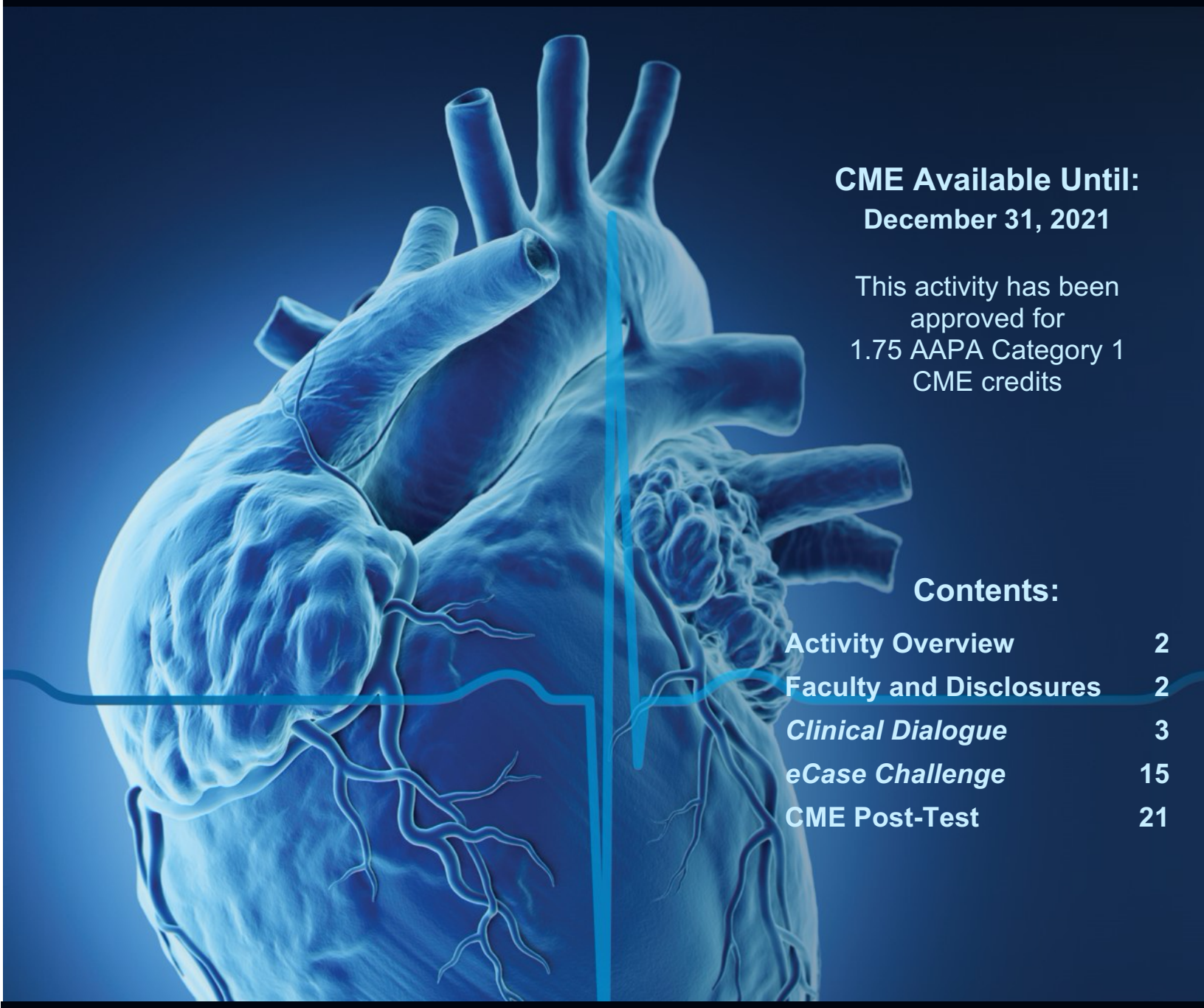
A CALL TO ACTION

The Role of the PA in Improving Outcomes for Patients with Heart Failure



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This activity has been approved for 1.75 AAPA Category 1 CME credits

Contents:

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ACTIVITY OVERVIEW

Heart failure (HF) exacts a significant toll on affected individuals, placing them at risk of morbidity, diminished functional abilities, lesser quality of life, and mortality. More than 5.8 million Americans have HF, with over 550,000 diagnosed each year. The prevalence of HF is expected to continue to increase as the U.S. population ages, underscoring the need for PAs to stay abreast of current treatments, the respective roles of these therapies in HF management as specified in evidence-based guidelines, and the management of comorbidities. As newer therapies have become available, it is particularly important that PAs be knowledgeable about these treatments and the latest recommendations concerning their use. Despite progress in HF management, deficiencies remain, as reflected in persistently high rates of readmission. Given all these considerations, it is imperative that PAs be prepared to meet the challenges of HF treatment.

AAPA TAKES RESPONSIBILITY FOR THE CONTENT, QUALITY, AND SCIENTIFIC INTEGRITY OF THIS CME ACTIVITY.

EDUCATIONAL OBJECTIVES

At the conclusion of this activity, the PA should be better able to:

- Recognize key diagnostic features of HF and use appropriate diagnostic tests to diagnose chronic HF early in the disease course.
- Outline the most up-to-date evidence-based guidelines for the management of chronic HF, including the use of newer pharmacotherapies.
- Use appropriate management strategies when addressing T2DM in patients with chronic heart failure.

ACCREDITATION STATEMENT

This activity has been reviewed by the AAPA Review Panel and is compliant with AAPA CME Criteria. The activity is designated for 1.75 AAPA Category 1 CME credits. PAs should only claim credit commensurate with the extent of their participation. Approval is valid through December 31, 2021.

Estimated time to complete this activity: 90 minutes.

HOW TO RECEIVE CREDIT

There are no fees for participating and receiving CME credit for this activity. Participants must: 1) read the educational objectives and faculty disclosures; 2) study the educational materials; 3) complete the post assessments in Learning Central.

In order to receive credit, participants must complete the post-test and evaluation. You will be able to access your certificate of completion in Learning Central as soon as you complete the post-test with a minimum score of 70%. Your certificate will be available under "Transcript" for your records.

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Clinical Dialogue

Lawrence Herman, DMSc, MPA, PA-C, DFAAPA: Hello, and welcome to this *Clinical Dialogue* and *eCase Challenge* program, "A Call to Action: The Role of the PA in Improving Outcomes for Patients with Heart Failure." I'm Dr. Lawrence Herman, President of Palantir Healthcare LLC in Boiling Springs, South Carolina, and a Past President of the American Academy of PAs in Alexandria, Virginia.

Joining me in this conversation are two expert clinicians, Daniel Thibodeau and Viet Le. Dan is an Associate Professor and Director of Clinical Education, Recruitment and Support for Eastern Virginia Medical School in Norfolk, Virginia. Viet is faculty and cardiovascular researcher and Intermountain Heart Institute Cardiovascular Research in Murray, Utah.

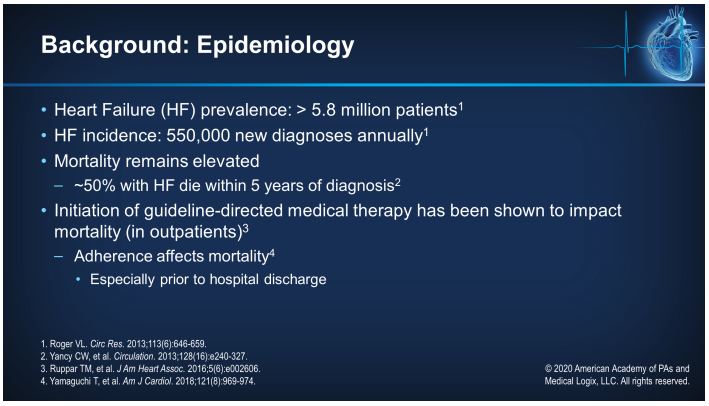
My thanks to both of you for your involvement in this important continuing medical education activity. So, let's get started.

So, before we get into the heart of the matter, let's discuss a bit of background on heart failure. And please allow me to put this into perspective. Between now and 2050, more new patients in this country will develop heart failure than the population of Manhattan, New York. That's the increased number of patients, and why this discussion is so important. So, Dan, I'd like to turn things over to you.

Daniel Thibodeau, MHP, PA-C, DFAAPA, AACC: Well, Larry, thanks for this. And Viet, it's always good working with my fellow colleague again. One of the things that I think we need to be mindful of is that we really need to start thinking about heart failure much more frequently in our clinics. And so, I would challenge all of my colleagues to think about heart failure the same way that they think about screening patients for hypertension and diabetes.

You know, Larry, you mentioned it well. And right now, there are more than 5.8 million patients who have heart failure, and each year we have about 550,000 new diagnoses that are made of heart failure.

So, as we think about it, heart failure mortality remains elevated, and approximately 50% of the patients who have heart failure die within 5 years. And that really hasn't changed much, and that's why the significance of this disease is still on the top of our minds, and should be on the top of everyone's mind.



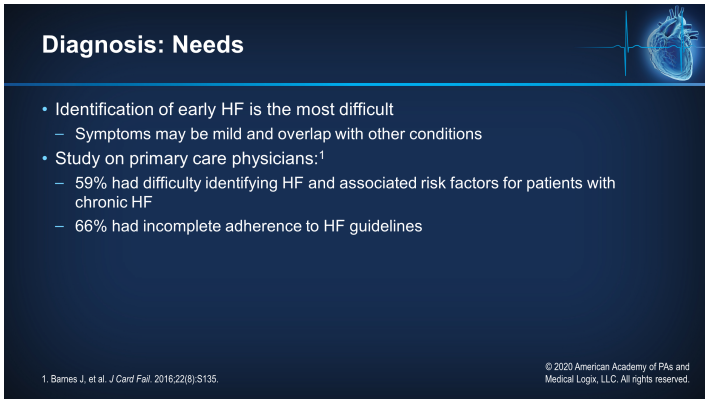
So, the real important parts is that the initiation of guideline-directed medical therapy in the outpatient setting has been shown to impact mortality, as does ongoing medication adherence to those guideline-directed medical therapies. And this is especially true before hospital discharge, just really focusing in on our patients who are in the hospital, making sure that we have those guideline-directed medical therapies in order before they go home.

Lawrence Herman: Dan, in the primary care setting, we typically see patients every 12 to 15 minutes, and it seems like it's even a shorter period than that. This is a difficult diagnosis to make. Can you comment on that, please?

Daniel Thibodeau: Well, Larry, you're right.

So, it's very difficult in the beginning, as symptoms are commonly mild, they overlap with other conditions.

So when testing primary care physicians on their heart failure practices and barriers, researchers actually found that 59% of primary care physicians really had difficulty in identifying heart failure and risk factors for patients with chronic heart failure, while 66% of these same patients had incomplete adherence to the guidelines.



