure for all substances of abuse. This study is the first to use the ASSIST to screen a trauma population.

METHODS: A cross-sectional screening study using the ASSIST was conducted which included all patients admitted to the trauma service at Rhode Island Hospital during July and August 2012 who met inclusion criteria.

RESULTS: The ASSIST categorized 25% of participants as needing a brief intervention for alcohol and an additional 6.3% as needing more intensive treatment. At least a brief intervention was indicated for at least one other substance besides alcohol in 37% of participants.

CONCLUSIONS: The ability of the ASSIST to identify misuse of multiple substances makes it a good candidate for the screening measure used by trauma centers.

KEYWORDS: trauma, substance abuse, ASSIST

INTRODUCTION

The literature shows a definite link between alcohol or illegal drug use and injury from physical trauma. At one urban trauma center, heavy alcohol use was associated with nearly double the risk of violent injury.[1] Another study of a trauma center population found that at the time of their admission, 24% of trauma patients were alcohol dependent and 18% were currently drug dependent, versus 7% and 4%, respectively, in the general population of the United States.[2]

One successful strategy developed to reduce the impact of substance abuse is the Screening, Brief Intervention, and Referral to Treatment (SBIRT) algorithm. In 2006, the American College of Surgeons Committee on Trauma (ACS COT) began requiring that a SBI program for alcohol be in place as a prerequisite to level I trauma center certification.[3] This study examines a newly validated screening measure from the WHO, the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST), as a potential screening measure for a trauma population that could expand an SBI program infrastructure to screen for multiple substances.[4]

The ASSIST uses eight questions to assess lifetime substance use and substance use within the past three months. It uses scaled multiple choice responses to create individual scores for each substance of use, and stratifies these scores into low, moderate, and high risk categories, based on past three month use.[5] A PubMed search returned a total of 29 studies using the ASSIST, the majority of which assessed substance abuse in primary care populations.[6] This study is the first to use the ASSIST measure to describe substance abuse patients admitted to a trauma center, and compares this description to that provided by the standard screening already in place.

METHODS

The study setting was the trauma service at Rhode Island Hospital (RIH), the level I trauma center serving the entire state of Rhode Island, as well as nearby areas in Massachusetts and Connecticut. Rhode Island has a population of just over one million, and is made up of 76% white non-Hispanic persons, as well as 12% Hispanic persons and 6% African-American persons.[7]

All patients admitted to the trauma service at RIH between July 16 and August 21, 2012 were screened for study eligibility. The selection criteria were designed to be as inclusive as possible, only requiring that the participant be at least 18 years old, proficient in English, and able to complete the survey on their own. If patients were not initially eligible, then they were evaluated daily for eligibility until their discharge from the hospital, or until permanently ineligible due to disability or death.

After receiving verbal consent to participate in the study from eligible patients, the ASSIST V3.0 measure was administered via a tablet computer with an internet connection using DatStat™ software (Seattle, WA), a HIPAA compliant web-based survey program. Each participant used the tablet computer to complete the ASSIST screening measure, but entered no identifying information other than gender. All survey data was collected confidentially and anonymously and not shared with the clinical staff. A five-dollar gift certificate was given as compensation for study participation. The study protocol was reviewed by the RIH institutional review board and deemed exempt.

RESULTS

During the time of the study, 272 patients were admitted to the trauma service. Of those, 134 were eligible for the study and 112 elected to participate. [**TABLE 1**] The trauma service population was 35% female, and of the study participants, 36% were female.

Responses to the ASSIST showed that 31% of participants were categorized as needing at least a brief intervention for alcohol, with 6.3% needing referral to more intensive treatment. [**TABLE 2**] In comparison, responses to the CAGE screen were positive in 12% of the trauma population, and detectable blood alcohol levels were found in 36% of the trauma population. [**TABLE 3**]

The ASSIST also individually screened for the use of other substances of abuse, showing that interventions were indicated for anywhere between 29% of the participants (marijuana) to 1% (inhalants). In total, 37% of participants were categorized as needing at least a brief intervention for at least one substance other than alcohol. In comparison, the urine toxicology screen for a wide range of substances was positive in 68% of the trauma population.

Table 1. Eligibility

Patients on Trauma Service	272
Medically Able and Contacted before Discharge	134
Non English Speaking	8 (6.0%)
Declined to Participate	14 (10%)
Participants	112 (84%)

Table 2. ASSIST Results (with % of eligible participants)

Substance	Brief Intervention	More Intensive Treatment
Alcohol	28 (25%)	7 (6.3%)
Any other substance	35 (31%)	7 (6.3%)
Marijuana	28 (25%)	4 (3.6%)
Cocaine	6 (5.4%)	1 (0.9%)
Amphetamines	3 (2.7%)	2 (1.8%)
Inhalants	1 (0.9%)	0
Sedatives	7 (6.3%)	1 (0.9%)
Hallucinogens	7 (6.3%)	0
Opioids	6 (5.4%)	0

Table 3. Standard Trauma Service Screening Tests

	Positive Result	Negative Result	Unknown
Urine Toxicology Screen	93 (68%)	43 (32%)	136
Blood Alcohol Level	69 (36%)	123 (64%)	80
CAGE Questionnaire	18 (12%)	129 (88%)	125

The urine toxicology screen detects the presence of amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, methadone, opiates, and phencyclidine. A positive result for Blood Alcohol Level (BAL) indicates detection of any amount of ethanol. Percentages indicate percentage of known results, and does not include those patients for which results were still pending at the time of data analysis.

DISCUSSION

Our results demonstrate that use of the ASSIST is feasible in the trauma center as it was completed by 84% of those eligible for the study. This level of participation by eligible patients may be slightly inflated in comparison to participation outside of a study due to our protocol of anonymous data collection as well as small compensation for participation. On average, the screening took nine minutes (mean = 9.4; SD = 5.3, range = 1-28) to complete. Furthermore, allowing the patient to complete the screening on their own using the tablet computer allowed for a minimal time commitment from those administering the screen.

The ASSIST and CAGE questionnaire both identified a sub-population of the trauma service for which an intervention for alcohol misuse was indicated. This study does not attempt to conclude which is a more appropriate screen for alcohol misuse in the trauma population.

The ASSIST also identified numerous other specific substances of abuse for which an intervention was indicated (and may not be currently provided). Determining whether using the ASSIST is measurably beneficial as compared to screening for alcohol only will depend upon future outcomes research demonstrating effective interventions with this population. The urine toxicology screen also identified substance use in many patients. However, it is used in practice at this center more for medical decision making than for assessing substance abuse patterns, as it documents only the presence, not the amount or manner in which a substance is used, and does not differentiate between prescription medicine use and misuse.

One of the main limitations of this study is the comparison between the participant's ASSIST data and the standard screening data from the entire trauma population, rather than a direct comparison of individual participant's data. This was due to the anonymity of the ASSIST data collection, and makes it difficult to compare the sensitivity or specificity of the two screening methods. Also, the subset of the trauma population who were participants likely underrepresented those who were more seriously injured due to the exclusion criteria, and it is unclear if this would have increased or decreased those identified as having substance abuse issues. Finally, the data gathered is useful for an accurate description of the substances being abused by the trauma population at our center. However, our findings may not apply to trauma centers in other locations which may have different substance abuse patterns or currently clinically screen for substance abuse using other measures.

In conclusion, our study confirmed that substance abuse

is present in a substantial portion of the adult trauma population at our center. We found that an electronic version of the ASSIST is a feasible screening measure to assess multiple types of substance abuse and offers an opportunity to detect and intervene for substance abuse during a trauma admission. In what may be a trauma patient's only encounter with the health care system, screening only for alcohol abuse is clearly a missed opportunity for intervention. If this level of substance abuse prevalence is consistent across other trauma patient populations, it may suggest that the recommendations of the ACS COT could be extended to include other substances besides alcohol.

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References

1. Hayman AV, Crandall ML. Deadly partners: interdependence of alcohol and trauma in the clinical setting. *Int J Environ Res Public Health*. 2009 Dec;6(12):3097-104.
2. Soderstrom CA, Smith GS, Dischinger PC, McDuff DR, Hebel JR, Gorelick DA, Kerns TH, Ho SM, Read KM. Psychoactive substance use disorders among seriously injured trauma center patients. *JAMA*. 1997 Jun;277(22):1769-74.
3. Gentilello LM. Alcohol and injury: American College of Surgeons Committee on Trauma requirements for trauma center intervention. *J Trauma.* 2007 Jun;62(6 Suppl):S44-5.
4. Humeniuk RE, Ali RA, Babor TF, Farrell M, Formigoni ML, Jittiwutikarn J, Boerngen de Larcerda R, Ling W, Marsden J, Monteiro M, Nhiwhatiwa S, Pal H, Poznyak V, Simon S. Validation of the Alcohol Smoking and Substance Involvement Screening Test (ASSIST). *Addiction*. 2008 Jun;103(6):1039-1047.
5. The Assist Project [Internet]. Geneva (Switzerland): World Health Organization; 2013 [cited 2013 Feb 1]. Available from: http://tinyurl.com/7d4do6n
6. PubMed.gov [Internet]. Bethesda (United States): National Center for Biotechnology Information, US National Library of Medicine; 2013 [cited 2013 Aug 11]. Available from: http://tinyurl.com/kdp84ek
7. State and county quick facts: Providence, Rhode Island [Internet]. Washington (DC): United States Census Bureau; 2013 [cited 2013 Feb 1]. Available from: http://tinyurl.com/a3wyxgt

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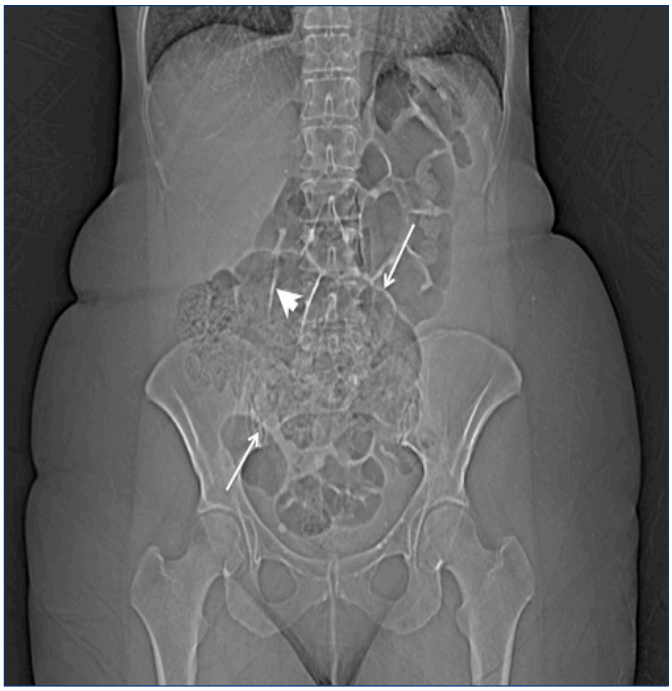
Cecal Volvulus Diagnosed on CT in Two Distinct Clinical Settings

JOSEPH FARNAM, MD; MICHAEL WALLACH, MD

Figure 1. CT topogram demonstrates a dilated stool filled bowel loop in the mid abdomen (arrow) with preserved haustral markings (arrowhead).



CASE 1

A 55-year-old white female presented to the emergency department in moderate distress with sudden onset severe lower abdominal pain, progressive over twelve hours with a "twisting" character that worsened with movement. She denied nausea or vomiting and reported having a normal bowel movement just prior to symptom onset. Her past medical history included a distant history of breast cancer but was otherwise negative. Her vital signs were normal. Her abdomen was mildly tender at the lower quadrants, as well as mildly distended and tympanic without peritoneal signs. Bimanual exam was normal. Laboratory analysis was non-revealing. A contrast-enhanced CT of the abdomen and pelvis was obtained. The CT topogram (**Figure 1**) revealed a loop of dilated, stool-filled bowel in the mid abdomen, confirmed to represent dilated cecum on coronal CT imaging (**Figure 2**). Axial CT imaging (**Figure 3**) demonstrated a decompressed ascending colon with transition to cecal dilation at the level of a CT whirl sign. The patient proceeded to emergent exploratory laparotomy where a torsed and markedly dilated cecum was encountered. A right hemicolectomy with functional side-to-side end iliocolocstomy was performed. The patient experienced an uncomplicated post-operative course and was discharged on day 5 following the procedure.

Figure 2. Coronal CT image at the level of the iliocecal valve (arrowhead) confirms a dilated, stool filled cecum (arrows).