Lawrence Herman: So, I have to believe that that's primary care physicians. That is also true for PAs who function in primary care roles, correct?

Daniel Thibodeau: That's exactly right.

Lawrence Herman: So, Dan, how do you like to make the diagnosis, especially in those patients who have more subtle signs or symptoms of heart failure?

Daniel Thibodeau: So one of the things that we have to think about as early risk factors for heart failure are issues such as hypertension, diabetes, dyslipidemia, things that would give us increased risk for atherosclerotic heart disease.

Then, as we start thinking about symptoms related to heart failure, we want to key in on things like dyspnea. Dyspnea has been shown to be one of the most sensitive and specific complaints of a patient with heart failure, especially early-onset heart failure.

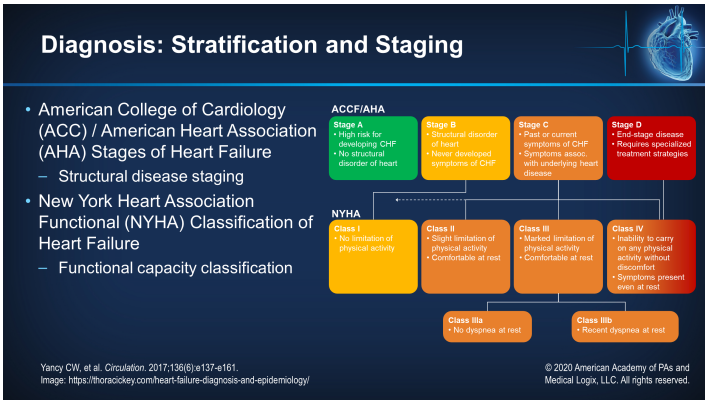
What gets really complicated with heart failure, though, are the other types of multifactorial reasons why people get shortness of breath or have signs and early symptoms of heart failure.

Lawrence Herman: Dan, we have a couple of different ways we can assess this, one being New York Heart Association and the other being the American Heart Association. Can you describe those and what the differences are?

Daniel Thibodeau: We have the American Heart Association's stages of heart failure, and then we have the New York Heart Association classes of heart failure. The way I explain it to my students here at EVMS is that the American Heart Association stages is what is wrong with the heart. So, we're looking at structural disease more than anything else. And then when I look at the New York Heart Association, that's really more, "what can the patient do?".

And so, to give an example of this, let me start with the American Heart Association's stages, which go A through D. So, when we think about stage A, there is no evidence of cardiovascular disease, patient has no symptoms, and there's no limitation to their normal, ordinary physical activity.

As we get into stages B, C and D, we start increasing the amount of disease from minimal to moderately severe to severe disease, which is stage D.



I think the one thing that I like using for my patients more is the New York Heart Association classes. And we commonly will give patients questionnaires in the waiting room asking them how they're doing with their symptoms.

At class I, there's no limitations of physical activity, and their normal, ordinary physical activity doesn't cause them to get fatigued, have palpitations, shortness of breath.

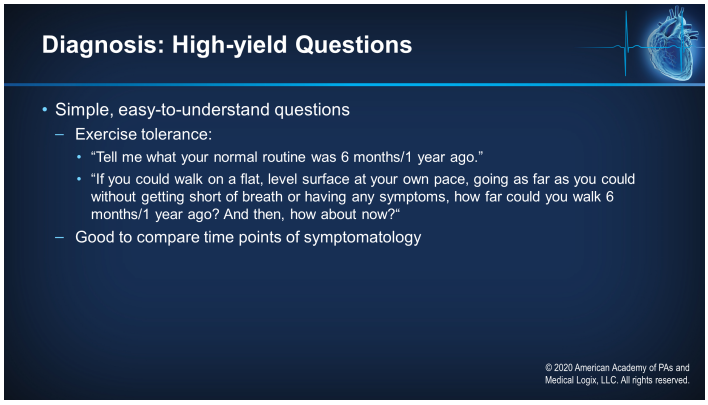
And then as we get into the higher classes, especially in II and III, which is where most heart failure patients live, we start getting into the limitations of physical activity.

When we get to the refractory level of class IV, they're short of breath all the time. Their physical activity is extremely limited.

Lawrence Herman: So, Dan, in a very busy primary care practice, what would be the one or two questions that you might ask this patient to rule in or rule out early symptoms of failure?

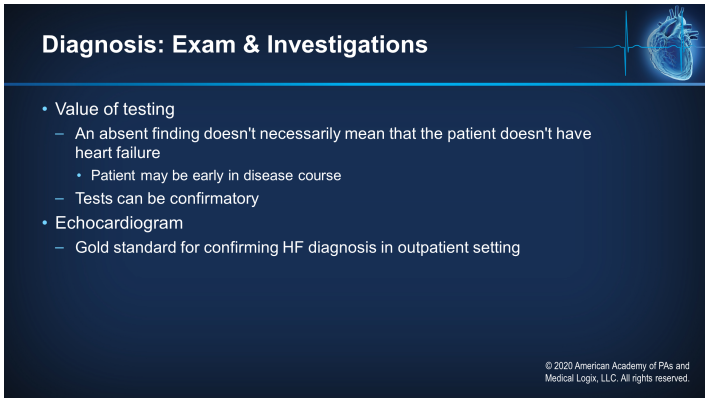
Daniel Thibodeau: Well, Larry, there's really important questions you can ask patients that are very simple and easy for the patient to understand. So, the first thing that I think about is exercise tolerance. "Tell me what your normal routine was 6 months ago or a year ago."

Sometimes I'll ask, "If you could walk on a flat, level surface at your own pace, going as far as you could without getting short of breath or having any symptoms, how far could you walk? And then, how about now?" And so that comparison between 6 months to a year is very helpful.



Lawrence Herman: Thank you for that. Viet, let's talk a little bit about positive predictive values and negative predictive values, without getting into statistics here. But if someone has an absent physical exam finding, it doesn't necessarily mean that the patient doesn't have heart failure. Tests can be confirmatory, so if the symptoms are strong but the exam findings tend to be on the weaker side or are, in fact, absent, we still need to consider the diagnosis of heart failure. So, we can begin with very basic things like echocardiograms, correct?

Viet Le, MPAS, PA-C, AACC: That's right. I mean, an echocardiogram is actually one of the gold standard studies that you can do in the outpatient setting. Barring the availability of cardiac MRI or other studies, the echocardiogram is my first go-to if I'm suspicious.



And I like what you said. The absence of physical exam findings does not mean the absence of heart failure. What it does mean is that typically you're a little early in the process of the heart failure development.

But having said that, we should probably talk about those physical exam findings that you should look for, or that are in general pathognomonic or more likely to discover heart failure if you're focusing on them.

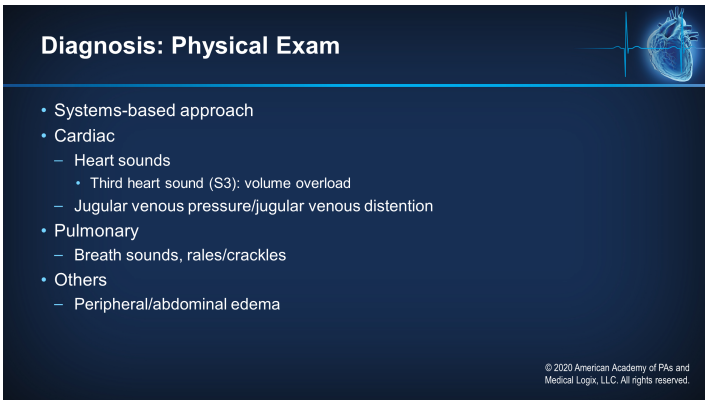
And so, these would be going through a systems-based approach. On a physical exam, when we're looking at a cardiac evaluation, you do want to listen to heart sounds.

In that, you always hear about an S3. Typically, that's much later in the game, where you are listening to blood volume that's already in there, and as it drops in passively, you'll hear an S3 sound. Jugular venous pressure, as you have your patient laying at a 45-degree angle.

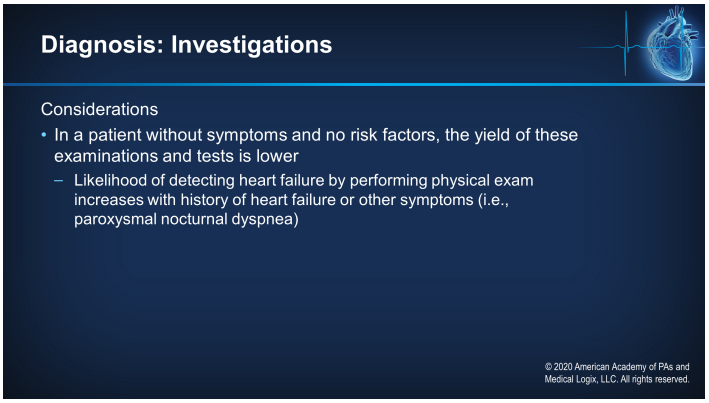
But it is uncommon to hear S3, while it's much easier and much more common to see jugular venous pressure, or JVD. And then it's just a matter of recording to what level that pressure is up along the sternocleidomastoid and the angle of the jaw.

From a lung standpoint, pulmonary evaluation. You know, you're listening for breath sounds, but what are you hearing? We're listening to rales. Now, with crackles and rales, you should be highly suspicious that this is heart failure.

Along the line of systems, then, you're just thinking about the pathophysiology. As fluid backs up from the heart into the lungs and then out into the system -- this is congestion back towards the heart -- then, you know, in the extremities you may find that there's -- well, often termed edema. And then it's just a matter of looking at severity there in the lower extremities, as well as, you know, don't forget this can back up into the abdomen, as well.

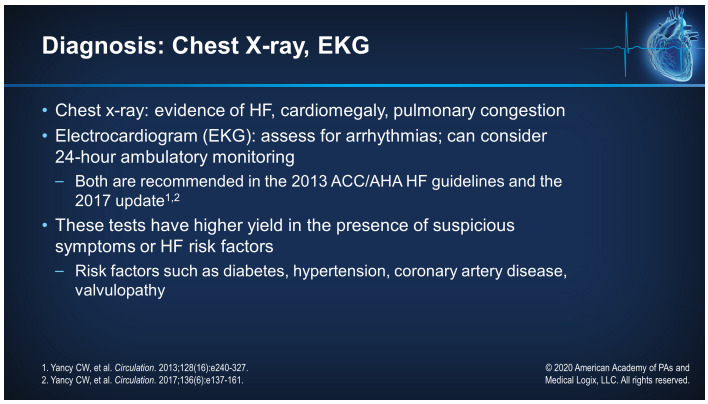


Lawrence Herman: Now each of these actually can be a predictor for failure, heart failure. Can you go through some of the ones that have specific statistical ties to heart failure?