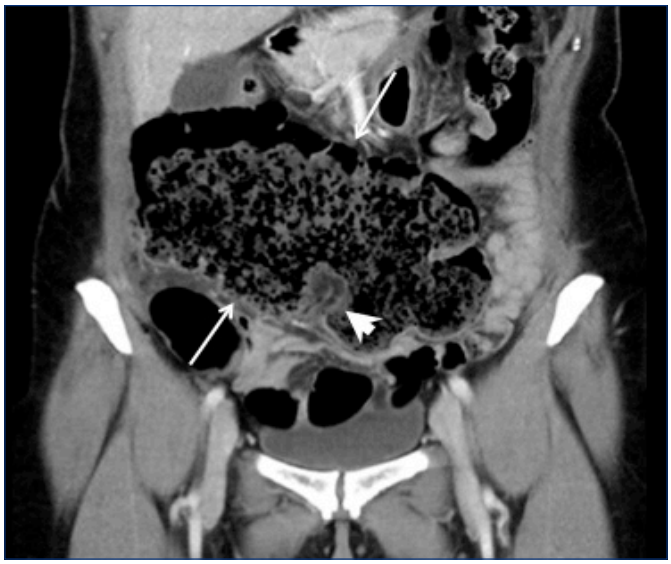
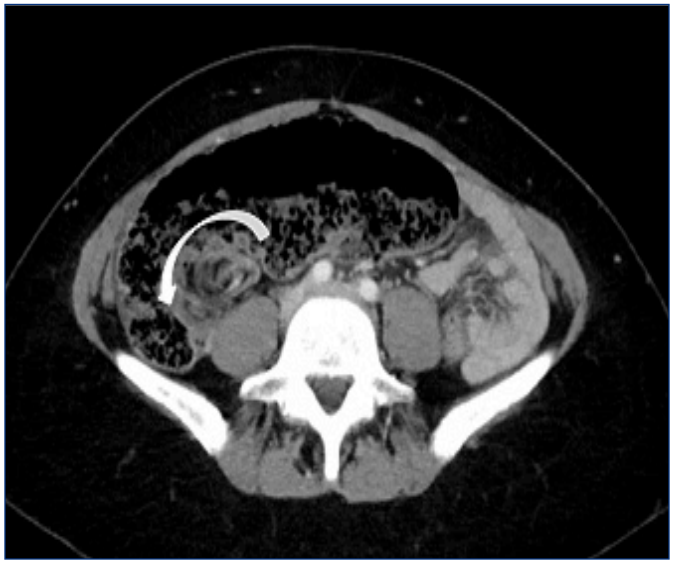


Figure 3. Axial CT demonstrates a whirl sign (curved arrow) at the level of the dilated cecum.



CASE 2

A 17-year-old wheel chair-bound female with a history of spina bifida and congenital hydrocephalus presented to the emergency department after failing outpatient treatment for a presumed viral gastroenteritis with two days of anorexia, extensive vomiting, diarrhea and fever. She reported one episode of bright red blood per rectum and her temperature at home was elevated up to 104°F. Additional past medical history included recurrent urinary tract infections likely related to daily routine self-catheterization. On physical exam her abdomen was distended and markedly tender at the epigastrium. She was febrile to 100.8°F with mild hypotension, marked tachycardia and tachypnea. Her oxygen saturation remained normal on room air. Her laboratory analysis was remarkable for mild hyponatremia (sodium 131) and leukocytosis (white blood cell count 13.3). An abdominal radiograph showed a dilated viscus in the left upper quadrant containing a single air fluid level. A subsequent CT examination (Figures 4, 5) revealed midgut malrotation with a dilated cecum twisted on its mesentery in the left abdomen. The patient was immediately taken to the operating room for emergent exploratory laparotomy with a presumed diagnosis of cecal volvulus. This was confirmed intra-operatively along with midgut malroatation. The cecum and terminal ileum were both necrotic and therefore resected. A primary end-to-end ilioccecostomy with a diverting loop ileostomy was performed. The patient recovered rather uneventfully and was discharged on post-operative day 10. Unfortunately, she has since developed multiple recurrent small bowel obstructions.

Figure 4. Supine (a) and lateral decubitus (b) views of the abdomen demonstrate a dilated viscus in the left upper quadrant (arrow) containing a single air fluid level (arrowhead)..

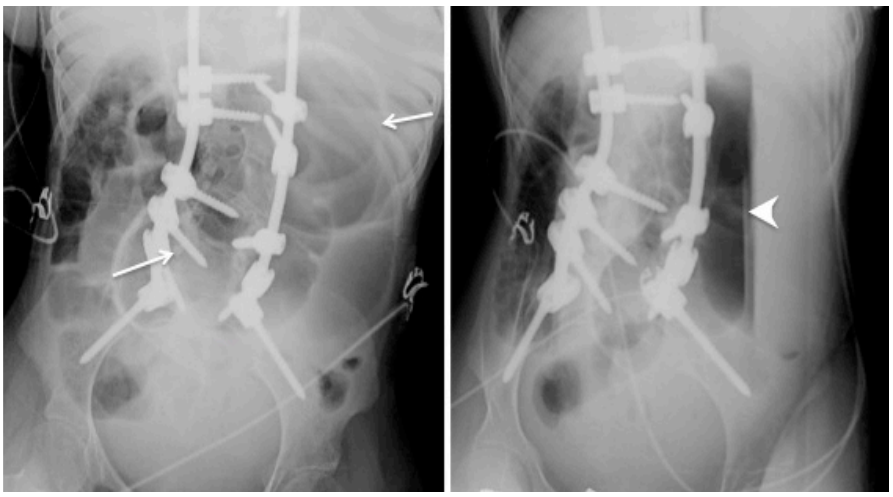
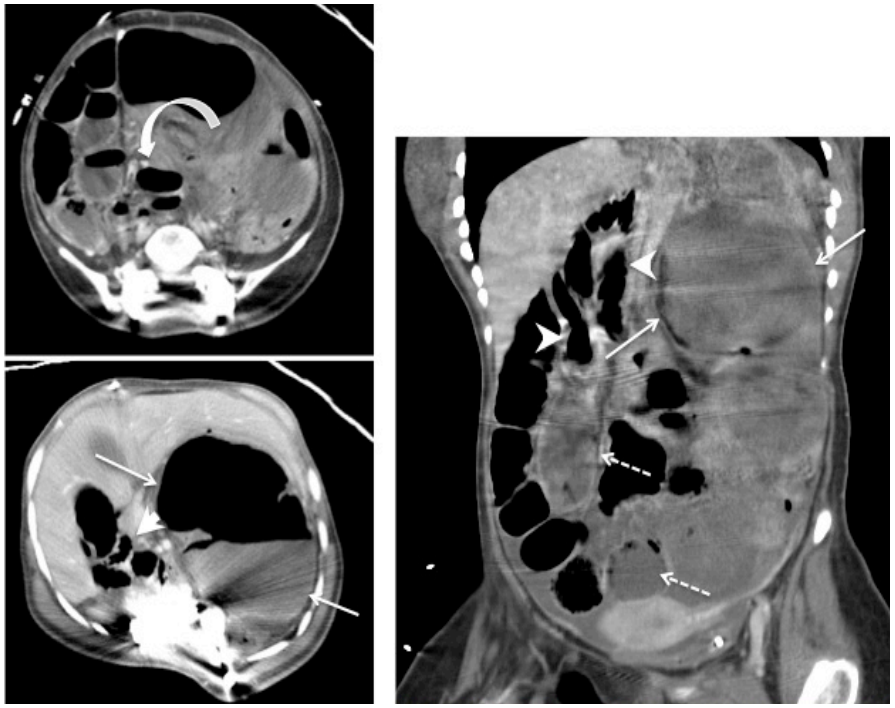


Figure 5. Axial (a and b) and coronal (c) CT images of the abdomen demonstrate a markedly dilated cecum located in the left upper quadrant (arrows) that is twisted with a whirl sign (curved arrow) in the mid abdomen. Note the predominance of bowel loops in the right abdomen (arrowheads) with distal small bowel dilation (dashed arrows).



DISCUSSION

Cecal volvulus is a rare gastrointestinal condition that presents with nonspecific symptoms, has historically been diagnosed at laparotomy or barium enema and more recently by computed tomography (CT). Emergent surgery is required to prevent colonic ischemia and perforation. It was first described by Rokitansky as "intestinal strangulation" of the cecum in 1837.[8] Pathophysiology is related to a combination of an abnormally fixated or rotated right colon and risk factors that can include anything acting as a fulcrum at the cecum (colonic mass, adhesion, etc) or colonic distension (chronic constipation, ileus, distal obstructing lesion, colonoscopy, etc).[9] While 10-25% of the general population has an abnormally fixed ascending colon,[10,11] cecal volvulus is rare, accounting for only 1% of bowel obstructions.[12] It can occur in one of three types: axial, loop and bascule. The axial and loop type require a twist of the cecum along its long axis

while in the bascule type, the cecum does not twist but folds anteriomedially along a fibrotic band, acting as a flap valve mechanism.[13] All three types of volvulus result in a closed loop obstruction at risk of mesenteric ischemia according to Laplace's law. In addition, the axial and loop-type volvuli have an underlying mesenteric twist that causes vascular strangulation and higher rates of mesenteric ischemia. With all types of cecal volvulus patients present acutely with non-specific symptoms of bowel obstruction, including generalized abdominal pain, nausea, vomiting, constipation and abdominal distension. The acute presentation can be preceded by a recurrent intermittent pattern of symptoms in 50% of patients, referred to as the mobile cecum syndrome.[14] On physical exam patients classically present with a tympanic mass; however, this is rarely encountered clinically.[3] Although several "classic" plain film findings have been described, their sensitivity and specificity are low, frequently necessitating a contrast enema. More recently, computed tomography has been used to make the diagnosis non-invasively, much quicker and with greater diagnostic accuracy, replacing contrast enema for diagnosis. Management of acute volvulus is surgical, most commonly with right hemicolectomy, regardless of underlying bowel viability. A subsequent primary iliocolonic anastamosis is performed in most cases, unless there is evidence of free perforation in which case temporary colonic diversion is advocated.[15]

IMAGING

Cecal volvulus can be encountered at several imaging modalities, including radiography, contrast enema and computed tomography. Classic radiographic findings include a single dilated, comma-shaped colonic loop ectopically located in the left upper quadrant containing a single air fluid level with preservation of haustral markings.[1] In contrast, sigmoid volvulus presents with two colonic limbs that take an inverted U or coffee bean appearance with two separate air-fluid levels and loss of haustral markings.[2] Despite the classic imaging appearance, findings are relatively insensitive and very nonspecific with the diagnosis made in only 17% of cases.[3] The location and presence of cecal dilatation is highly variable and small bowel dilatation can oftentimes obscure underlying colonic abnormalities, confusing the diagnosis.[3, 4] Contrast enema increases both sensitivity and specificity with findings that include distal colonic decompression with beak-like tapering at the level of the volvulus.[5] However, contrast enema can delay diagnosis.

In comparison, CT is much quicker, non-invasive and has several imaging signs with superior sensitivity and specificity. Nearly all cases of axial or loop-type volvulus demonstrate a whirl sign, defined as a twisting of mesenteric vessels and bowel loops around central mesenteric fat. Most cases are accompanied by distal colonic decompression.[6] By "running the bowl" in a retrograde fashion starting at the rectum, one can usually identify the anatomic site of the whirl sign and in turn distinguish sigmoid from cecal volvulus. When a redundant mesentery or scant intra-abdominal fat makes this determination difficult, the location of the whirl sign in the right or left abdomen can reliably diagnose cecal and sigmoid volvulus respectively.[7] A very rare exception to this search pattern and algorithm occurs with midgut malrotation, as presented above, where cecal volvulus is very difficult or impossible to distinguish from sigmoid volvulus. In addition, the whirl sign is not seen in the bascule type, therefore making this diagnosis more challenging. However, this type represents a minority (approximately 10%)[13] of cases and its diagnosis is still suggested by abnormal cecal configuration, cecal dilatation and distal colonic decompression. In all, CT provides excellent diagnostic utility and should be regarded as the test of choice for the diagnosis of cecal volvulus.

References

1. Anderson JR and Mills JOM. Caecal volvulus: a frequently missed diagnosis? *Clinical Radiology*. 1984;35:65-69.
2. Burrell HC et al. Significant plain film findings in sigmoid volvulus. *Clinical Radiology.* 1994;49(5):317-319.
3. Rabinovici et al. Cecal volvulus. *Dis Colon Rectum.* 1990;33(9):765-769.
4. O'Mara CS at al. Cecal Volvulus: analysis of 50 patients with long-term follow-up. *Ann Surg*.1979;189(6):724-731.
5. Ericksen AS et al. Use of Gastrointestinal Contrast Studies in Obstruction of the Small and Large Bowel. *Dis Colon Rectum*. 1990;33(1):56-64.
6. Rosenblat J et al. Findings of cecal volvulus at CT. *Radiology*. 2010;256(1):169-175.
7. Macari M et al. Can the location of the CT whirl sign assist in differentiating sigmoid from caecal volvulus? *Clinical Radiology.* 2011;66:112-117.
8. Rokitansky C . Intestinal strangulation . *Arch Gen Med*. 1837;14:202–204.
9. Radin DR, Halls JM. Cecal volvulus: a complication of colonoscopy. *Gastrointestinal radiology.*1986;11(1):110-111.
10. Wolfer JA et al. Volvulus of the cecum. *Surgery Synecol Obstet.*1942;74:882-894.
11. Donhauser JL et al. Volvulus of the caecum. *Arch Surg*. 1949;58:129-148.
12. Halabi WJ et al. Colonic Volvulus in the United States: Trends, Outcomes, and Predictors of Mortality. *Annals of Surgery*. 2013;electronically published ahead of print.
13. Delabrousse E et al. Cecal volvulus: CT findings and correlation with pathophysiology. *Emergency Radiology*. 2007;14:411-415.
14. Rogers RL, Harford FJ. Mobile cecum syndrome. *Dis Colon Rectum*.1984;27(6):399-402.
15. Madiba TE et al. The management of cecal volvulus. *Dis Colon Rectum*. 2002;45(2):264-267.

Authors

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Sexual Orientation and Health Risks among RI High School Students

BRUCE CRYAN, MBA, MS

According to a youth survey, 8% of Rhode Island (RI) public high school students (3,500 students) identify as lesbian, gay or bisexual (LGB). This paper examines if there are any differences in health risk behaviors and exposures for this population versus their heterosexual peers.

METHODOLOGY

Every two years, RI high school students participate in the Youth Risk Behavior Survey (YRBS). The YRBS is a sample survey examining the major causes of disease and injury morbidity and mortality.

The YRBS asks the following question: "Which of the following best describes you? 1) heterosexual; 2) lesbian or gay; 3) bisexual, or 4) not sure." Student responses are parsed into two categories, those indicating either #1 (heterosexual), or #s 2 or 3 (lesbian, gay or bisexual).

Fourteen risk measures are examined, relating to mental health, violence, tobacco, drugs and alcohol, and sexual activity. Each measure is a negative indicator, so lower values are preferred. As the YRBS is a sample survey, two years of data (2011 and 2013) are combined to yield samples of sufficient size (>100) to be statistically representative of the LGB cohort. All the differences in values presented here (between LGB and heterosexual students) are statistically significant at the 95% confidence level.

RESULTS

Demographically, lesbian, gay or bisexual students are more likely than their heterosexual classmates to be female (70% versus 48%), Hispanic (28% versus 19%), and poor academic performers (15% versus 7%).

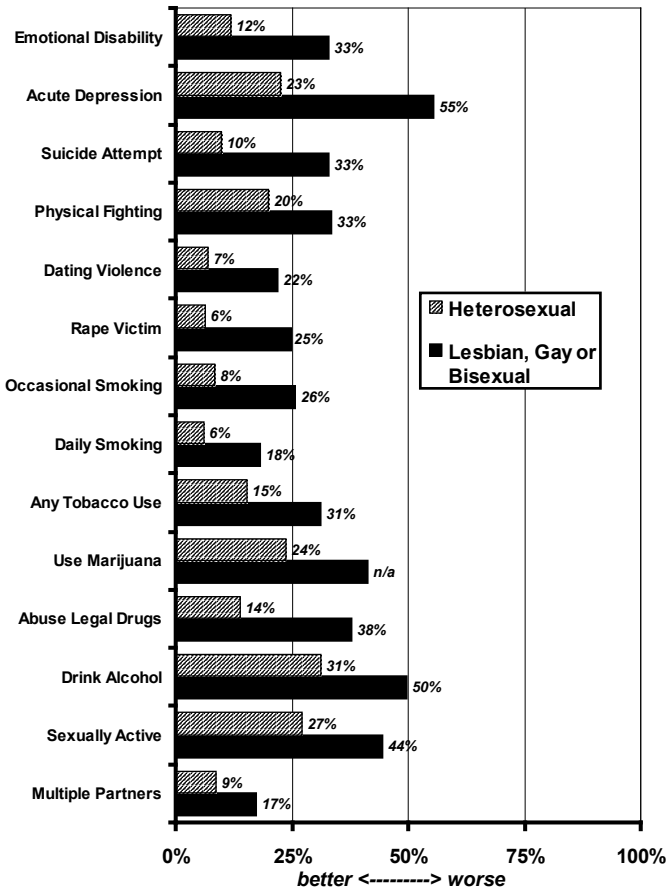
LGB students report more mental health issues when compared to their heterosexual peers. Emotional disability is almost three times more common (33% versus 12%), depression is twice as prevalent (55% versus 23%), and the attempted suicide rate is three times higher (33% versus 10%)[1]

Compared to their heterosexual classmates, reported violence is much more common among LGB students. They are more likely to engage in physical fighting (33% versus 22%), three times more likely to experience dating violence (22% versus 7%), and four times more likely to be a victim of sexual assault (25% versus 6%).

Reported tobacco, alcohol and substance use is higher among LGB high school students compared to their heterosexual peers. Occasional smoking is three times higher (26% versus 8%), as is daily smoking (18% versus 6%), and the use of any tobacco product is twice as high (31% versus 15%). LGB students have higher rates of alcohol drinking (50% versus 31%), marijuana use (41% versus 24%), and abuse of legal drugs (prescription and 'over-the-counter') (38% versus 14%).

More LGB high school students report being sexually active compared to heterosexual students. LGB students are more likely to engage in intercourse (44% versus 27%) and twice as likely to have had multiple (4+) sexual partners (17% versus 9%).

Table. Health Risks Among High School Students by Sexual Orientation Rhode Island, 2011 and 2013



Source: Rhode Island Youth Risk Behavior Survey, Rhode Island Department of Health

DISCUSSION

Lesbian, gay or bisexual students are clearly a vulnerable population displaying a higher prevalence of health risks across every measure examined. Dating violence (1 in 5 LGB students), forced sexual intercourse (1 in 4 LGB students) and attempted suicide (1 in 3 LGB students) are particularly alarming. Equally disturbing are the rates of drinking (1 in 2 LGB students), depression (1 in 2 LGB students) and emotional disability (1 in 3 LGB students).

Reducing health disparities requires concerted effort in identifying the prevention needs and susceptibilities of this group of youth. Strategic interventions, such as increased access to physical/mental health services and prevention education, are needed to change negative social behaviors (e.g., smoking, drinking) and to help avoid victimization from exposure to other negative situations (e.g., rape, dating violence).

Footnote

1. The "Attempted Suicide" rate is based on the proportion of students who reported they had attempted suicide one or more times in the 12 months prior to the survey. During past years, the attempted suicide rate among Rhode Island high school students has been 8%-9%, and in 2011, it was 8.7%. This rate was higher than the overall rate for the United States, which was 7.8% in 2011 (the most current data available). However, in 2013, the self-reported attempted suicide rate among all Rhode Island public high school students rose to 14.3%, which prompted the Department of Health to confirm the data with the Centers for Disease Control and Prevention (CDC), which sponsors the survey and weights the state's data to be representative of the population. The CDC conducted an audit of their 'weighting' methodology for this measure and concluded the 2013 value was correct. It should also be noted that these data are different than other data, such as hospitalization data for suicide attempts, since not all attempts result in a hospital admission. For example, in Rhode Island during 2012, there were 17.2 per 10,000 (less than 1%) hospitalizations for suicide attempts among teens aged 13-19.

Author

Bruce Cryan, MBA, MS, is the YRBS Coordinator in the Center for Health Data and Analysis at the Rhode Island Department of Health.

VITAL STATISTICS
MICHAEL FINE, MD
DIRECTOR, RHODE ISLAND DEPARTMENT OF HEALTH
COMPILED BY COLLEEN A. FONTANA, STATE REGISTRAR

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

	REPORTING PERIOD		
VITAL EVENTS	AUGUST 2013	12 MONTHS ENDING WITH AUGUST 2013	
	Number	Number	Rates
Live Births	1,012	11,594	11.0*
Deaths	753	9,867	9.4*
Infant Deaths	5	81	7.0#
Neonatal Deaths	2	59	5.1#
Marriages	966	6,304	6.0*
Divorces	254	3,338	3.2*
Induced Terminations	No data available		
Spontaneous Fetal Deaths	No data available		
Under 20 weeks gestation	No data available		
20+ weeks gestation	No data available		

* Rates per 1,000 estimated poulation
# Rates per 1,000 live births

	REPORTING PERIOD			
Underlying Cause of Death Category	FEBRUARY 2013	12 MONTHS ENDING WITH FEBRUARY 2013		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	239	2,391	227.0	3,419.5
Malignant Neoplasms	144	2,172	206.2	5,834.5
Cerebrovascular Disease	32	459	43.6	689.5
Injuries (Accident/Suicide/Homicide)	57	639	60.7	8,844.0
COPD	42	509	48.3	470.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 estimated population of 1,052,567 (www.census.gov)
(c) Years of Potential Life Lost (YPLL).

NOTE: Totals represent vital events, which occurred in Rhode Island for the reporting periods listed above.
Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

CME EVENT

Eleventh Hour Education Event

May 17, 2014, 7:00 am
Crowne Plaza Hotel
801 Greenwich Avenue, Warwick RI 02886

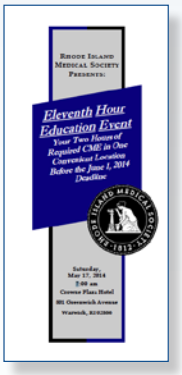
The RI Medical Society has organized your opportunity to obtain required Continuing Medical Education (CME) on Saturday, May 17, 2014.

The required topics to be covered are **Pain Management** and **Risk Management**, while we will also cover important education on a non-required topic.

The Rhode Island Department of Health states that "unless you were in training or became Board Certified or Re-Certified within the past two years, (physicians) need to complete 40 hours of Continuing Medical Education (CME) during each two-year license cycle. The current license renewal cycle requires that you obtain and submit your credits no later than **June 1, 2014**. At least two hours of this education must be related to one of the following topics:

- Risk management
- Opioid pain management/chronic pain management
- End of life/palliative care
- Ethics"

Registration



Program and Registration form

The program agenda and registration details for this event can also be found at www.rimed.org. RIMS members may log onto the Member Portal to register or complete the form and return as noted.

If you are not a RIMS member but would like to join, please complete the online membership application. The member rate will be offered to applicants upon receipt of your membership application.

Please email Megan E. Turcotte with questions, or call 401-331-3207.

NOTICE

The Rhode Island Medical Society no longer endorses the collection agency **IC System** and is currently seeking a high-quality, professional collection agency that will provide superior service to RIMS members at favorable rates.

Steve DeToy; Susan Bailey, MD, Vice Speaker, AMA House of Delegates; Michael E. Migliori, MD

AMA State Legislative Strategy Conference

Tucson, Arizona
January 9–13, 2014

RIMS was represented at the annual AMA State Legislative Strategy Conference by Steven R. DeToy, Director of Government and Public Affairs, and Chair of the AMA Advocacy Resource Center; and Michael E. Migliori, MD, Chair of the RIMS Public Laws committee. The conference was sponsored by the AMA Advocacy Resource Center.

The SLSC brings together stakeholders from state and specialty medical societies, state and federal government, and consumer advocacy groups to discuss issues and initiatives going on across the country. This year some of the topics covered include the transformation of Medicaid, physician-led health care teams, prescription drug abuse and diversion, and health care exchanges.

Michael E. Migliori, MD; Carrie Armour, JD, Senior Legislative Attorney, AMA Advocacy Resource Center; Steve DeToy,

Why You Should Join the Rhode Island Medical Society

The Rhode Island Medical Society delivers valuable member benefits that help physicians, residents, medical students, physican-assistants, and retired practitioners every single day. As a member, you can take an active role in shaping a better health care future.

RIMS offers discounts for group membership, spouses, military, and those beginning their practices. Medical students can join for free.

Above: State House press conference on health care, Brown MSS at the AMA, CPT update seminar, bike helmet distribution, medical student volunteers; Upper right: Meeting of RIMS membership committee

APPLY FOR MEMBERSHIP ONLINE

RIMS MEMBERSHIP BENEFITS INCLUDE:

Discounts on career management resources
Insurance, collections, medical banking, and document shredding services

Discounts on Continuing Medical Education
InReach online CME program discounts;
RIMS is an ACCME accrediting agency

Powerful advocacy at every level
Advantages include representation, advocacy, leadership opportunities, and referrals

Complimentary subscriptions
Publications include *Rhode Island Medical Journal*, *Rhode Island Medical News*, annual *Directory of Members;* RIMS members have library privileges at Brown University

Member Portal on www.rimed.org
Password access to pay dues, access contact information for colleagues and RIMS leadership, RSVP to RIMS events, and share your thoughts with colleagues and RIMS

SPECIAL NOTICE: 2014 AMA DUES PAYMENTS

The American Medical Association (AMA) will direct bill its Rhode Island members for their 2014 dues. Beginning August 2013, AMA members will receive a separate dues statement from the AMA instead of paying AMA membership dues through the Rhode Island Medical Society (RIMS) membership invoice. This is simply an operational change so that both RIMS and AMA can concentrate on their respective member satisfaction. There remains no requirement for RIMS members to join the AMA.

Please let us know if you have questions concerning this change by emailing Megan Turcotte or phoning 401-331-3207.

Providence doctor testifies at federal hearing on UnitedHealthcare's network contraction

BY MARY KORR
RIMJ MANAGING EDITOR

RAYMOND H. WELCH, MD, a Providence dermatologist for almost three decades, testified January 22 at a federal hearing held in Hartford, Conn. It focused almost entirely on UnitedHealthcare's (UHC) termination of physicians from its Medicare Advantage (MA) provider network, which went into effect February 1.

Dr. Welch and an estimated one-third of Rhode Island physicians were cut; but he noted that a review of the list of UHC active Ocean State dermatologists "included a doctor who is dead. And one is me, under an old EIN number and different address."

'…Doctors are not interchangeable widgets. There will be delays in diagnosis and treatment, and increased morbidity and suffering and possibly death for some of my patients.'

R.I. Sen. Sheldon Whitehouse, a member of the U.S. Senate Special Subcommittee on Aging, which held the field hearing, had invited Dr. Welch to speak. Among its charges, the subcommittee studies issues and makes recommendations related to Medicare and Social Security.