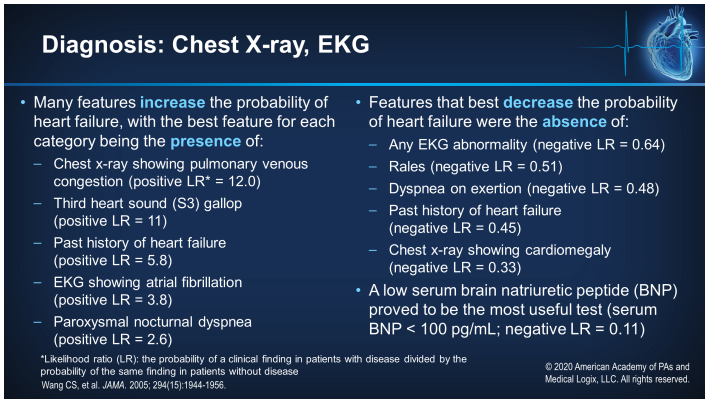


Viet Le: Sure. And first, before, we must preface that you shouldn't try to do all of these exams in someone that's fully asymptomatic and does not have any risk factors. So, your likelihood of picking up heart failure by going through this physical exam increases if they have a past history of heart failure, already a symptom of paroxysmal nocturnal dyspnea. I mean, that should be a clue that you should be looking, a sign of the third heart sounds.

And then chest radiographs, electrocardiograms. I mean, these are things that you would add on when you assess someone that comes in with dyspnea or has stage A and B, where diabetes, hypertension exist, maybe a history of coronary disease without MI or structural disease, such as valve. Then, as they come in with complaints of lower extremity edema or dyspnea, then, yeah, the likelihood increases as you do these exams.

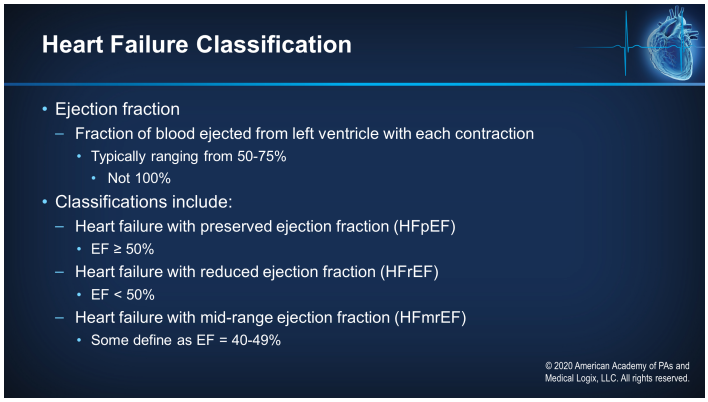


So getting a chest radiograph, obtaining an electrocardiogram, looking for jugular venous pressure -- I believe we'll have a slide here with the likelihood ratios -- but these are the high-impact exams that you should do in a very busy primary care practice. There's no way that one in 12 to 15 minutes can take care of everything and then add on these extra, special tests and signs.



But certainly, if you have a patient that comes in with dyspnea or complaints of lower extremity edema and has a history of heart failure in the past, then looking for these on the physical exam is very helpful.

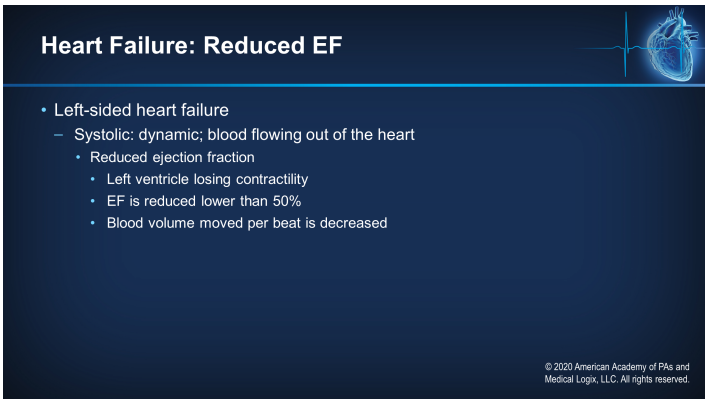
Lawrence Herman: We actually have learned a great deal about heart failure, where we now have new terms, where people have heart failure with reduced ejection fraction and preserved ejection fraction. And then we have intermediate stages of heart failure, and these all go by different names that some of our audience may not be familiar with. Can you talk a little bit about that?



Viet Le: Thank you for asking that. Actually, if I may, let me remind our audience that ejection fraction is really -- I mean, what is that? It's the fraction of blood flow that's ejected with each heartbeat. It's 50 to 75%, or one-half to three-quarters of blood volume that's ejected out normally. It's not 100%.

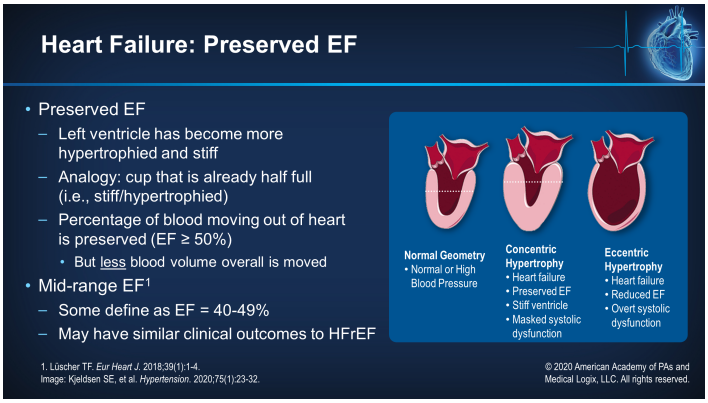
So then as we talk about heart failure, think of it from the left or right side, but in this case, we think of the left side, and this refers often to systolic, that beat, that dynamic beat of blood flow out of the heart.

And when that left ventricle begins to lose its contractility, then you reduce even further, from 50 to 75%, down below that, and so then it's a reduced ejection fraction. That heart just can't push -- it doesn't produce enough force to push out that volume. And then we have this drop in that blood volume with each beat.



As we look at preserved ejection fraction, the other way to think about this is an 8-ounce glass, where you're trying to fill it up and drink out of it, but about 4 ounces is already cement. It's stiff. And so you effectively only get 4 ounces ejected because that heart is so hypertrophied or stiff that it no longer really gets enough volume.

However, the 4 ounces that you put in, you get out, so you preserve that ejection fraction. But the reason why you have heart failure is because there's so much less that's pumping out overall when that ventricle is so stiff. Hopefully that helps to kind of put into context why preserved ejection fraction has congestion or heart failure.



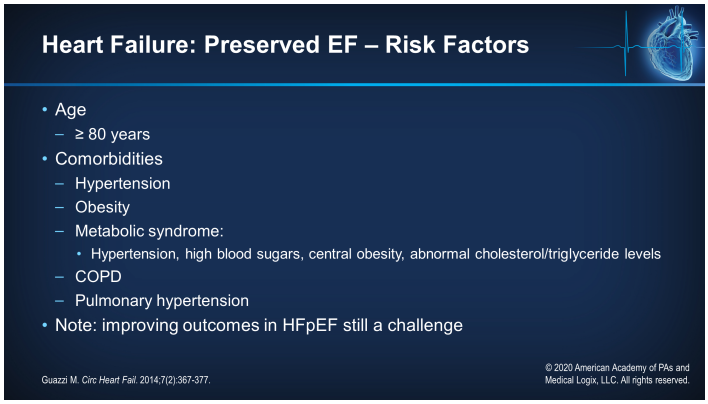
Lawrence Herman: Dan, can you take a moment to speak about HFpEF and the cohort of patients that that tends to be associated with?

Daniel Thibodeau: Sure. Well, one thing that PAs need to think about when we're trying to risk-stratify patients for potential heart failure -- specifically now we're talking about HFpEF -- is advanced age, and we're really talking about patients that are in their 80s or older. They pose an increased risk for HFpEF from developing. And those individuals who have hypertension, our patients who are obese, and those who have metabolic syndrome all are potential patients that could develop HFpEF.

Now, the overwhelming one that we have to really think about are our patients who have COPD. Those are very commonly associated with HFpEF. And this is where I referred to a little bit earlier where multifactorial reasons for why people are short of breath come into play.

Now, patients also with COPD present with fatigue, but that's also a symptom of heart failure.

The other thing that you have to think about with these patients is pulmonary hypertension, which also plays a factor. So, try to imagine a patient who has pulmonary hypertension, COPD and HFpEF all at once. This can actually present quite common.



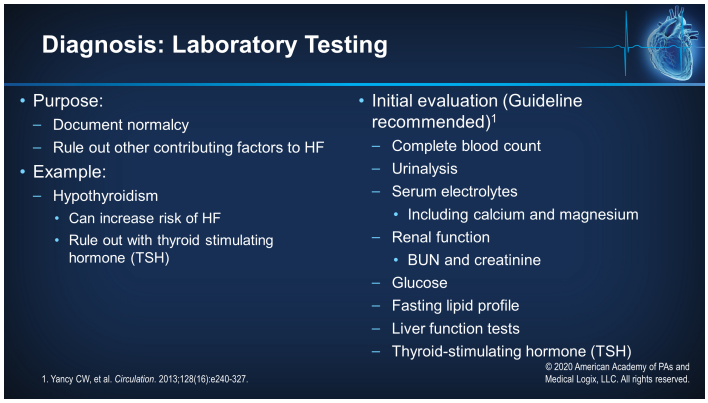
So, when it comes to HFpEF, there's no clear one treatment that has demonstrated to improve outcomes for patients with HFpEF compared to when we look at the studies and the treatment options for HFrEF.

Lawrence Herman: Let's take a moment to circle back and talk about the overall diagnosis of heart failure and the role of laboratory tests in both chronic, worsening and acute failure. What role did they play in your diagnostic armamentarium?

Daniel Thibodeau: So, what I explain to our students when we're teaching them is, one of the things that we want to do when we evaluate patients is to document normalcy. There are tests to rule out other possible contributing conditions that can make heart failure worse.

So, as an example, hypothyroidism can increase the risk of heart failure. So, if you have a patient who possibly has this, or you're thinking about it, you may be ordering thyroid studies as well to rule that part out as a contributor to heart failure.

Now, in 2013, the guidelines recommend that patients with signs and symptoms of acute decompensation, where they had not been previously diagnosed with heart failure, need to have an initial evaluation. And that initial evaluation includes a complete blood count, so a CBC, urinalysis, looking at serum electrolytes, including calcium and magnesium, which are very important when we look at heart failure patients.



Renal function -- so BUN and creatinines. Glucose. Fasting lipid profile. And once again, we're risk-stratifying for coronary or atherosclerotic disease. Liver function tests and TSHs, which I mentioned before.