GINA WELCH

Dr. Raymond H. Welch prepares to testify at a U.S. Senate subcommittee hearing on United Healthcare's dismissal of physicians from its Medicare Advantage provider network held January 22 in Connecticut.

"You would think a high-value network would be able to pick up the deadness of a doctor," Whitehouse later observed, after an insurance trade association's legal counsel (not speaking for UHC) emphasized the industry's commitment to building "high-value" networks; this remark was questioned in this particular case by two physicians on the panel of witnesses.

In a subsequent interview with the *Rhode Island Medical Journal*, Dr. Welch described some of his patients as veterans of World War II, and the Korean and Vietnam wars. "In fact, of our 120 affected patients, over 90% have had skin cancers or pre-cancers. Almost 10% of our patients with UHC's Medicare Advantage plan are 89 years old or older," he said.

One such patient of his is an elderly man with a heart-transplant who has had more than 140 pre-cancerous and cancerous lesions removed as a result of the immuno-therapy he is on. "These are patients that need our continuity of care. But, of course, skin cancer care incurs higher costs," Dr. Welch said.

Circuit court sends UHC, physicians to mediation

If mediation is unsuccessful, judges will render decision

NEW YORK, N.Y. – In December, the Hartford and Fairfield medical associations in Connecticut sued UnitedHealthcare (UHC) as a result of its actions in the termination of physicians from its Medicare Advantage (MA) network. The suit claimed the insurer violated federal laws by dropping the physicians without a stated reason and recourse to appeal the reasons for the decision.

In December, a state district court issued an injunction and temporary restraining order against UHC, which then appealed the decision. Initial oral arguments were heard Jan. 21 in the U.S. Court of Appeals for the Second Circuit in Manhattan before a three-judge panel.

On Jan. 23, the court ordered the groups to mediation this week, which is overseen by a court-appointed attorney. Typically mediation lasts a day and if a settlement or agreement is not reached, the three-judge panel will then issue a ruling, expected within a two-month period.

The Medical Society of New York also filed suit on Dec. 23. in the Eastern District Court of N.Y. "By terminating numerous physicians from the . . . network, United seeks to stem financial losses occasioned by reduced federal payments under the Affordable Care Act," the suit claims. It is in abeyance until a decision is made in the Connecticut case.

At the U.S. Special Subcommittee on Aging hearing held in Hartford on Feb. 22, Connecticut's Sen. Richard Blumenthal, a subcommittee member who presided over the hearing, didn't mince words on UnitedHealthcare's (UHC) actions, which resulted in several thousand Connecticut physicians jettisoned from the UHC MA provider list.

"It is an outrageous abuse and should not be permitted. It is unacceptable and unjustifiable in terms of the doctors and probably illegal under present law," he said, "but if we need to change the law we will," he said.

— *Mary Korr*

Appeals' process

When Dr. Welch queried UHC on the metrics it used to determine the cuts, he was informed that was considered "proprietary" information. "Our 'appeal' was held via a conference call with a UHC moderator and two of its medical directors. The only question under discussion was: 'Did I feel we were properly and legally notified?' I said no."

He questions UHC's stated reasons – that the contraction of the network was to "create a more focused network to allow UHC to work more closely with providers to improve outcomes and, ultimately, lower costs."

Dr. Welch said no avenue has been provided to refute the implied statement that doctors are not providing high quality, cost-effective care for their patient population. "UHC has not improved quality by reducing one-third of the dermatologists, as well as other subspecialists, in its Rhode Island network. For patients who need to find new doctors, there is a significant loss in continuity of care. I know these patients and their cancer history. Doctors are not interchangeable widgets. There will be delays in diagnosis and treatment, and increased morbidity and suffering and possibly death for some of my patients."

Where does this leave his patients? Dr. Welch said the State of Rhode Island was able to negotiate an out-of-network benefit for retirees to allow them to continue to see the terminated providers, if the providers are willing to accept an out-of-network fee schedule. He also noted that about half of the remaining patients have switched their insurance to other carriers rather than lose their doctors. Others have switched to the traditional Medicare A/B plans with Medigap or supplemental insurance.

And then there are those who are bound by their retirement plan to remain with UHC MA who may have to wait longer for appointments with new physicians, or may be unable to find ones accepting new patients. "Some of advanced years may give up trying to find another doctor. This is truly unacceptable. I cannot believe that the government ever thought that giving Medicare Advantage plan contracts to publicly-held corporations would result in a limitation of access to care," Dr. Welch said.

He ended his testimony at the hearing by stating: "I have dedicated my life to serving and caring for my patients in accordance with the Oath I professed 33 years ago. In that oath, I vowed:

> *That above all else I will serve the highest interests of my patients through the practice of my science and my art;*
>
> *That I will be an advocate for patients in need and strive for justice in the care of the sick.*

"This is why I am here today and I hope that you will join me in protecting and advocating for these Medicare patients."

Sen. Whitehouse summed up the hearing by stating that UHC's actions was a consumer-protection problem because it placed the burden on the sickest and most vulnerable patients. He likened it to "Medicare gamesmanship."

The MA program, he said, was supposed to "compete head-to-head with Medicare and was being paid 14 percent more than the traditional plan." The Affordable Care Act (ACA), he said, eliminates that premium and "may enhance the incentive by insurers to 'cherry-pick' patients," which amounts to "privatizing profits and socializing costs." He said UHC's actions raise a "flag of suspicion."

Sens. Whitehouse and Richard Blumenthal (CT) called for greater oversight of the plans by CMS. "If CMS does not have the resources to do this, we need to address that," Blumenthal said.

UHC declined an invitation to participate in the hearing; however, a UHC representative was in the audience, according to a news report in the *Hartford Courant*. ❖

Alpert students seek volunteers for newly-formed human rights asylum clinic

Physicians, healthcare professionals invited to forensic training conference to be held Saturday, February 8

BY MARY KORR
RIMJ MANAGING EDITOR

MARY KORR

From left, William Berk (MD'16), Rebecca Slotkin (MD'16) and Andy A. Hoang (MPH, MD'17) view the website of the Brown Human Rights Asylum Clinic.

PROVIDENCE – A group of Alpert medical students have formed a student-run clinic to provide forensic psychological and medical evaluations to survivors of persecution seeking asylum in this country. A training session will be held this Saturday and space remains available. *(See details, link to program on next page.)*

Called the Brown Human Rights Asylum Clinic (BHRAC), it is one of a handful nationwide, modeled on the Weill Cornell Center for Human Rights in New York City, the first student-run asylum clinic, which was formed several years ago. Its medical director, 1977 Brown graduate Joanne Ahola, MD, a psychiatrist, will serve on the expert panel at the Saturday conference. She has trained health professionals nationwide in evaluating and documenting the psychological effects of torture and other forms of persecution.

The Brown clinic partners with Physicians for Human Rights (PHR), which acts as the referral organization for asylum seekers, via immigration attorneys. Brown Professor Eli Y. Adashi, MD, PHR board member and former dean of the medical school, serves as faculty advisor.

REBECCA SLOTKIN MD'16, one of the founders of the Brown clinic, an outgrowth of her interest in global health issues, said volunteers are needed to perform physical, psychological and gynecological evaluations to those seeking asylum. "We need physicians who are interested in doing these kinds of evaluations and who are passionate about this kind of work," she said.

Her words aptly describe the motivations of two of her peers who helped found the group. **WILLIAM BERK, MD'16**, said his experience as a 17-year-old working on an Indian reservation for five months sparked his interest in domestic refugee populations. And a summer stint last year brought him face-to-face with the plight of migrants. Last summer he volunteered with an organization called No More Deaths on the Mexican-Arizona border in the Sonoran Desert, "shuttling food, water and medical supplies to areas where migrants come across the border," he said. The *New York Times* featured this humanitarian effort in an August article. Berk's boots-on-the-ground approach is, he said, "apolitical." He describes asylum seekers as encompassing a wide range of individuals – from artists, to political dissidents, to victims of state-sponsored violence.

Co-founder **ANDY A. HOANG**'s passion for this work is deeply rooted. At age 7, he arrived here from Vietnam with his family. "My grandfather, my

COURTESY OF WILLIAM BERK

Alpert student William Berk, at left, volunteered last summer with a group called No More Deaths. He and other volunteers deposited food, water, and first-aid supplies to areas in the Sonoran Desert, Arizona, where migrants traverse and where many have perished.

PHOTO COURTESY BHRAC

Alpert medical students instrumental in the formation of the asylum clinic are, from left, Sean Love (MD'17), Andy Hoang (MD'17), David Corner (MD'17), Nat Nelson (MD'17), Peter Kaminski (MD'15), Liam Sullivan (MD'17), Michelle Chiu (MD'17), Caitlin Ryus (MD'17), Josh Rodriguez-Sdrenicki (MD'16), Rebecca Slotkin (MD'16), William Berk (MD'16), and Linnea Sanderson (MD'17). The Yellow Lab is Penny, the therapy dog.

father, and my uncle were political prisoners. My dad spent half a decade in a re-education camp, and my uncle and grandfather spent a decade. Our entire family was considered traitors to the state; they were blackballed from all forms of formal employment, and we lived in abject poverty up until we came to the United States.

"My memories of Vietnam are just images of poverty and hopelessness," he continues. "My childhood, like that many asylum seekers, was colored by many social and economic difficulties even after coming to the Unites States. But we were given asylum and a right to resettle in the United States. Not everyone is as fortunate as we were. The clinic will serve to help other victims of torture and abuse receive the same opportunity."

Before attending medical school, Hoang, MD'17, who also has a master's degree in public health, worked with children with disabilities and as a consultant for PHR.

Slotkin describes the clinic concept as a medico-legal arrangement, rather than the traditional doctor/patient relationship. According to these students, the affidavits the medical students draft under the physicians is crucial information judges use to determine whether or not to grant asylum.

The trio was trained as medical student evaluators at a conference in Chicago last year. They said the clinical examinations help determine if the injuries or trauma sustained, the "sequelae of the events," are consistent with the accounts of those seeking asylum. Hoang said the trauma may have happened decades before applying for asylum and the effects are not readily apparent.

Currently, those seeking asylum must travel to New York or Boston to undergo evaluation. The Brown clinic will fill a much-need gap in services, these students believe.

Hoang concludes from the heart. "Doctors occupy unique positions – not leveraging that power to push for the protection of human rights is a missed opportunity," he said.

The eventual commitment on the part of medical volunteers who join them in this effort would be two hours a month at a local clinic location. The students will coordinate the schedules and logistics involved. ❖

For more information, contact andy_hoang@brown.edu, or visit https://sites.google.com/a/brown.edu/phr/brown

Asylum Training: Documenting Torture and Other Human Rights Abuses

BHRAC Brown Human Rights Asylum Clinic

PROGRAM Forensic medical evaluators and legal experts will train conference participants in the skills needed to diagnose, evaluate and document the physical and psychological after-effects of torture and severe human rights violations in order to create a pool of trained evaluators in the state. View program brochure

WHEN Sat., February 8, 2014, 9 am to 5 pm

WHERE Alpert Medical School, 222 Richmond St., Providence

COST $40 residents; $60 medical and legal professionals (Includes program, parking, breakfast, lunch)

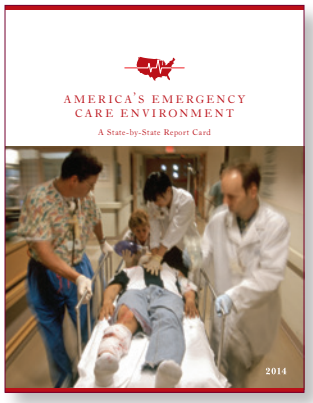
SPEAKERS

Joanne Ahola, MD, Medical director, Weill Cornell Center for Human Rights

Jillian Tuck, JD, Asylum Program Manager, Physicians for Human Rights

Sarah Kimball, MD, MPH, Asylum network trainer, Physicians for Human Rights

National Emergency Physicians' Group Issues Report Card for Nation



WASHINGTON – Emergency physicians on January 16 sounded a warning that the continuing failure of state and national policies is endangering emergency patients, citing as proof a grade of D+ for the nation in the 2014 American College of Emergency Physicians' (ACEP) state-by-state report card on America's emergency care environment ("Report Card").

The District of Columbia ranked first in the nation with a B-, surpassing Massachusetts, which held the top spot in the 2009 Report Card. Wyoming ranked dead last, receiving an F overall.

The top ranked states were:

- The District of Columbia (1st, B-),
- Massachusetts (2nd, B-),
- Maine (3rd, B-),
- Nebraska (4th, B-) and
- Colorado (5th, C+).

Rhode Island received an overall C- grade.

The Report Card forecasts an expanding role for emergency departments under Obamacare and describes the harmful effects of the competing pressures of shrinking resources and increasing demands.

The report also evaluates conditions under which emergency care is being delivered, not the quality of care provided by hospitals and emergency providers. It has 136 measures in five categories:

1. Access to Emergency Care (30% of grade)
2. Quality and Patient Safety (20%)
3. Medical Liability Environment (20%)
4. Public Health and Injury Prevention (15%)
5. Disaster Preparedness (15%)

"Rhode Island continues to have strong public health and disaster preparedness policies, but its rankings have dropped significantly in the category of Quality and Patient Safety," said **DR. ACHYUT KAMAT**, president of the Rhode Island Chapter of ACEP. "We have the 7th longest emergency department waits times in the nation, and our medical liability environment received a failing grade. Policymakers need to make emergency care a top priority in our state."

The report evaluates conditions under which emergency care is being delivered, not the quality of care provided by hospitals and emergency providers.

RI strengths noted in report card

- Ranks first in the nation with:
  - Proportion of hospitals developing a diversity strategy or plan (62.5%)
  - Proportion of patients with acute myocardial infarction given percutaneous coronary intervention within 90 minutes of arrival (98%).
- Ranks second in the nation by dramatically increasing its burn center capacity; and the state also requires that all emergency medical services (EMS) personnel be trained in disaster management and response.
- The state supports the second largest emergency medicine resident population, with 70.5 per 1 million people.
- Continues to benefit from low rates of traffic fatalities, fatal occupational injuries, homicides, and suicides. The proportion of traffic fatalities due to alcohol has fallen significantly in the past 5 years. The state also has banned smoking in restaurants, bars, and worksites.

http://www.emreportcard.org

http://www.emreportcard.org/uploadedFiles/States/Rhode_Island/RhodeIsland.pdf

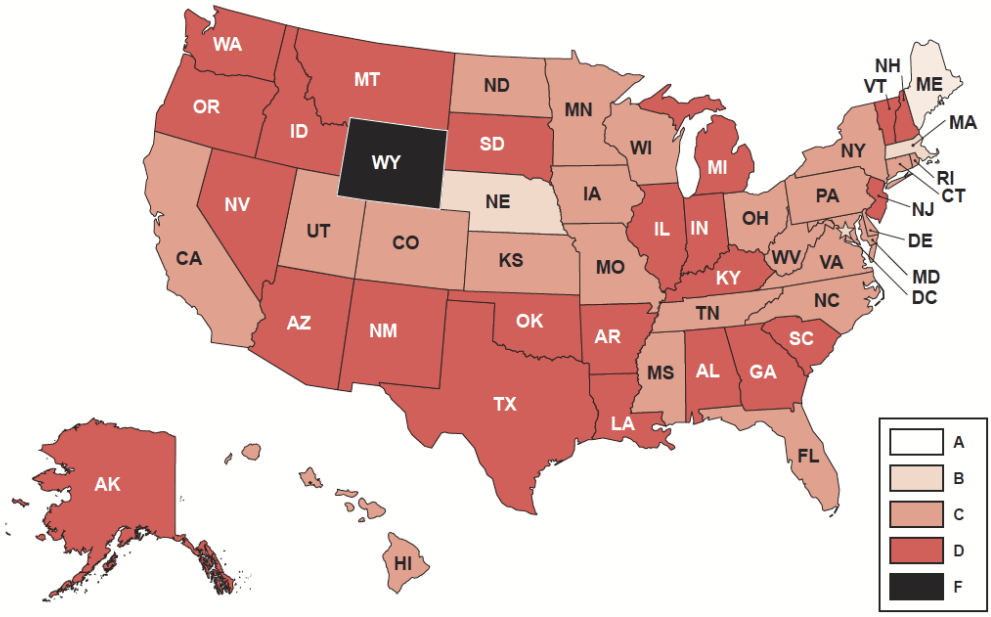
RI results

- In the category of Access to Emergency Care, Rhode Island received a C, dropping from the B- grade it received in 2009. According to the Report Card, Rhode Island has a low rate of emergency departments for its population and a high hospital occupancy rate (72.5 per 100 staffed beds). The state also has suffered a severe decrease in the availability of psychiatric care beds since 2009 (from 37.2 to 25.9 per 100,000 people). These factors all likely contribute to the seventh longest ER wait times in the nation (343 minutes from arrival to departure for admitted patients).
- The state received a D+ in category of Quality and Patient Safety, ranking 35th in the country — compared with an A grade and 7th place ranking in 2009. According to the Report Card, Rhode Island does not fund quality improvements of the EMS system and no longer has a funded

state EMS director. The state also lacks a uniform system for providing pre-arrival instructions, field trauma triage protocols or guidelines and a statewide trauma registry.

- Rhode Island received an F in the category of Medical Liability Environment, ranking it 46th in the nation. According to the Report Card, the state has not passed any meaningful liability reforms, and the average malpractice award payments are increasing, which reduces the number of medical specialists who are willing to care for emergency patients. Average medical liability insurance premiums for primary care physicians and specialists are well above the average across the states. Insurance premiums for specialists ($82,426) are a particular concern at more than 43% above the national average ($57,459). At the same time, the average malpractice award payment has increased markedly from $260,388 in the 2009 Report Card to $355,199.

OVERALL STATE GRADES



RHODE ISLAND REPORT CARD

	2009		2014	
	Rank	Grade	Rank	Grade
Access to Emergency Care	10	B-	10	C
Quality & Patient Safety Environment	7	A	35	D+
Medical Liability Environment	49	F	46	F
Public Health & Injury Prevention	8	B+	15	B
Disaster Preparedness	13	B+	9	B-
OVERALL	2	B-	18	C-

- While Rhode Island's B grade in Public Health and Injury Prevention worsened somewhat, the state continues to benefit from low rates of traffic fatalities, fatal occupational injuries, homicides, and suicides. The proportion of traffic fatalities due to alcohol has fallen significantly in the past 5 years. The state also has banned smoking in restaurants, bars, and worksites. Rhode Island has strengthened its adult seatbelt laws to include primary enforcement of the law.
- Rhode Island received a B- in the category of Disaster Preparedness. The state has dramatically increased its burn center capacity, currently making it second in the nation, and the state also requires that all emergency medical services (EMS) personnel be trained in disaster management and response.

Recommendations

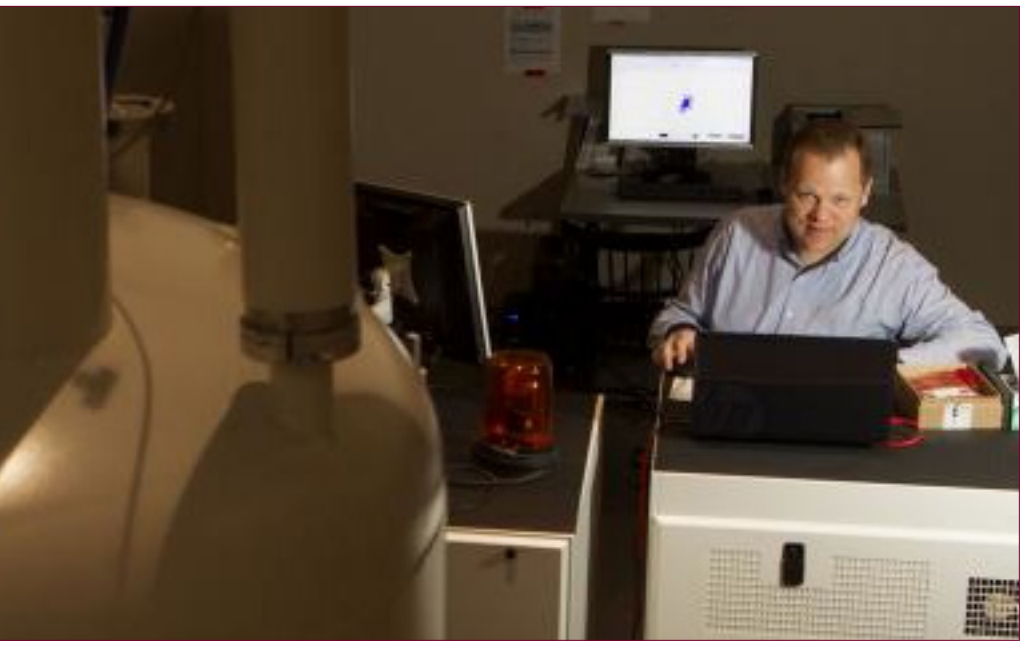
The Report Card's recommendations for Rhode Island improvement included:

- Increase the availability and accessibility of hospital inpatient beds and psychiatric care beds.
- Enact medical liability reform to encourage specialists to provide on-call services for emergency patients; recommended reforms include strengthening expert witness rules to include case certification and requiring expert witnesses to be licensed to practice medicine in the state.
- Decrease emergency department wait times.
- Increase access to substance abuse treatment and outpatient mental health services. ❖

With $1.6M award, biochemist tackles diabetes

BY DAVID ORENSTEIN
BROWN UNIVERSITY SCIENCE OFFICER

PROVIDENCE – **WOLFGANG PETI**, a biochemist who studies the structure, motions, and interactions of proteins at the atomic scale, has won a five-year, $1.625-million New to Diabetes Research Accelerator Award announced January 9 by the American Diabetes Association. Peti is one of only five researchers around the country to win.



MIKE COHEA/BROWN UNIVERSITY

Brown's powerful new NMR magnet will allow Wolfgang Peti to study the motion and timing of protein interactions, advancing the effort to understand and possibly to improve insulin signaling in people with type 2 diabetes.

His goal is to help develop drugs to improve the body's insulin signaling so that injections become unnecessary. As it is for millions of people around the world, the pervasive condition is personal for Peti. His grandmother battled it for decades.

"It affected her ability to see, her ability to walk through the mountains of Austria, and her ability to eat all the traditional foods she grew up eating and cooking," Peti said. "And while she successfully battled the disease for many years, eventually the doctors had to amputate both of her legs (first at age 80, second at age 88) and she was confined to a wheelchair for the last eight years of her life."

Although he hasn't focused specifically on diabetes before, decades of research have given him a deep expertise in the atomic structure and behavior of some of the key proteins of insulin signaling. He and his collaborators have refined these proteins in the lab to the degree that they and their interactions can now be fully analyzed with advanced techniques such as nuclear magnetic resonance spectroscopy and X-ray crystallography.

Last year, when Brown acquired a powerful new NMR magnet, Peti gained a rare degree of capability to study the dynamic motions of these proteins and the timing of their interactions, as well as their basic structure.

Peti's ambitious goal is to enable the development of medicines that improve on the status quo so greatly that insulin injections might no longer necessary.

"The easiest thing would be if you have type 2 diabetes instead of injecting insulin, you'd just take a tablet," he said. "If you can control the insulin-signaling pathway with a drug, that would make your life much easier."

Three targets

Peti still sees the insulin-signaling pathway as rife with potential new leads. He plans to look in novel ways and in novel places at the interactions of three main proteins in particular.

One target is the binding between insulin and the insulin receptor. That step activates the "TK" domain, or section, of the receptor, kicking off the cascade of protein signaling that leads to the metabolism of glucose. This may seem like an obvious place to start, but the complexity comes from trying to observe the movements of the TK domain and the specific timing that may be going awry in type 2 diabetes.

Peti and his colleagues have been able to model it all in E. coli bacteria, which will allow them to observe it precisely with NMR. That will allow Peti see how the TK domain reshapes and moves, how quickly and when. That could yield a clear understanding of whether a drug could block or slow a key movement that is happening too soon or too quickly.

Peti also plans to work with fellow Brown biologist Marc Tatar to take the ideas into the fruit fly where they can investigate the differences made by known genetic mutations.

Another target is an enzyme called PTP1B, which can shut off insulin signaling. Because the goal in treating type 2 diabetes is to improve insulin function, Peti wants to stop PTP1B.

PTP1B has proven time and again to be tough to block without unintended consequences, but Peti hopes a less direct approach than others have taken will make a difference. Rather than targeting the main catalytic parts of the enzyme directly, he's looking at the behavior of a more peripheral but nevertheless influential structure called the "c-terminal segment." It's an underexplored region that could be targeted very specifically, likely with a combination of surgical strikes on more than one area. A key requirement of any drug is that it only affects insulin signaling and not other interactions by similar enzymes.

Sure enough, along with colleague Nicholas Tonks at the Cold Spring Harbor Laboratory, Peti has begun to characterize a drug that works in this area. They plan to use NMR to improve the understanding of the drug's workings further and use that knowledge to improve its abilities.

Peti's third approach under the ADA award is more traditional in that it depends "simply" on characterizing the structure of a complex of proteins, together known as GM:PP1. That complex controls the balance between storing glucose in the form of a larger "glycogen" molecule and breaking glycogen down into glucose. GM:PP1 accomplishes the latter by turning on an enzyme called glycogen phosphorylase.

Peti's idea is to figure out how a drug could inhibit GM:PP1's recognition of glycogen phosphorylase so that it doesn't break down glycogen into glucose so readily. Peti already knows where he wants to look on the proteins to try the idea and has developed a means of screening drugs that might interact with those areas.

Success with any of the three approaches is hardly guaranteed, but if there is a chance he can save anyone else from the kind of difficulty his grandmother endured, Peti is eager to try. ❖

NIH awards URI pharmacy professor $1.3M grant to fight cancer with nanoparticles

KINGSTON — The National Institutes of Health have awarded a University of Rhode Island pharmacy professor a $1.3 million grant to further study a new class of inorganic nanoparticles that target primary cancer, and help control the disease's spread (metastases) and recurrence.

WEI LU, assistant professor of biomedical and pharmaceutical sciences in the College of Pharmacy, has discovered in his preliminary research that hollow copper sulfide nanoparticles are effective in delivering chemotherapy and heat through a laser that can burn the tumor.

The Kingston resident will be using the four-year NIH grant to further his laboratory study with a focus on breast cancer, the second most frequently diagnosed malignancy in women worldwide.