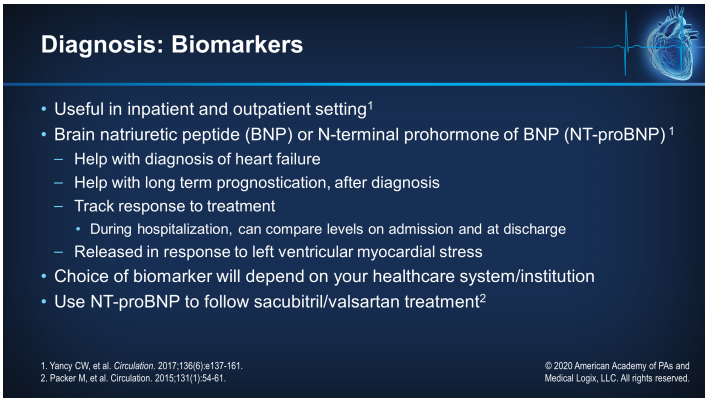
Lawrence Herman: Viet, we've talked a little bit about the use of biomarkers for detecting heart failure. And that's traditionally been done in the hospital setting. But we can also use those identical tests in the clinic. I'm certain you find them useful. That's a rhetorical question. In my opinion, they're underutilized. How do you feel about that?

Viet Le: I feel the same. It's - for guidance. You know, when we look at fasting lipid profile for risk stratification, once you start therapy, you want to check from time to time. And a brain natriuretic peptide, or NT-proBNP, can be helpful for long-term prognosis once you have a patient that's been diagnosed with heart failure.

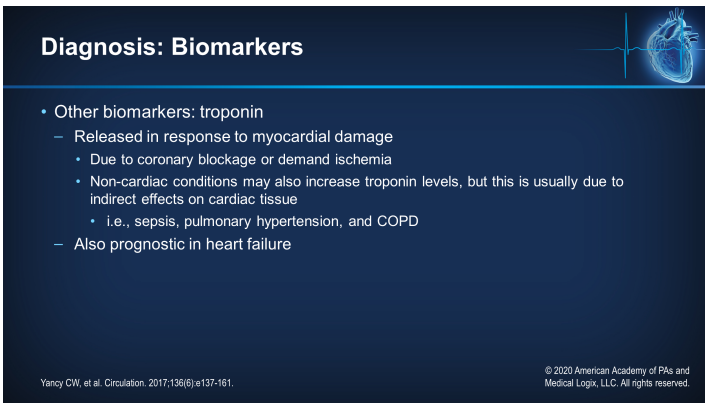
So those are the two biomarkers that are now commonly used to diagnose heart failure, but also to follow them for prognosis and for therapy. I do find it useful to know what the value is at the beginning of a hospitalization, and whether we were able to get it down to a certain level. I mean, that talks to prognosis, and that helps you as you speak to the patient in the outpatient setting.

But, you know, I think it depends on your system. It depends on the clinic. But I think BNP and NT-proBNP are two markers that certainly the primary care provider can use in the outpatient setting. Just know that they're both released equally in the bloodstream, and it's through myocardial stress in that left ventricle.

You could choose either to follow, and we'll talk about a little bit later with regards to sacubitril and valsartan therapies, typically NT-proBNP is what you would follow.



Other markers would include troponin, and I think this speaks more to what Dan was talking about in terms of risk factors.



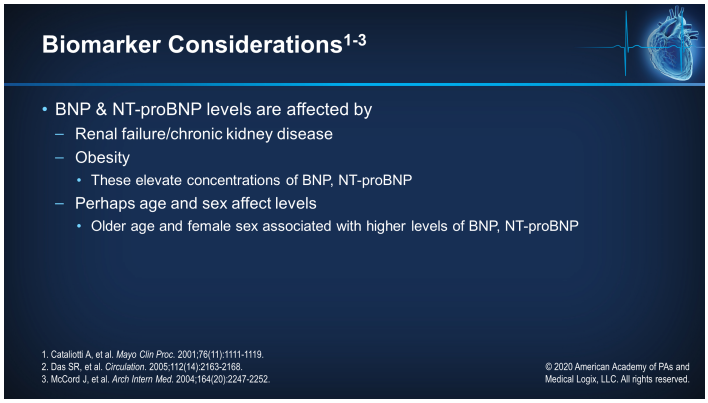
Well, you know, troponin, if it's elevated, obviously, speaks to myocardial damage. But that can be from coronary or it can be from demand ischemia, some other factor going on that's causing decreased blood flow to the heart. But that troponin is also prognostic in heart failure.

Lawrence Herman: What's more important is to understand that regardless of which one is the test that your health care system uses, there are things that impact the level, and those things need to be accounted for, correct?

Viet Le: That's correct. Once you get past which one to order -- because it'll be decided for you -- then you have to understand that brain natriuretic peptide and NT-proBNP are affected by renal failure and chronic kidney disease. Obesity also affects this.

Now, with regards to chronic kidney disease and renal failure, what happens is – and you're going to find this in most of the folks that have heart failure as a comorbid condition, the concentrations of BNP and NT-proBNP will be elevated. So, the baseline is already high.

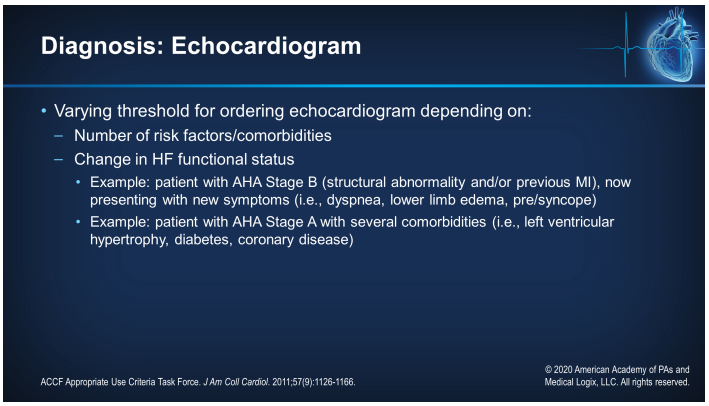
You have to understand what the baseline is for that patient, whether they have obesity, or whether they're obese, which their BNP and NT-proBNP will be lower to begin with. You just look at the change based on those things. There is some evidence that age affects this, as well as gender. It tends to be a little bit higher in both those that are older as well as female, of women.



Lawrence Herman: Where are we, or where are you in terms of the threshold for ordering an echo, or what do you recommend, more importantly, for the person in a primary care setting?

Viet Le: These are great questions. I think if we go back to the ACC/AHA classifications, you know, someone with a known stage B -- so they have a structural abnormality and/or have had a previous MI -- and then they also present with dyspnea -- you know, the shortness of breath -- or lower extremity edema or syncope or presyncope, my threshold lowers real quickly, meaning I would order an echocardiogram in those individuals.

With those that are stage A, well, presumably, if they have symptoms, then the question is, is this now stage C? But, you know, those with hypertension, known left ventricular hypertrophy, diabetes, coronary disease without an event yet, then my threshold for ordering echocardiogram in those individuals using those wonderful questions that Dan alluded to, where you're trying to figure out when the dyspnea occurs in relation to prior activity level, so that's when I would order an echocardiogram.

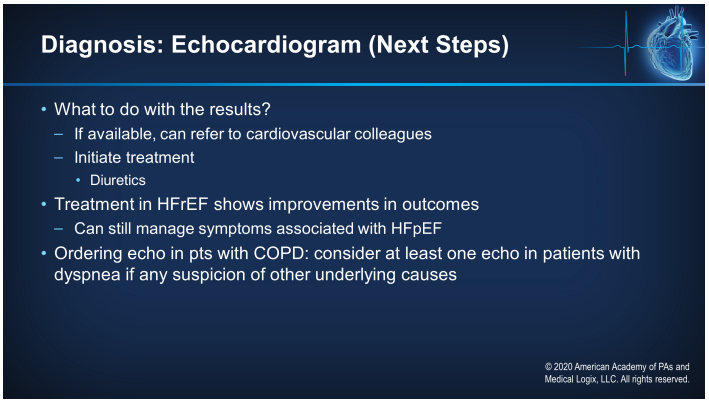


Now, you know what to do with the results, right?

Well, if you don't have tight cardiovascular backup, then you can treat. Certainly, we know that when you have LV dysfunction, and someone has heart failure symptoms, you can start diuretics.

You know, while I've mentioned that you can start treatment in HFrEF, again -- and we'll talk about this later -- HFpEF, unfortunately, has not many treatments that are good for outcomes, but we can at least help with symptoms.

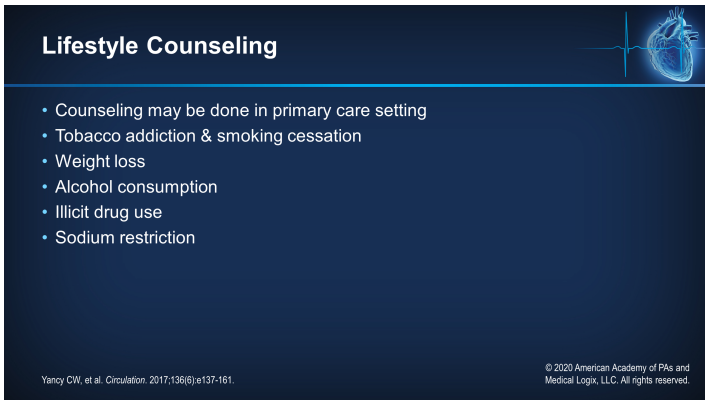
Lawrence Herman: In my practice in the past, if I have any doubt that someone that I've diagnosed with COPD, and their dyspnea is not exclusively related to their COPD, if I have any hint of it perhaps having more than one underlying cause, I'll order at least one echo to rule that out as a possibility or rule it in, of course, and go ahead and treat them. And I think that's a reasonable thing for our audience to do, that single echocardiogram.



I do also think it's important for us to talk for a moment about -- regardless of whether this is HFrEF, HFpEF or that midrange -- there are many lifestyle changes that each and every one of these patients should undergo and can easily be done relatively easily, I should say, in a primary care setting. And that includes tobacco addiction and smoking cessation.

These folks ideally should lose weight. That will help all of our patients.

We need to question them about alcohol consumption. We need to limit that, as well as talk to them honestly about illicit drugs that they may be using and trying to determine that. Of course, sodium restriction is a good thing.

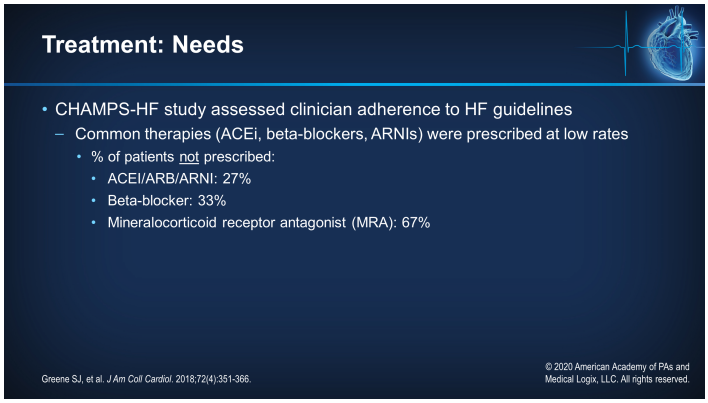


Dan, we've spoken up until this point about the diagnosis. Let's talk about therapies, initial therapies in particular for patients who have heart failure.

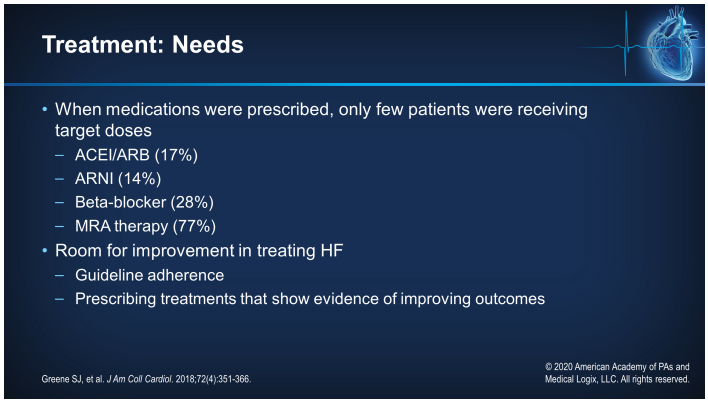
So, let's just spend a few minutes talking about how comfortable PAs who are primary care providers should be in prescribing therapeutics for heart failure, and which ones.

Daniel Thibodeau: So, Larry, one other thing that I wanted to mention relative to treatment is that we as PAs need to do better when it comes to adhering to our own guidelines and making sure we're doing what we need to do for our patients.

A study a couple of years ago called the CHAMPS-HF heart failure study actually showed almost embarrassing low percentages of clinician adherence to the guidelines to where, in some cases, the common therapies that we mentioned with ACE inhibitors, beta blockers, ARNIs were at very low rates.



So the vast majority of us are just not doing as good of a job as we need to when it comes to prescribing these medications and getting with the guidelines.



Whether they know it or not, they're treating a lot of the risk factors for heart failure, and so they're initially treating these things anyway.

Let's start with hypertension. Follow the guidelines of the JNC and keep the optimal blood pressure under control, and that really helps reduce the risk of heart failure from developing in the first place. And getting the patient adherent on the meds is absolutely key. It's a big challenge, but we all need to try harder, educating our patients on the importance of why getting blood pressure under good control is important.

But we also have a lot of heart failure agents that we're going to counteract that neurohormonal, you know, activation. And so, one of the first things that we're going to use is either an ACE inhibitor or an ARB. And that's especially important in heart failure, as are beta blockers.

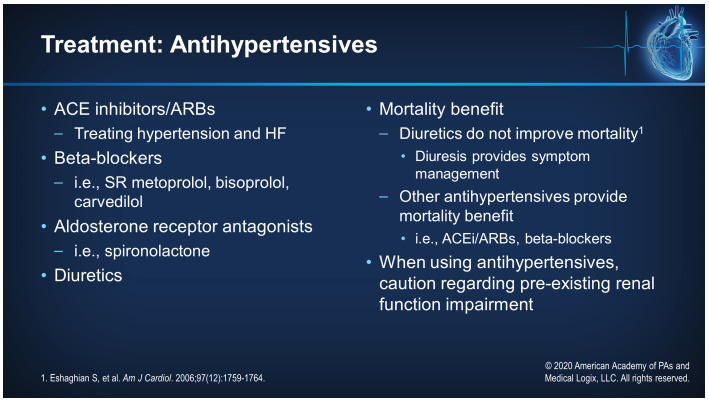
Now, they have dual roles, because some of our patients who have hypertension may be on an ACE inhibitor for hypertension, as well, and so you're dually treating both the hypertension and the risk for heart failure, or if they have heart failure, you're treating that, as well.

Aldosterone receptor antagonists -- so spironolactone comes to mind -- is another very common therapy that's used, as well as diuretics.

All of the other medications, especially with ACE inhibitors and beta blockers, they have been shown to improve and reduce overall mortality and morbidity in patients with heart failure.

Diuretics don't do that. You don't improve the function of heart failure with diuretics. All you're doing is treating the symptoms of shortness of breath and the edema that patients have by using diuretics.

I should also mention that one of the patient populations we all have to be careful with in treating is our patients who have some form of early or known kidney disease, as well. And so that's going to modify how we treat certain patients based on what their renal function is doing, as well.



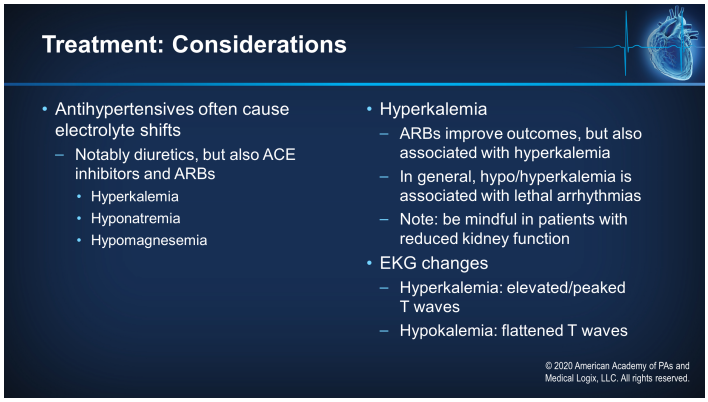
Lawrence Herman: The other thing that happens is, when we are using some of these medications, and it includes ACEs, ARBs, diuretics and others, you get shifts in some of the ions, whether it be intracellular or extracellular, and we need to be mindful of both monitoring and potential treatments if that does occur. What are the data associated with that complication?

Viet Le: I'm glad you bring that up, because the therapies that we use all -- I mean, that's their mechanism of action, right, especially if you're thinking of the diuretics. But ACEs and ARBs also can contribute to electrolyte shifts.

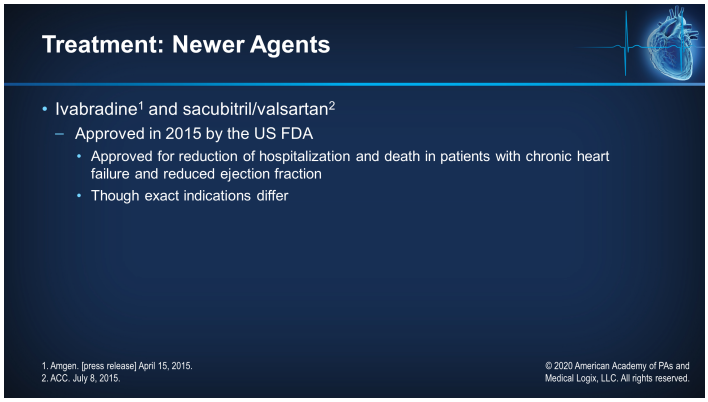
And so, you have to look at serial or surveillance labs, such as basic metabolic panel, looking at magnesium levels. And we've had a couple of patients with hypomagnesemia that it just didn't occur to me initially to look for that.

But one of the medications in particular, the aldosterone receptor antagonists -- again, let me remind you that the evidence is very good for mortality outcomes and improvement -- those can cause hyperkalemia, which -- either way, hypo or hyper, can cause lethal arrhythmias. And so it makes it difficult to add these medications on board when you have someone that already has reduced kidney function, and then they begin to have potassium increases.

Lawrence Herman: All the more reason to do periodic EKGs on these patients. As our PA students know, potassium lives under the T wave, and elevated T waves may, among other things, imply elevated potassium levels, where flattened T waves may imply hypokalemia or low potassium levels, allowing you then to get a metabolic panel to make a definitive determination.



Viet, let's now shift for a moment and speak about two relatively recently approved agents for the treatment of chronic heart failure, and they are ivabradine and sacubitril/valsartan. Take a moment and walk us through the importance of these drugs, what the clinical trials showed, and how they fit into your practice.



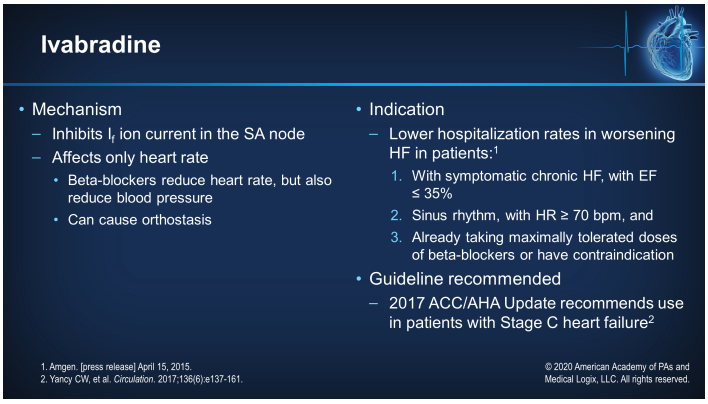
Viet Le: Both of them were approved in 2015 by the U.S. Food and Drug Administration for the reduction of hospitalization and death in patients with chronic heart failure and reduced ejection

fraction. So, that's important to know that the studies enrolled that type of patient, chronic heart failure and reduced ejection fraction. And what they were looking for in the primary outcome was to reduce death as well as hospitalization.

So ivabradine, interestingly enough, affects only the heart rate, and that's nice, because then you're not having an effect on heart contractility or blood pressure, which is a common problem in those with heart failure. So paradoxically, they're fluid overloaded, but they have not much blood pressure to work with. So, using the beta blockers to help reduce heart rate tends to affect their blood pressure and then you have patients with severe orthostasis.

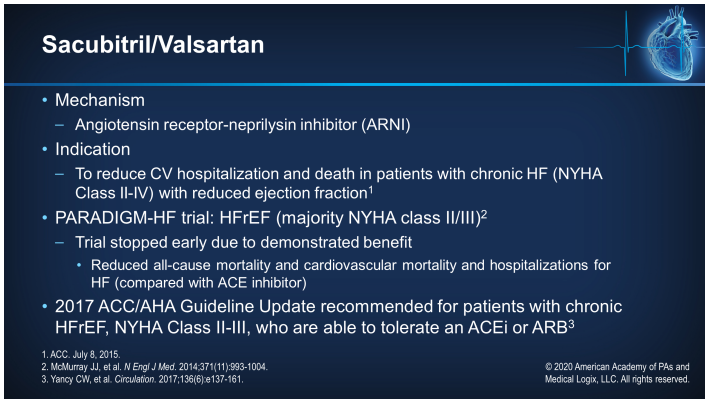
In this case, ivabradine is indicated for lowering hospitalization rates. And those that you should think about using ivabradine in: they're stable, but they have symptomatic chronic heart failure, and their EF is less than or equal to 35%. They have a sinus rhythm with a heart rate of greater than or equal to 70 beats, and they're already taking maximally tolerated doses of beta blockers or have contraindications to them. And let me remind you that maximally tolerated may be little to none.