"We are developing a novel cancer therapeutic technology that has several innovative features: biodegradability, multimodality and simplicity," said Lu, who is teaming with Pharmacy Professor Bingfang Yan, a specialist in genetic and environmental factors that combine to regulate the expression of genes involved in drug response and the cellular switches related to tumor formation.

"One nanoparticle can carry hundreds or even thousands of drug molecules to a target like a tumor cell," Lu said.

He wants to enhance photothermal ablation therapy, a process that uses lasers in cancer treatment.

"As is the case with surgical removal of a tumor, getting all of the cancer is critical, " Lu said. "The new nanoparticles provide a three-way punch to the tumor: a more widespread ability in a tumor to distribute heat and burn the tumor, a more efficient and comprehensive way to deliver chemotherapy, and better use of heat to activate the chemotherapeutic agents and immunotherapeutic agents. The new nanotechnology offers promise in tumor eradication.

"Such nanoparticles are introduced intravenously and are absorbed into a tumor." Lu said. "This study is using near-infrared laser light instead of ultraviolet light or visible light because it penetrates tumor tissue better and has much lower side effects. In addition, these particles are readily degradable in the body, minimizing potential organ toxicity."

URI PHOTO BY JOE GIBLIN

Wei Lu, assistant professor of biomedical and pharmaceutical sciences in URI's College of Pharmacy, in his lab conducting research on novel nanoparticles to battle metastatic breast cancer.

Lu, who came to the University in 2010, said he could not have competed for the NIH award if it weren't for the support of the Idea Network of Biomedical Research Excellence, a $45 million initiative funded by NIH and headed by URI to increase research capacity among biomedical faculty in Rhode Island. ❖

Hasbro study finds high number of pediatric injuries caused by school violence

Article published in Pediatrics *implicates bullying and violence*

PROVIDENCE – **SIRAJ AMANULLAH, MD, MPH**, an emergency medicine attending physician at Hasbro Children's Hospital, recently led a study that found children between the ages of five and 19 still experience a substantial number of intentional injuries while at school. The study, titled "Emergency Department Visits Resulting from Intentional Injury In and Out of School," has been published online ahead of print in the journal Pediatrics.

Dr. Amanullah's team analyzed data from the National Electronic Injury Surveillance System All Injury Program from 2001 to 2008 to assess emergency department (ED) visits after an intentional injury. Of an estimated 7.39 million emergency department visits due to injuries occurring at school, approximately 736,014 (10 percent) were reported as intentional, such as those from bullying and peer-to-peer violence.

"This study is the first of its kind to report such a national estimate," said Dr. Amanullah. "The 10 percent number may not seem large, but it is alarmingly high when you consider that such a significant number of intentional injuries are occurring in the school setting, where safety measures meant to prevent these sorts of injuries, are already in place."

The study also identified gender and age disparities. Boys were most likely to be identified as at risk for intentional injury-related ED visits from within the school setting, along with all students in the 10- to 14-year age group; whereas girls were most at risk for intentional injury-related ED visits from outside of the school setting, along with the 15- to 19-year age group.

Additionally, both African-American and Hispanic ethnicities were found to be associated with higher risks for intentional injury in the school setting compared to outside school. "The important point about these disparities related to specific ethnicities and specific age groups is that the findings suggest that preventive safety efforts in the school setting may need to be tailored for the groups that carry much of this injury burden," said Dr. Amanullah.

JAMES LINAKIS, MD, PHD, associate director of pediatric emergency medicine at Hasbro Children's Hospital and co-author of the study, added, "We know that the risk of hospitalization was found to be higher from intentional injury-related ED visits versus unintentional injuries." Dr. Linakis continued, "In supervised environments such as schools, we have a great opportunity to implement additional prevention strategies and reduce the number of seriously injured children who we are seeing in emergency departments nationwide."

Siraj Amanullah, MD

James Linakis, MD

Michael Mello, MD

HASBRO CHILDREN'S HOSPITAL/DEPT. OF EMERGENCY MEDICINE

The study highlights the continued public health impact of bullying and peer-to-peer violence. While there are substantial numbers of emergency department visits due to intentional injuries occurring in U.S. schools, there are still likely many others that do not result in ED visits.

MICHAEL MELLO, MD, MPH, director of the Injury Prevention Center at Hasbro Children's Hospital who also contributed to the study, added a reminder that these injuries not only affect the physical health, but also the emotional health of children, families and both victim and perpetrator. "As parents, guardians and physicians we need to keep talking to our children and patients about this physical and mental health burden. It is our responsibility to address the issue of violence and bullying, both in and out of school, just like prevention efforts for any other medical illness," said Dr. Mello. ❖

News Briefs

BROWN

Josiah D. Rich, MD

Medicaid expansion improves health care services for prison population

PROVIDENCE – As Medicaid eligibility expands under the Affordable Care Act, prison systems are increasingly supporting prisoners' enrollment in Medicaid as a way to help lower prison system costs and improve prisoners' access to health care upon release. These are the findings of a nationwide survey of state prison administrators that was led by **JOSIAH D. RICH, MD, MPH**, director of the Center for Prisoner Health and Human Rights, based at The Miriam Hospital and professor of medicine and epidemiology at the Alpert Medical School. The study is published online in advance of print in the *American Journal of Public Health.*

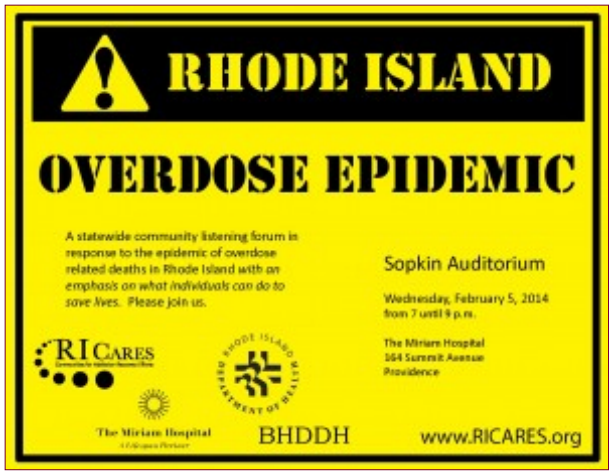
"This study is unique because of the timing with the expansion of Medicaid. We know that an increasing number of prison systems, although far from all, are helping prisoners enroll in Medicaid in preparation for their return to the community," explained Dr. Rich. "Enrollment improves access to basic health services, including substance use and mental health services, and can in turn benefit the health of the communities and families to which prisoners return. There is a possibility that there will be decreased recidivism as people get treatment for their mental illness and addiction." ❖

BCBSRI awards Thundermist $75,000 to fight childhood obesity

WOONSOCKET – Thundermist Health Center, a non-profit community health center that provides health care regardless of ability to pay, has received a $75,000 grant from Blue Cross & Blue Shield of Rhode Island (BCBSRI) to fund its new pilot initiative Impacting Obesity Together: Woonsocket, which focuses on increasing healthy diets and physical activity among low-income Woonsocket families.

The initiative will receive this funding as part of the 2014 BlueAngel Community Health Grant Program (BACHG), which supports nonprofit organizations addressing critical health issues in Rhode Island.

The Impacting Obesity Together pilot program will marry Thundermist's "ThunderKids" program with the YMCA's "Join for Me" program and Farm Fresh RI's "Healthy Foods, Healthy Families" and farmers market programs. ❖



Spike in drug overdose deaths prompts warnings, action

PROVIDENCE – RICares, a grassroots alliance of people in recovery, their family and friends, and concerned members of the community, is holding a forum on overdose prevention Wednesday, Feb. 5, from 7 p.m. to 9 p.m. at the Sopkin Auditorium, Miriam Hospital.

In mid-January the Department of Health reported that there have been 22 deaths due to apparent accidental drug overdose since the first of the year. This alarming number is twice the number of deaths seen for this same time period last year. The deaths were geographically spread throughout the state, and the age range of the decedents is 20-62 years old. The deaths happened most frequently on weekends, with 18 of the 22 happening between Fridays and Mondays. Tests are still pending on the specific substances involved.

The figures were announced by Michael Fine, MD, Director of Health. He was joined by Craig S. Stenning, Director of Rhode Island Department of Behavioral Healthcare, Developmental Disabilities and Hospitals, and Lt. Robert S. Wall of the Rhode Island State Police.

The three also highlighted the state's Good Samaritan Drug Overdose Prevention Act, which provides some legal immunity to people who call 911 to report drug overdoses. ❖

AG Kilmartin's Medicaid Fraud and Control Unit recovers more than $8M

State gets $5.6M from settlement with Johnson & Johnson, Janssen Pharmaceuticals

PROVIDENCE – In 2013, Rhode Island Attorney General Peter F. Kilmartin's Medicaid Fraud and Control Unit (MFCU) recovered more than $8.1 million for the state's Medicaid budget.

"Medicaid is one of Rhode Island's most expensive programs and cannot afford to be plagued with fraud, waste and abuse," said Attorney General Kilmartin. "From big pharma looking to pocket tens of millions of dollars in profits through the off-label marketing of drugs to individual caregivers who defraud the system a few hundred dollars at a time, each must be held accountable."

Last year, the MCFU entered into 16 settlement agreements with major pharmaceutical companies who engaged in off-label billing and/or overbilled the state for drugs totaling $6.8 million in monies returned to the Medicaid budget. The year's single largest settlement was announced in November; Rhode Island received $5.6 million as its share of a multistate and federal settlement with Johnson & Johnson and its subsidiary, Janssen Pharmaceuticals, Inc., to resolve civil and criminal allegations of unlawful marketing practices to promote the sales of their atypical antipsychotic drugs, Risperdal and Invega.

The MFCU also recovered $1,276,530 in civil penalties from physician practices for overbilling and coding errors, including a $244,923 settlement with a former Rhode Island physician, Dr. Hafeez Kahn. In addition, the Unit secured court-ordered restitution of $81,365 from individuals convicted of Medicaid Fraud or patient abuse. ❖

OHIC report: Primary care spending up

PROVIDENCE – On January 17, the State of Rhode Island Office of the Health Insurance Commission (OHIC) released *2013 Primary Care Spending in Rhode Island*. It reported data on primary care spending that each insurer submits to OHIC on a quarterly basis, covering actual spending between 2007 and 2012 and projections for 2013 and 2014.

Highlights include:

- **Overall, insurers spend 9.1% (or $65m) of total premium on primary care**, a 60% increase from 2008 (5.7%, $47m).
- **Insurers are hitting their targets:** In 2012, Blue Cross Blue Shield of Rhode Island and United Healthcare met their primary care spending targets and project doing so in 2014. Though Tufts Health Plan does not yet have a target, it spent roughly the same percentage on primary care as the other two companies did in 2012.
- **Patient Centered Medical Homes (PCMHs)** and other non-Fee for Service (FFS) methods drive the rise in primary care spending. ❖

THE MIRIAM HOSPITAL

Miriam introduces ultraviolet technology

Xenex system shown to be effective in fighting C. diff, MRSA and more

PROVIDENCE – As antibiotic-resistant germs become harder to fight, The Miriam Hospital is using a new tool to disinfect patient areas. The Xenex room disinfection system uses ultraviolet technology to get rid of highly infectious pathogens such as Clostridium difficile (C.diff), Methicillin-resistant Staphylococcus aureus (MRSA), norovirus and even influenza.

Julie Nakos, director of environmental services at the hospital, said, "We are rolling out the use of the Xenex system in our most vulnerable areas first, and eventually we will expand it throughout the hospital. Not only is it portable and easy to use, but based on the reports, we feel confident that we are better able to destroy those pathogens that pose a threat to our patients."

Because the Xenex device is portable, it can be used in virtually every area within the hospital if and when needed. The other benefit is how rapidly it works – the environmental staff at the hospital is able to completely disinfect a patient room in five to 10 minutes. ❖

Kent offers new therapy for dysphagia

WARWICK – The Rehabilitation Program at Kent Hospital has added VitalStim Therapy designed to treat dysphagia, as part of its speech and swallowing program. It is an FDA-approved, non-invasive external electrical stimulation therapy that re-educates the muscles needed for swallowing. ❖

Transitions

Dr. Schlissel appointed president of Univ. of Michigan

ANN ARBOR, MICH. – With a unanimous vote of the Board of Regents, **MARK S. SCHLISSEL, MD, PhD**, was appointed the 14th president of the University of Michigan on January 24.

Dr. Schlissel, currently serving as provost of Brown University, will succeed Mary Sue Coleman July 1, 2014. Coleman is retiring after 12 years leading U-M.

Dr. Schlissel, 56, is a nationally recognized biomedical researcher who has risen through the ranks of academic and administrative positions in higher education. Before being named provost at Brown in 2011, Dr. Schlissel was University of California at Berkeley's Dean of Biological Sciences in the College of Letters & Science and held the C.H. Li Chair in biochemistry.

A graduate of Princeton University, Dr. Schlissel earned both MD and PhD degrees at the Johns Hopkins University School of Medicine. He did his residency in internal medicine at The Johns Hopkins Hospital and was a postdoctoral research fellow at the Massachusetts Institute of Technology's Whitehead Institute for Biomedical Research. His research program has focused on the developmental biology of the immune system. ❖

MARY KORR

Gov. Lincoln Chafee and Brown University Provost Mark S. Schlissel, MD, PhD, shown at a healthcare showcase held in the fall at the Alpert Medical School.

Dr. Doberstein named interim chief of neurosurgery, interim dept. chair at Brown

PROVIDENCE – **CURTIS DOBERSTEIN, MD**, has agreed to serve as interim chief of neurosurgery at Rhode Island and The Miriam hospitals and as interim chair of the Department of Neurosurgery at the Alpert Medical School.

The announcement on Jan. 29 from Lifespan and the Alpert Medical School came after **GARTH REES COSGROVE, MD, FRCSC**, stepped down for personal reasons as chief of the Department of Neurosurgery at Rhode Island Hospital and The Miriam Hospital and Stoll Professor and as chair of the Department of Neurosurgery at the Alpert Medical School. Dr. Rees also served as clinical director for the Norman Prince Neurosciences Institute and was a member of the Brown Institute for Brain Science.

The announcement stated: "Dr. Rees has been an important part of the creation of a nationally recognized neurosciences institution with the establishment of the Norman Prince Neurosciences Institute. He is credited with advancing the neurosurgical academic, clinical and research programs since his arrival in 2010 and for helping to forge strong collaborations across the academic medical center among neuroscience, neurology, neurosurgery and psychiatry and human behavior. He has been critical to efforts aimed at advancing brain science collaborations among our institutions. Dr. Rees was also instrumental in bringing the BodyTom intraoperative, portable CT scanner to Rhode Island Hospital.

"We are extremely grateful to Dr. Rees for his contributions to the field of neurosurgery and the broader enterprise of brain science in Rhode Island and for his tireless advocacy and compassion for his patients."

A national search for his replacement will be led by **KAREN L. FURIE, MD**, chief of the Department of Neurology at Rhode Island Hospital and The Miriam Hospital and the chair of neurology at Alpert Medical School. ❖

Recognition

RWMC honors Drs. Skowron, Calenda

PROVIDENCE – **GAIL SKOWRON, MD** and **CHARLES CALENDA, MD** were recently honored by the medical staff of Roger Williams Medical Center (RWMC) for their outstanding contributions to the hospital. Dr. Skowron, a nationally recognized expert in HIV antiretroviral therapy and HIV immunology, is RWMC's chief of the Division of Infectious Diseases and a professor of medicine at the Boston University School of Medicine.

Dr. Calenda, who has been director of Ophthalmology at Roger Williams since 1987, is a member of the American Academy of Ophthalmology, the American Society of Cataract and Refractive Surgeons, a charter member of the American College of Eye Surgeons, and also has membership in the Rhode Island Medical Society and the Kent County Medical Society. ❖

RWMC

Pictured here at the ceremony are, from left, Edwin J. Santos, chairman of the CharterCARE board, Dr. Charles Calenda, Roger Williams medical staff president Dr. Mark Braun, Dr. Gail Skowron, and CharterCARE President and CEO Kenneth H. Belcher.

Recognition

W&I's oncology program awarded $50,000 for patient mentoring program

CNE

Cornelius "Skip" Granai III, MD

PROVIDENCE – Ovarian Cancer Research Fund (OCRF) recently awarded a $50,000 grant to the Program in Women's Oncology at Women & Infants Hospital of Rhode Island for the creation of a Woman to Woman patient-to-patient mentoring program at the hospital.

Woman to Woman, sponsored nationally by QVC, pairs gynecologic cancer patients with survivors, supporting women and their families through all phases of treatment, recurrence and recovery. The program will begin at Women & Infants in 2014.

"Being diagnosed with any type of cancer can be traumatic and can leave a patient feeling like no one truly understands her fears and anxiety," said **KATINA ROBISON, MD**, a gynecologic oncologist with the Program in Women's Oncology who will oversee Woman to Woman with **DIANE THOMPSON**, director of Social Services for the Program. "Through Woman to Woman, gynecologic cancer patients at Women & Infants will receive vital emotional support and mentoring from our survivors. The result is an improved quality of care for these women. They will also feel more empowered to advocate for themselves going forward."

"Our goal at the Program in Women's Oncology is to give women whatever it is they need to make their cancer journey easier," said **CORNELIUS "SKIP" GRANAI III, MD**, director of the Program in Women's Oncology. "That's a very personal need and might mean having an appointment for acupuncture, joining a poetry workshop or sitting with a survivor who understands the emotional and physical difficulties of a cancer journey.

"We are thrilled that Ovarian Cancer Research Fund has given our patients this opportunity."

Thompson added that the Woman to Woman Program will be available for women who want to meet face to face, but will also tap social media to connect women.

"We are in the golden age of electronics, which will help us make the Woman to Woman experience available to more isolated women through any medium they have. We have young patients who are blogging, older women who text throughout the night because they have only each other," she explains. ❖

Coastal's Moss honored with health care leadership award

COASTAL

Meryl Moss

PROVIDENCE – **MERYL MOSS**, COO, Coastal Medical, was honored with the annual "Regent's Award" January 16 by the American College of Health Care Executives (ACHE). The award recognized Moss for her leadership role in advancing the PCMH model of care at Coastal Medical, as well as for supporting Coastal's use of Health Information Technology.

The ACHE leadership also expressed gratitude to Moss for lending her voice to various ACHE and MGMA educational discussions and programs to help others understand how to translate "lessons learned" into their own improved PCMH transformation, and Health IT use and development.

Moss studied economics at Boston University, received her Master's in Administration from Harvard's Kennedy School and completed post-graduate work at Boston College's Carroll School of Management. She is currently attending the Executive Masters in Healthcare Leadership Program at Brown University. Also an accomplished public speaker, Meryl presents to groups across the nation on a wide range of topics, some of which include: The Electronic Health Record as a Business Tool • Building a Physician Owned/Governed Practice from the Ground Up.

Coastal Medical is Rhode Island's first Medicare Shared Savings ACO. ❖

WESTERLY HOSPITAL

Westerly's Hospital's **Erin Kennedy, RN**, was recently honored at the "Celebration of Excellence in Hospital Care," an annual awards ceremony held by the Hospital Association of Rhode Island (HARI) at the Crowne Plaza Hotel in Warwick. She was recognized along with employees of the year from HARI's member hospitals by the HARI Board of Trustees for exemplary performance and dedication to health care.

Recognition

Healthcentric Advisors awarded $835,000 grant to evaluate public reporting of home health care outcomes

PROVIDENCE – Healthcentric Advisors has been awarded a three-year $835,000 research and evaluation grant from the Agency on Healthcare Research and Quality (AHRQ). AHRQ is the lead federal agency charged with improving the quality, safety, efficiency and effectiveness of the nation's health care primarily through the funding of health services research that will improve healthcare quality and promote evidence-based decision-making.

The research study, Evaluating the Impact of Patient-Centric Home Health Quality Reports, takes advantage of Healthcentric Advisors extensive experience in measuring healthcare outcomes and public reporting.

Although information about health care quality is increasingly available on public and private websites, little is known about what consumers look for when choosing providers and how the format of the information provided affects their choices and outcomes. This study will ask consumers what they would find helpful when choosing home health agencies, and incorporate their preferences into a new report format. Researchers at Healthcentric Advisors will examine the impact of the new report on patients' home health agency choices and the quality outcomes they experience. Healthcentric Advisors is partnering with Lifespan and Brown University to conduct this work.

"This grant attests to Healthcentric Advisors' growing national reputation for applied healthcare research," says H. John Keimig, President and CEO at Healthcentric Advisors. "We have more than 15 years of experience measuring health care outcomes and assisting providers in improving health care quality, locally and nationally."

"In Rhode Island, we've published information about home health agencies and other care providers since 1999," says Rosa Baier, MPH, Senior Scientist at Healthcentric Advisors and principal investigator of the AHRQ study. "We believe public reporting improves health care quality by changing provider and purchaser behavior. This study will help us demonstrate that consumer-centric public health care reports can improve patients' choices of providers and ultimately the quality of the care they receive." ❖

Newport Hospital birthing center earn WHO, UNICEF re-designation

LIFESPAN

NEWPORT – Through its Noreen Stonor Drexel Birthing Center, Newport Hospital has again earned the prestigious Baby-Friendly designation from the World Health Organization (WHO) and the United Nation's Children's Fund (UNICEF). The designation recognizes the commitment and dedication the hospital and staff embrace for breastfeeding mothers and their babies.

"Earning this re-designation was truly a team effort and is something all of us in the birthing center are committed to each and every day," said Debra Venancio, RN, manager of maternal and child health at Newport Hospital. "Being recognized as Baby-Friendly means our moms and their families know that we maintain an environment that promotes, protects and supports breastfeeding."

The Baby-Friendly Hospital Initiative, which was launched in 1991, is a global program of the WHO and UNICEF. The initiative encourages and recognizes hospitals and birthing centers that offer an optimal level of care for infant feeding and mother/baby bonding.

Newport Hospital first earned Baby-Friendly designation in 2003 and at the time was one of only 40 U.S. hospitals to have achieved it. Today, there are 172 hospitals that have been honored as Baby-Friendly. To meet the requirements of the designation, Newport Hospital had to successfully implement the Ten Steps to Successful Breastfeeding, and also was required to implement the International Code of Marketing of Breast-milk Substitutes. This means the hospital offers educational materials that promote human milk rather than other infant food or drinks. The hospital also does not accept or distribute free or subsidized supplies of breast milk substitutes or other feeding devices. Through the birth center, Newport Hospital offers a breastfeeding class, as well as a breastfeeding support group. The hospital also has four International Board Certified Lactation Consultants on staff. ❖

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Obituaries

MILTON W. HAMOLSKY, MD, 92, died on January 18, 2014. He was the husband of the late Virginia (Maglin) Hamolsky, and the beloved husband of Sandra (Rosman) Hamolsky for 34 years. Born in Lynn, MA, he was a son of the late Israel and Sophie (Cremer) Hamolsky. A graduate of Harvard College and Harvard Medical School, Class of 1946, he was an accomplished physician. He was an Assistant Professor at Harvard Medical School, and while serving as a physician at Beth Israel Medical Center he discovered the T3 Uptake Thyroid Test.

Dr. Hamolsky was the first full time Physician-In-Chief of Medicine at Rhode Island Hospital and a Professor of Medical Science at Brown University where he helped develop the Brown University Medical School. He was the first Chief Administrative Officer of the Board of Medical Licensure & Discipline for the State of Rhode Island. He continued to be an active board member of Home & Hospice Care of Rhode Island and beloved by his colleagues; he has numerous awards within the medical community named in his honor. He was a member of many medical associations.

Dr. Hamolsky was a member of Temple Beth El. Besides his wife, he is survived by his children, Deborah Hamolsky and her spouse Toby Dyner of San Francisco, David J. Hamolsky and his spouse Tina L. of Rindge, NH, Joy Scharfman and her spouse Stewart of Roslyn, NY, and Robin Folk and her spouse Ron of Long Beach, NY; his siblings, Dorothy Stern of Chattanooga, TN, and Sidney Hamolsky of Portland, OR; and his grandchildren, Adam, Johnathan, Johanna, Rachel, Ginny and Sydney.

He was the father of the late John S. Hamolsky and grandfather of the late Spenser Scharfman. Contributions in his memory may be made to Home & Hospice Care of RI or to the Dr. Milton Hamolsky Lectureship Fund.

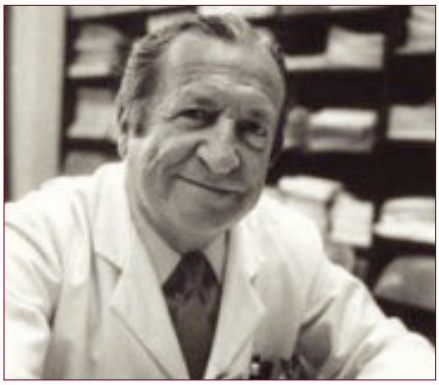
HHCRI

Home & Hospice Care of Rhode Island (HHCRI) honored Milton W. Hamolsky, MD, center, with its annual Human Dignity Award presented at an annual breakfast Sept. 24, 2013. From left are, Vince Mor, PhD; Rabbi Leslie Gutterman, Sandra Hamolsky, Dr. Hamolsky, Joseph Chazan, MD, and Diana Franchitto, President & CEO of HHCRI.

TRIBUTE

Milton W. Hamolsky, MD: Four decades of leadership

STANLEY M. ARONSON, MD



BROWN

(Editor's note: The following commentary first appeared in 2009, in a compilation of Dr. Aronson's work called *Perilous Encounters, Commentaries on the evolution, art and science of medicine from ancient to modern times.*)

A decade before Brown University's medical school became a reality, Brown already had a professor of medicine.

Back in 1963, Rhode Island Hospital recognized that its future as a tertiary care medical center, as well as its contemplated role in providing a site for the clinical training of medical students, depended upon the recruitment of a full-time director of an internal medicine service.

This appointment would represent the first crucial step in transforming the hospital from a community institution managed by physicians in private practice to one with an expanded role to include medical and health care education at all levels, basic and applied research as well as rigorous supervision of the care rendered to its patients. The appointment of a director of internal medicine is typically the first critical undertaking in the transition of a community hospital to an academic medical center.

A search committee examined the credentials of many physician-candidates for this critical post. They finally selected a 42-year-old Massachusetts physician, then an assistant professor of medicine at the Harvard Medical School and an attending physician at Boston's Beth Israel Hospital. His name was Milton William Hamolsky.