So, the 2017 guidelines that just came out as an update recommends that we use ivabradine primarily to reduce heart rate in those with stage C heart failure. So if you will remember, these are the folks that swing back and forth from II, III and then IV in the New York Heart Association classes, and then have an EF of less than 35%.



Lawrence Herman: Dan, would you speak about sacubitril/valsartan? And obviously, valsartan is a drug that our audience is very familiar prescribing, but this is a combination of two agents in a single tablet.

Daniel Thibodeau: That's right. So this came along the same time as ivabradine. It's a single tablet. It's referred to as an angiotensin receptor neprilysin inhibitor, or ARNI. And just as Viet said with ivabradine, this is for HFrEF patients who are class II through IV with a low EF.

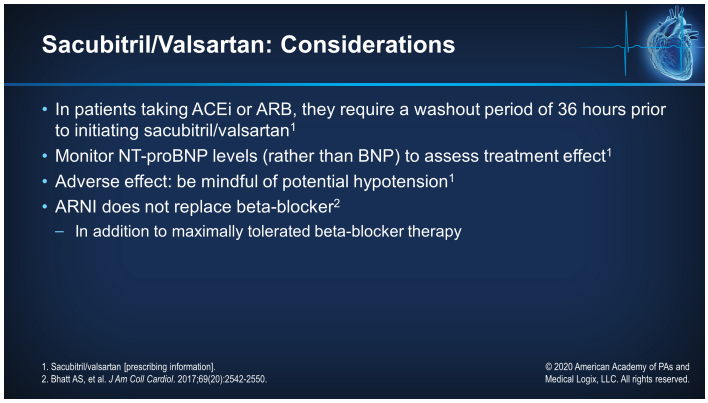


A big trial named PARADIGM-HF was the study. It was actually stopped early because it reduced overall cardiovascular mortality and hospitalizations for heart failure. And so this is also in the guidelines and recommendations now that were updated in 2017 for those symptomatic patients who have heart failure with reduced ejection fraction, either class II or III, who also are able to tolerate an ACE or an ARB.

So, in a lot of these patients, they might already be on an ACE or an ARB. You'll have a washout period for at least 36 hours before you can start them on sacubitril/valsartan.

And then what we do is we monitor the NT-proBNP levels for these types of patients because of how it works. And so, we need to watch for those higher levels that indicates an increasing symptomatology of heart failure.

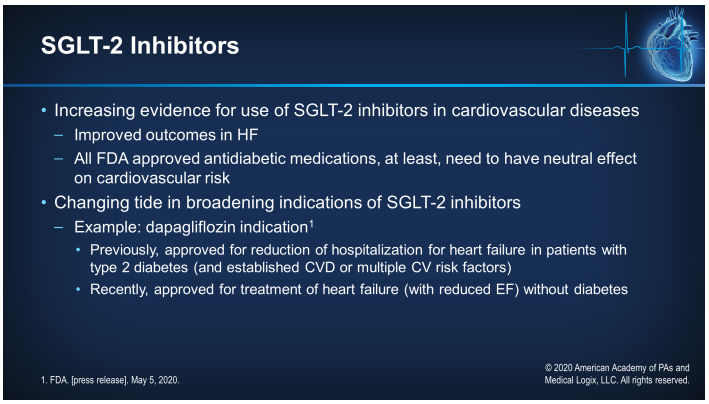
Lawrence Herman: It's important to note, because a lot of people don't understand, this is a replacement for an ACE or an ARB, and you have that washout period. But this does not replace your beta blocker. This is in addition to maximally tolerated beta blockers.



Interestingly enough, Viet, there has been a flurry of information regarding drugs that were originally in the diabetic realm which now are utilized in the cardiovascular field.

And in particular, for heart failure, what we're talking about are SGLT-2 inhibitors.

And something that seems counterintuitive, but we discovered that they have an effect on failure and preventing progression, and actually preventing failure at all. And this is huge news. Talk a little bit about this.



Viet Le: It's very exciting. So, while we're looking at it in heart failure, just know that it also reduces cardiovascular disease. The FDA put in place that any diabetic or antidiabetic medication has to prove that it doesn't increase cardiovascular risk. In this case, it reduced cardiovascular disease rather than just a neutral effect.

So when we look at these medications, you know, dapagliflozin is a great one to look at. It was looked at in those with type 2 diabetes and heart failure with reduced ejection fraction. And it now has the indication -- it was just approved for heart failure without diabetes.

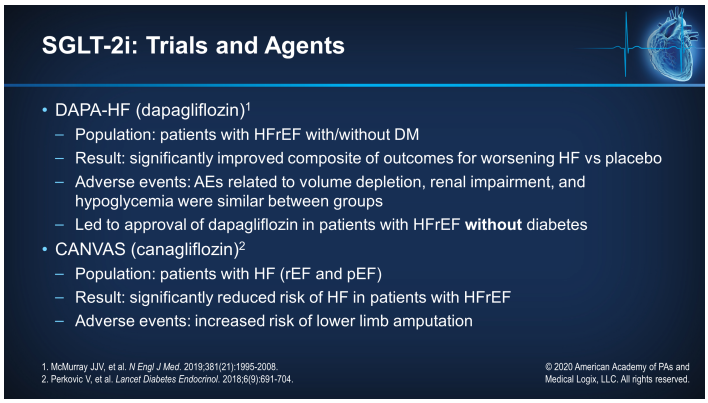
But in general, I would say that the effect on diabetes is low enough that I don't think you have to adjust medications necessarily. If someone's already on antidiabetic medications, such as metformin, a GLP-1 or insulin, it doesn't have such an effect that you would get scared in using SGLT-2 inhibitors.

Just know that from my standpoint, it's a cardiovascular drug, and it also protects kidneys. There's great data, and in fact indication now in chronic kidney disease to use the SGLT-2 inhibitors.

So just kind of running down the line here, the DAPA-HF study looked at a composite of worsening heart failure compared with placebo, and the results were looking at with or without diabetes, and, well, led to the approval in the U.S. for treatment of heart failure in patients with heart failure with reduced ejection fraction. And again, that's with and without diabetes.

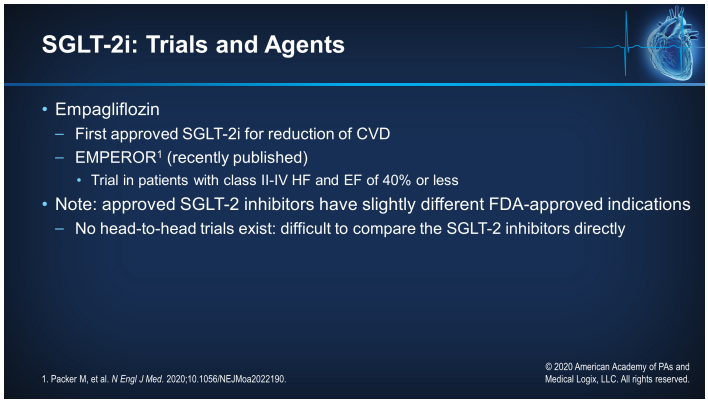
Going down further, to canagliflozin, the CANVAS trial was looking at lowering -- well, actually, what it saw was that there was a lowering of risk of heart failure in patients with already reduced ejection fraction, but it also looked at those with heart failure with preserved ejection fraction.

I don't mean to minimize this, because there was lower leg amputation with its use, or at least it was seen when the trial was moved forward.



Moving on to empagliflozin. So. there's multiple drugs in this class of SGLT-2 inhibitors, and empagliflozin was actually the first approved for reduction of cardiovascular disease.

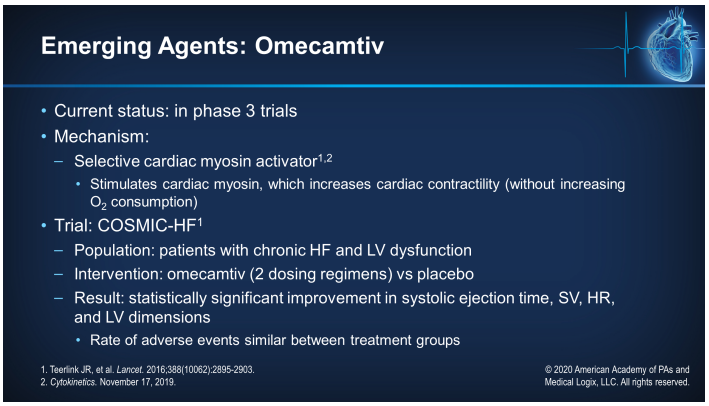
But there is a great case for SGLT-2 inhibitors in heart failure, and in particular with those that have chronic kidney disease and diabetes. But I wouldn't stop there, and there is an indication now in those that have heart failure without diabetes.



Lawrence Herman: I think it's important for our audience to recognize that, number one, every one of these drugs has a slightly different indication from the FDA. None of these drugs have had a head-to-head trial, so we can't compare the risk and the benefit and the alternative for each of them. It is important to go back to the package insert and look at the FDA approved indication, because some have indications for different things.

Viet Le: So, in COSMIC-HF -- it's a phase 2 trial -- it was looking at patients with chronic HF and left ventricular systolic dysfunction, and they were given omecamtiv at 25 mg twice daily or 25 mg with dose escalation to 50 twice daily versus placebo.

In that dose escalation group, there was a statistically significant improvement in the systolic ejection time, the stroke volume and heart rate, and also showing improvement in the left ventricular and systolic and diastolic dimensions compared to placebo.

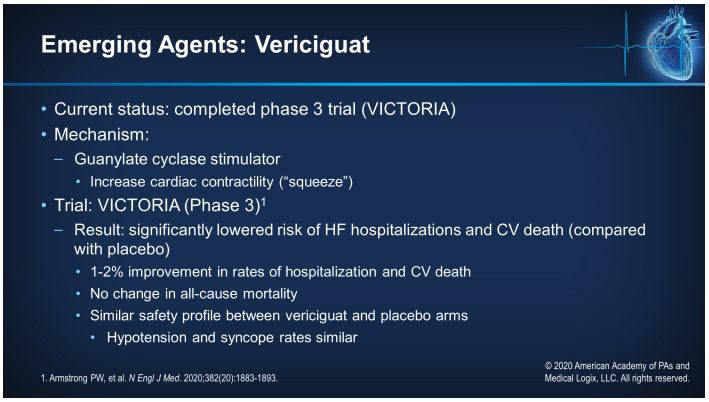


Lawrence Herman: And Professor Thibodeau, there's a second agent, as well. Can you talk to us about that one?