Hamolsky was born in Lynn, Mass. (and not Milton, Mass., as some of his admirers had claimed). He was the son of a local shopkeeper and a member of a closely-knit family that cherished learning above all other graces. Milton (named after his grandfather, Mordecai) attended Harvard College graduating *summa cum laude.* He then went on to Harvard Medical School in 1943.

The nation was in the depths of World War ll and medical education was accordingly shorn of all its summer vacations, thus accelerating the process of educating future physicians to three years. Hamolsky received his medical degree in 1946 and his diploma bore those seldom-imprinted words, *magna cum laude,* signifying his station as the school's outstanding student.

In the summer of 1946, Hamolsky entered into a long and productive relationship with Beth Israel Hospital, beginning with an internship on the medical service, followed by a three-year medical residency which culminated in his appointment as chief resident physician in medicine.

In the midst of his graduate training, Hamolsky entered the armed services and was assigned to the Army Medical Research Facility at Fort Knox, Kentucky, where he conducted extensive investigations on the diagnostic and therapeutic uses of newly devised radioactive chemicals in a variety of human diseases. He was discharged in 1950, with the rank of captain, returning then to his beloved Beth Israel Hospital. In 1951, he was appointed both to the hospital's attending staff and, concurrently, to Harvard's Dept. of Medicine. And for the succeeding decade he established himself as one of the hospital's authorities on endocrine diseases, particularly ailments of the thyroid gland. By 1958, he was promoted to chief of endocrinology and assistant professor of medicine at Harvard.

During much of this productive interlude, Hamolsky invested his spare time in studying the role of iodine in the metabolism of the thyroid gland, both in normal and abnormal conditions. This investigation was so promising that the Commonwealth Foundation underwrote a research fellowship allowing Hamolsky to devote an entire year (1961-'62) to his investigative pursuits. He chose the College de France, in Paris, to undertake this research, which led to the discovery of a laboratory test, used to this day, as a standard diagnostic procedure in determining the status of thyroid function. This research brought him to the attention of medical centers beyond Boston. And, in1963, Rhode Island Hospital recruited him as their physician-in-chief, a position he held until 1987.

And what had he accomplished on behalf of Rhode Island Hospital during those 24 years?

He maintained a superb residency training program, certainly the finest in Rhode Island and one of the best in New England. There are, here in Rhode Island and elsewhere in the United States, hundreds of practicing internists who learned both their clinical skills and their high ethical standards from Milton Hamolsky. In addition, he recruited outstanding full-time chiefs of the subspecialties of internal medicine, including cardiology, pulmonary, gastroenterology, nephrology and other disciplines. And in doing so, he created the groundwork for a multidisciplinary clinical service that could easily accommodate the educational needs of a medical school. Brown, in its wisdom, appointed him as professor of medicine despite the absence of any medical school in 1963 or even a corporate commitment to create a medical school in the foreseeable future.

Hamolsky's contributions to health care in Rhode Island extended beyond the portals of the Rhode Island Hospital. He was senior consultant to The Miriam Hospital and the Veterans Administration Hospital, served concurrently as chief at Women and Infants Hospital, worked on countless committees under the aegis of the state government, the state medical society and private organizations such as Planned Parenthood of R.I. During those active years he also served as presidents of the R.I. Heart Association and the R.I. Diabetes Association and governor of the American College of Physicians.

The internal medicine service of the Rhode Island Hospital, under Hamolsky's leadership, has now provided the core inpatient experience for 30 consecutive classes of Brown medical students. And, in rotation with his colleagues at the other Brown teaching hospitals, he had taken on the additional responsibilities of chairing Brown University's Department of Medicine.

In 1987, Hamolsky retired but only to assume yet another heavy responsibility as chief administrative officer of the state's Board of Medical Licensure and Discipline. Under his inspired stewardship, the board has been transformed into a superbly managed agency that has become a model for other states to emulate. And when the directorship of the R.I. Dept. of Health became vacant, it was Hamolsky who was called upon to briefly assume its leadership.

In 2002, Dr. Milton Hamolsky retired as a practicing physician. He has given Rhode Island almost four decades of dedicated and exemplary leadership as an administrator, as teacher, and as wise and humane practitioner. Rhode Island, its local medical school and its teaching hospitals, are collectively indebted to that anonymous search committee which, some 40 years ago, brought a gifted physician named Hamolsky to this community. ❖

Obituaries

WARWICK – **WILLIAM R. THOMPSON, MD**, 84, a towering and revered figure in his professional community of physicians and surgeons, nurses, aides, and administrators and a leader in the advance of surgical practice and medical education, died January 15, 2014, from cancer.

A member of the American College of Surgeons and many other professional societies, and the author of numerous medical science articles, Dr. Thompson was Clinical Professor of Surgery-Emeritus at Brown University's Alpert Medical School. He was a pillar of wisdom and commitment in his field, stepping forward to take the chairmanship of the Brown Department of Surgery and serving as Acting Surgeon-in-Chief of Rhode Island Hospital on two separate occasions when the duties of leadership called.

He grew up in the logging and paper mill town of Livermore Falls where he acquired that "State of Maine" stalwart common sense that characterized his life with family, friends, and co-workers ever after. A loyal University of Maine alumnus, he received his bachelor of science degree from Orono in 1951. He then entered Cornell University's School of Medicine and graduated in 1955.

Dr. Thompson's surgical training began at Rhode Island Hospital in 1955. Two years later he joined the United States Navy Reserve in which he served as an active flight surgeon, assigned first to Pensacola, Florida and then to Quonset, Rhode Island, attaining the rank of Lieutenant Commander. Upon leaving the Navy he joined the surgical staff of Rhode Island Hospital and Providence Lying-In/Women's and Infants Hospital and remained on the surgical staff of both institutions until reaching the honor of surgeon-emeritus.

In the early 1960s Dr. Thompson, along with his partner Dr. J. Robert Bowen, formed Surgical Group Inc., one of the first organized medical groups in Rhode Island, which later expanded to include Drs. Brian Dorman, Clarence Soderberg and Thomas Shahinian.

Throughout his long career, Dr. Thompson held numerous committee and association assignments, served on a variety of special boards and commissions, and earned awards for services performed for his profession, patients and the community. He was known not only for the breadth of his achievements but his compassion and selflessness, gaining him a distinguished reputation across Rhode Island, New England, and beyond.

In recognition of Dr. Thompson's 34 years of dedication to the practice of surgery and teaching of residents and medical students, University Surgical Associates established an endowment upon his retirement that supports the William R. Thompson MD Annual Lectureship in Esophagogastric Surgery, The Thompson Library at Rhode Island Hospital, and various resources for residents, including the annual sponsorship of a resident for surgical training in Africa.

Over the past two decades Dr. Thompson indulged his love for Maine through his rustic camp on a wooded point of land at Kennebago Lake where, during the kinder months of the calendar he could take out one or the other of his two "Rangeley Boats" to sharpen his art of fly-fishing and, at dawn and dusk, keep an eager look-out for moose and other wild neighbors of his cabin. And here he welcomed a steady flow of family and other visitors from near and far.

He is survived by his wife Diane Thompson and his stepson Daniel Brouillard; his former wife Sylvia (Sullivan) Thompson and their children Mary, an airline analyst; John, a bio-medical scientist; Kathryn, an attorney and legal ethicist; Norma, a college faculty member and academic administrator; and Bill, a wildlife biologist. Grandchildren include Jesse, Maegan, Kaila and Kiera Schedeen and Madeleine, Gary, and Kristen Thompson, and great-grandaughter Lilia Thompson.

A private memorial service is being planned and memorial donations may be made to the USA William R. Thompson Fund, PO Box 16149, Rumford RI 02916.

BROWN UNIVERSITY NEWS SERVICE

Sam Berns and his mother, Dr. Leslie Gordon.

FOXBORO, MA. – **SAM G. BERNS,** 17, passed away on January 10, 2014, following a lifelong battle with progeria. He was the beloved son of Leslie Gordon, MD, associate professor of pediatrics (research) and Scott Berns, MD, clinical professor of pediatrics at the Alpert Medical School. His parents confirmed Sam's passing in a statement on the website of the Progeria Research Foundation, which they founded in 1999 to battle the disease.

Sam was a junior at Foxboro High School, where he achieved highest honors and was recently selected to be a member of the National Honor Society. He was a percussion section leader in his high school band and achieved the rank of Eagle Scout in the Boy Scouts of America. He was a highlighted speaker at Tedx MidAtlantic in 2013 and is featured in the documentary "Life According to Sam."

Sam teaches us that every day is a gift, and that we can achieve anything we set out to do. Through his courage, spirit, kindness and love, Sam will forever inspire those who have come to know him.

Remembrances may be made to The Progeria Research Foundation, P.O. Box 3453, Peabody, MA 01961-3453. www.progeriaresearch.org.

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The Etymological Roots of the Specialties

STANLEY M. ARONSON, MD

A surgeon, etymologically, is a practitioner who does healing work with his hands; as opposed to one who achieves healing solely with pharmaceuticals. The ancient Greek term, *kheirurgia* defined someone who worked by hand, and resulted from the merger of *kheir* (meaning hand), and *ergon*, (meaning work.) An older English title for a surgeon, accordingly, was chirurgeon. (And a chiromancer is a palmist for foresees the future; while a chiropractor is one who treats disease by manual manipulation.)

Those who supervised the birth of infants, in Rome, were skilled individuals who stood (Latin, *stare*) before (*ob-*) their pregnant patients. And thus an ancient midwife was called an obstetrix. The vernacular term for such a practitioner, still employed in many nations, is midwife. The mid-prefix, however, means 'with' (as in the German, *mit*); and the root, wife, preserves the Old English meaning of 'adult woman.'And thus a midwife is a skilled person 'standing with a woman in labor.'

Pediatrics, the medical discipline of treating the health needs of growing children, is derived from the Greek prefix, *paedo-*, meaning child, and *iatros*, another Greek word meaning physician. The Latin prefix, *pedi-*, however, means foot (but not, child) and so gives rise to words such as pedestrian, pedestal, pedal, podium, pedigree and podiatry.

Orthopedics, in its original intent, defined the subspecialty of those who helped to straighten the limbs of growing children. And thus the Greek prefix *ortho-* (meaning straight, regular or correct), joined with the Greek root, *paedo-* (meaning child, as in the word paediatrics) has produced the name, orthopedics. The practitioners of this discipline are sometimes called orthopods which suggests, incorrectly, that the name describes those who straighten legs rather than straighten children.

Rehabilitation medicine relies upon the Latin *rehabilitare*, a transitive verb meaning to restore to good condition. This, in turn, is from the Latin, *habitatio*, meaning a dwelling; and still further back, to the Latin, *habitus*, borrowed from the Greek meaning to dwell (inhabit) or a habit or a manner of dressing.

The etymological origins of the names of many of the medical specialties are self-evident: radiology, dermatology, geriatrics, psychiatry, pathology, urology and gynecology.

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Original Articles

The Treatment of Chronic Cardiac Affections, with Special Emphasis Upon Diet Therapy*

By G. CARROLL SMITH, M. D.,
BOSTON, MASS.

Probably the two best cardiac tonics in our hands to-day are digitalis and opium, as they both slow the heart's action and strengthen the systole. Digitalis also acts in many instances as a diuretic, and is therefore clearly indicated in dilatation, slight or marked, with great exhaustion, and remember you may have great exhaustion with very little, as well as with great dilatation, because the exhaustion is due to the impairment of heart muscle affected, hence if there remains sufficient muscle intact to make itself known by increasing tone seen in the character of the pulse, the digitalis will be useful, otherwise not, and this undoubtedly explains the failure of this drug in so many instances, rather than the quality of it, though this may be at times the cause. I have for some time used the leaves prepared by Caesar & Loretz, of Germany, and it makes little difference whether one uses the infusion, tincture or the pills. They are all reliable, and when carefully used do not seem to irritate the stomach. I find it much stronger than that of Park, Davis & Co., and use not more than five drops of the tincture to begin with. An effect of digitalis often noticed by Cushing and Mackenzie, after using it a few days, is the nodal rhythm is established and the pause between the ventricular systoles is much prolonged. This, of course, is an indication to discontinue its use. Moreover, Mackenzie always stops it when the pulse rate drops one per minute, as he says further reduction will take place. In cases when it has no effect it should, of course, not be used. It may often be combined with squills and calomel to enhance their diuretic effect. The clearest indication for its use is cardiac exhaustion, accompanied with dilatation, scanty urine with high gravity and usually albu-

100 Years Ago: Digitalis, Opium as Adjunct Therapy in Treating Heart Disease

This excerpt is from an article on the treatment of heart disease which appeared in the January 1914 issue of *The Providence Medical Journal*. The author writes in the article: "Opium is a very valuable heart tonic by virtue of its quieting effect on the nervous system and its slowing the heart and increasing the force of the systole. … When given by mouth, only pleasant preparations should be selected, like McMunn's elixir of opium." He recommended that it may be given "at bedtime in doses of fifteen to twenty-five minums, or five to ten minums t.i.d."

NATIONAL LIBRARY OF MEDICINE

This print from 1737 by Elizabeth Blackwell in England shows the flower, fruit and seed of a foxglove plant, from which digitalis was derived.