Daniel Thibodeau: Right. So that's vericiguat, which is a guanylate cyclase stimulator, which is intended to help with squeeze. They had a phase 3 VICTORIA trial related to this drug.

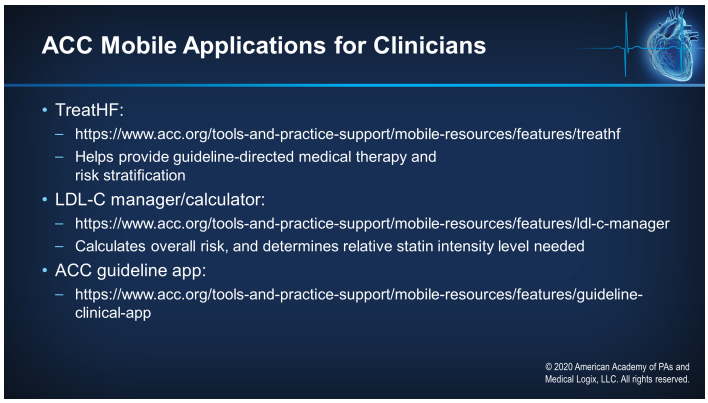
The VICTORIA trial showed that the vericiguat lowered the risk of heart failure hospitalizations and cardiovascular death when compared to placebo. However, it didn't show any change in all-cause mortality.

The improvements were about 1 to 2% when you compared hospitalizations to cardiovascular death, so there was a small improvement, but overall, it did show an improvement with no change in the risk of the safety profile. While they still had episodes of hypotension and syncope, they were not significantly increased by actively treating patients with vericiguat.

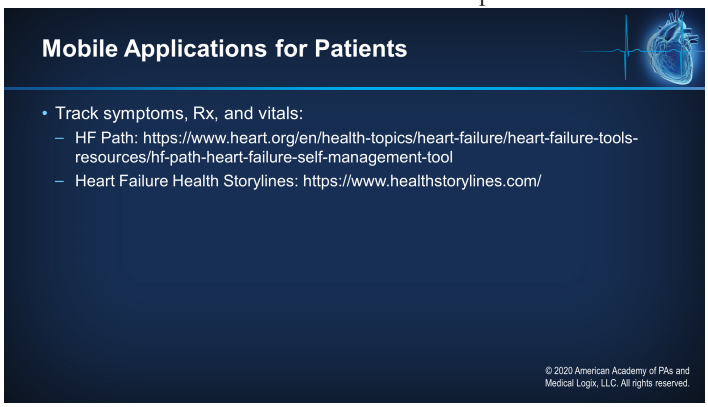


Lawrence Herman: I believe we all love our smartphones and the apps that are associated with them that make our lives much easier. Dan, would you speak about some of the apps that you believe that PA clinicians find helpful and useful in their practices?

Daniel Thibodeau: Sure. Well, there are several. The ones that are the most helpful to me, because they're free and I'm a member of the American College of Cardiology, I think a lot of PAs have found this helpful.



Lawrence Herman: And we have a slide that shows the apps, as well as the links for our audience to be able to download them and utilize them both for themselves and for their patients.

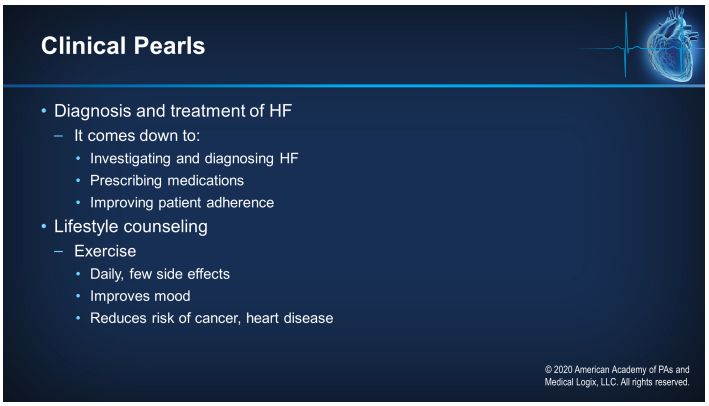


Viet, what would you like to leave our audience with in terms of a clinical pearl?

Viet Le: Larry, that's a great question. What are the clinical pearls? And I think it goes back to behavior, both for the patient and we as clinicians. Going back to Dan, speaking about therapies and the CHAMPS-HF trial, it comes down to whether or not we are going to prescribe and look for heart failure, but prescribe medications and whether or not patients will adhere to them.

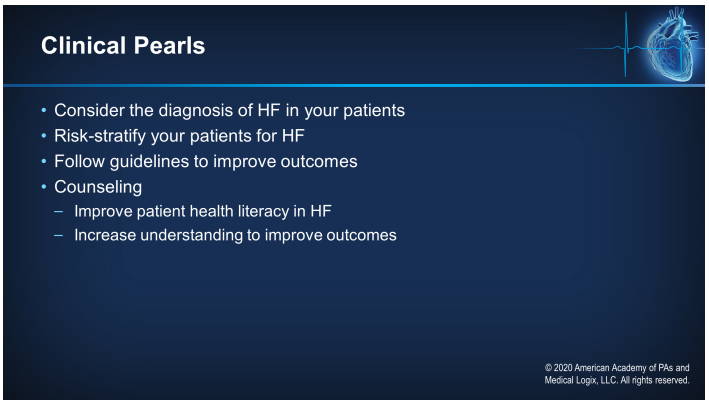
One of the things I like to tell my patients is -- we'll talk about lifestyle. I'll say, "Look, if there was a pill to make you live longer and stay healthier, would you do it? You'd have to take it once a day. It's for 30 minutes maybe a little difficult. You may experience some sweating, some fatigue, a little bit of symptoms, the palpitations. However, if you take it, it's been shown to make you feel better, during, even. You might have a better mood. You have less cancer, less heart disease, and you may enjoy other activities if you take it."

It's exercise. And if you just did it for 30 minutes, then that would help tremendously. And I would ask our clinicians to think about that in terms of behavior. If we just take a moment and think about heart failure, look for those risk factors and initiate them in our own practice, changing our behavior of how we think of medications and adherence. The clinical pearl here is that, keep it top of mind.



Lawrence Herman: Dan, what clinical pearl would you like to leave our audience with?

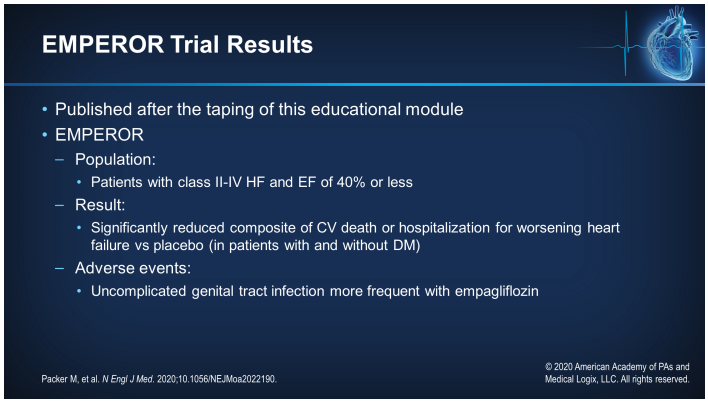
Daniel Thibodeau: Well, Larry, once again, thanks for allowing us to participate in this really important education for our colleagues. The things that I would take away as a pearl to my colleagues is, number one, is just really start thinking about your patient population and risk-stratify them. Really think about heart failure as a potential risk for these patients that you care for on a regular basis.



And then really hone in on the guidelines to make sure that you're doing what you can to give your patient the best chances for great outcomes.

I tell my kids all the time, it's the little things. And so, educating your patients as best you can in a very simple health literacy formatting for heart failure can go a long way. Heart failure is a very complicated disease, so trying to make it as easy to understand for your patients is going to be key.

Lawrence Herman: I would like to thank both of our expert faculty, Dan Thibodeau and Viet Le, for their great insights and discussion. And I'd like to thank you, our audience, for participating in this *Clinical Dialogue*.



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eCASE CHALLENGE

Sherryl is a 62-year-old office manager who is seeing you for a routine clinic visit. She was diagnosed with chronic heart failure 8 years ago, with her most recent echocardiogram (2 years ago) showing an ejection fraction (EF) of 35%. She also has a history of hypertension (15 years), atrial fibrillation (8 years) and hyperlipidemia (9 years). She does not have a personal history of diabetes. Previously, she reported no limitations in her functioning. She is currently maintained on furosemide 40 mg PO once daily, valsartan 160 mg PO BID, and carvedilol 25 mg PO BID. She also takes warfarin 2.5 mg PO once daily and atorvastatin 40 mg PO once daily.

On physical examination, the patient's current height is 5 feet 4 inches and her weight is 179 pounds (last year 172 pounds), with a body mass index of 30.7 kg/m^2, considered obese by most national standards. Her heart rate remains irregularly irregular at 72 beats per minute. Her blood pressure is 123/79. On lung auscultation, there are faint bibasilar crackles with no wheeze. Examination of her lower limbs reveals a pitting edema up to the mid shin, that disappears within 5 seconds. Other physical examination findings are normal.

Other laboratory results show liver function tests, electrolytes, serum urea nitrogen/creatinine ratio, and microalbumin levels were all normal. Sherryl's lipid profile shows total cholesterol of 151 mg/dL, low-density lipoprotein cholesterol of 79 mg/dL, high-density lipoprotein cholesterol of 52 mg/dL, and triglycerides of 101 mg/dL.

Biometrics:

- Height: 5 feet 4 inches
- Weight: 179 lbs.
- Current BMI: 30.7 kg/m^2

Vital Signs:

- Heart rate: 72 bpm, irregularly irregular
- BP: 123/79 mmHg
- Respirations: 16/minute

Past Medical History:

- Hypertension for 15 years
- Dyslipidemia for 9 years
- Atrial fibrillation for 8 years
- Chronic heart failure for 8 years

Family History:

- Father with T2DM managed with oral agents
- Older brother with previous MI and history of hypertension

Social History:

- Non-smoker
- Alcohol use: non-drinker
- Occupation: office manager
- Spouse: married, 1 child

Current Medications:

- Furosemide 40 mg PO QD (see above)
- Valsartan 160 mg PO BID
- Carvedilol 25 mg PO BID (see above)
- Warfarin 2.5 mg PO once daily
- Atorvastatin 40 mg PO once daily
- Potassium 20 mEq PO once daily (this now makes more sense with daily rather than BID)

Known Allergies:

- None

Recent Laboratory Findings:

- A1C, 1 year ago – 5.9%
- Liver function tests, normal
- Electrolytes, normal
- BUN/Creatinine, 24/1.1
- Total cholesterol, 151 mg/dL
- LDL-C, 79 mg/dL
- HDL-C, 52 mg/dL
- Triglycerides, 101 mg/dL

Question #1

Which of the following historical, physical examination or diagnostic findings most increases the probability of heart failure (i.e., highest positive likelihood ratio for heart failure)?

A. Paroxysmal nocturnal dyspnea
B. Bibasilar crackles
C. Third heart sound (S3)
D. EKG showing atrial fibrillation

To improve clinical acumen, the Journal of the American Medical Association has published a series of articles on the Rational Clinical Examination. The main purpose is to reveal the usefulness of various historical, physical examination, and investigation findings to rule in or rule out a specific condition.

For the specific question of "whether a dyspneic patient in the emergency department has heart failure", they showed that the following POSITIVE findings increased the likelihood of a heart failure diagnosis[4]:

- Past history of heart failure (positive likelihood ratio [LR] = 5.8; 95% confidence interval [CI], 4.1-8.0);
- The symptom of paroxysmal nocturnal dyspnea (positive LR = 2.6; 95% CI, 1.5-4.5);
- The sign of the third heart sound (S3) gallop (positive LR = 11; 95% CI, 4.9-25.0);
- The chest radiograph showing pulmonary venous congestion (positive LR = 12.0; 95% CI, 6.8-21.0); and
- Electrocardiogram showing atrial fibrillation (positive LR = 3.8; 95% CI, 1.7-8.8).

Of all the listed options in our question, presence of the third heart sound (S3) has the highest likelihood ratio, and its presence most increases the chance of a diagnosis of heart failure in this setting, thus making the correct answer C. It should be noted that chest radiograph showing pulmonary venous congestion has an even higher likelihood ratio, but this was not one of the listed options above in our question.

Similarly, the ABSENSE of specific historical features and exam/investigation findings leads a clinician away from the diagnosis of heart failure; these include[4]:

- Past history of heart failure (negative LR = 0.45; 95% CI, 0.38-0.53);
- The symptom of dyspnea on exertion (negative LR = 0.48; 95% CI, 0.35-0.67);
- Rales (negative LR = 0.51; 95% CI, 0.37-0.70);
- The chest radiograph showing cardiomegaly (negative LR = 0.33; 95% CI, 0.23-0.48); and
- Any electrocardiogram abnormality (negative LR = 0.64; 95% CI, 0.47-0.88).

Interestingly a low serum BNP proved to be the most useful test in ruling out heart failure (serum B-type natriuretic peptide <100 pg/mL; negative LR = 0.11; 95% CI, 0.07-0.16).

This brings us to our next clinical question.

Question #2

Which of the following agents is recommend by the 2017 ACC/AHA Guideline Update for lowering risk of hospitalization and death in patients with chronic heart failure, in sinus rhythm with a heart rate ≥70 beats per minute, and already on maximally tolerated doses of beta-blockers?

A. Candesartan
B. Carvedilol
C. Ivabradine
D. Sacubitril/valsartan

In the most recent 2017 American College of Cardiology (ACC) / American Heart Association (AHA) / Heart Failure Society of America (HFSA) heart failure guideline update, both ivabradine and sacubitril/valsartan are recommended for use in patients with HF though with slightly different specific indications.[3]

Ivabradine affects heart rate alone, while having no effect on heart contractility or blood pressure. Specifically, it works by inhibiting the I_f ion current in the sinoatrial (SA) node. It is indicated for lowering hospitalization rates in worsening HF in patients[5]:

(1) with stable, symptomatic chronic HF with a left ventricular ejection fraction (LVEF) ≤35%,
(2) who are in sinus rhythm with a heart rate of ≥70 beats per minute, and
(3) who are taking maximally tolerated doses of beta blockers or have contraindications to them.

Use of ivabradine is supported in the 2017 ACC/AHA/HFSA guideline update, primarily to reduce heart rate in patients with stage C HF and an LVEF ≤35% or less,[3] thus making the correct answer C.

In the SHIFT trial, patients' enrollment criteria reflect the above indication regarding reduced EF, sinus rhythm, elevated heart rate, and on maximally tolerated doses of beta blockers. A total of 6558 patients were randomly assigned to ivabradine or placebo groups.[6] Patients were followed for a median of 22.9 months.

The primary endpoint (a composite of CV death or hospital admission for worsening HF) was significantly lower in the ivabradine group compared with the placebo group: 24% vs 29% (HR 0.82, 95% CI 0.75–0.00, p<0.0001). This effect was largely driven by the reduction of hospital admissions for worsening heart failure. The authors concluded that this trial showed the importance of heart rate reduction, specifically with ivabradine, in the improvement of clinical outcomes in heart failure.

Overall, there were fewer serious adverse events in the ivabradine group compared with the placebo group. Though more patients in the ivabradine group had symptomatic bradycardia (5% vs 1%; p<0.0001). Visual side-effects (phosphenes) were reported by 89 (3%) of patients on ivabradine and 17 (1%) on placebo (p<0.0001).

Of note, ivabradine is not indicated in acute decompensated heart failure.[7]

The other additional recommendation in the 2017 ACC/AHA guideline update surrounded the use of the new agent sacubitril/valsartan. This brings us to our next clinical question.

Question #3

For what indication and in which population is sacubitril/valsartan recommended in the 2017 ACC/AHA guideline update?

A. To reduce composite of CV death or hospitalization for worsening heart failure vs placebo (in patients with reduced ejection fraction (EF)
B. To reduce mortality (in patients with diabetes mellitus)
C. To reduce composite of CV death or hospitalization for worsening heart failure vs placebo (in patients with preserved EF)
D. To reduce all-cause mortality (in patients with preserved and reduced EF)

Sacubitril/valsartan is a new single tablet angiotensin receptor-neprilysin inhibitor (ARNI) indicated for lowering cardiovascular death and hospitalization in patients with NYHA class II-IV HF with low ejection fraction.[8] Within the 2017 guideline update, the authors note, "[i]n patients with chronic symptomatic [heart failure with reduced ejection fraction (HFrEF)] NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality."[3] Given this recommendation, the correct answer to this question is A. To monitor efficacy of sacubitril/valsartan, decompensation of HF should be evaluated with NT-proBNP levels, with higher levels indicating increased HF.[9]

In the PARADIGM-HF trial, 8,442 patients with NYHA functional class II-IV HF with reduced EF (≤40%) were studied.[10] Researchers randomized patients to receive either sacubitril/valsartan or enalapril. Patients were followed for a median of 27 months. The trial was stopped early due to benefit, as the researchers found that the primary end point of cardiovascular (CV) death or HF hospitalization was significantly improved for the sacubitril/valsartan group compared with the enalapril group: 21.8% vs 26.5%, respectively (HR, 0.80; 95% CI, 0.73 to 0.87; P<0.001).

Regarding the frequency of specific selected outcomes, when comparing sacubitril/valsartan to enalapril, the mortality was 17.0% vs 19.8% (HR for death from any cause, 0.84; 95% CI, 0.76 to 0.93; P<0.001). Of these patients, 13.3% vs 16.5%, respectively, died from CV causes (HR, 0.80; 95% CI, 0.71 to 0.89; P<0.001). Similarly, sacubitril/valsartan reduced the risk of HF hospitalizations by 21% and decreased the symptoms and physical limitations of HF (P=0.001).

Adverse events within this trial showed that the sacubitril/valsartan group had higher proportions of patients with hypotension and nonserious angioedema. Interestingly, however, this agent was

associated with lower proportions of renal impairment, hyperkalemia, and cough than the enalapril group.

Sacubitril/valsartan is associated with fetal toxicity, which is a class effect of medications affecting the renin-angiotensin system.[8] The most common adverse events associated with this agent are hypotension, hyperkalemia, cough, dizziness, and renal failure. Thus, these potential adverse events should be monitored for.

Other classes of medications have new evidence for their use in heart failure as well, including SGLT-2 inhibitors. Most recently the EMPEROR-Reduced trial was published. This leads to the next question.

Question #4

In the EMPEROR-Reduced trial, which studied empagliflozin compared with placebo in patients with heart failure (NYHA class II-IV, EF ≤40%), what was the main outcome?

- **A. Significantly reduced composite of CV death or hospitalization for worsening heart failure vs placebo (in patients with and without DM)**
- B. Significantly increased mortality in patients without DM
- C. Significantly reduced composite of CV death or hospitalization for worsening heart failure vs placebo (in patients with preserved EF)
- D. Similar reduction in CV death and all-cause mortality as placebo

SGLT-2 inhibitors, though indicated for lowering blood glucose in patients with type 2 diabetes, have shown benefit in HF outcomes. Depending on the agent tested, this HF benefit has been seen in patients with or without diabetes.

Empagliflozin

Empagliflozin was given a Fast Track designation in 2019 for use in patients with chronic HF to reduce the risk of CV death and HF hospitalization. This designation was given based on the preliminary data from EMPEROR-Preserved and EMPEROR-Reduced trials. Both trials have primary outcomes of time to first event of adjudicated CV death or adjudicated hospitalization for HF in a 38-month period.[11]

The EMPEROR-Reduced trial was conducted in patients with New York Heart Association (NYHA) Functional Class II-IV HF and with reduced ejection fraction (EF 40% or less).[12] Patients with and without diabetes were enrolled. The primary outcome measure was a composite of CV death or hospitalization for worsening heart failure. The trial authors found that this composite measure was significantly reduced in the empagliflozin group compared with the placebo group, even in patients without diabetes; thus, making the correct answer A.

Hypoglycemic event rates were similar between groups. Most adverse event rates were similar between groups, though uncomplicated genitourinary tract infection was more frequent with empagliflozin.[12]

Dapagliflozin

Dapagliflozin was recently approved, based on the results of the DECLARE-TIMI 58 CV trial, for use in adults with type 2 diabetes and CV disease or multiple CV risk factors to reduce the risk of hospitalization with HF.[13]

Subsequently, the phase 3 DAPA-HF trial studied the effect of dapagliflozin versus placebo on patients with NYHA class II-IV HF and LVEF ≤40%. Dapagliflozin significantly reduced the composite measure of worsening HF compared with placebo, and the same results were seen in patients with or without diabetes. This led to dapagliflozin's approval in 2019 for the reduction of risk of hospitalization to heart failure or CV death, regardless of diabetes diagnosis. Adverse events were similar between groups, the most common being volume depletion, renal dysfunction, and hypoglycemia.[14]

Canagliflozin

Researchers analyzing the CANVAS study program looked at the potential benefit of canagliflozin in patients with type 2 diabetes, HF, and a history of atherosclerotic CV disease/CV risk factors.[15] Patients were labeled as having preserved EF if EF was ≥50% at admission, and reduced EF if EF was <50% or if the patient previously had reduced EF and no documented recovery. This analysis showed that canagliflozin lowered the risk of HF in patients with HFpEF and HFrEF. One risk, however, is the potential for lower leg amputation when used in patients with type 2 diabetes and CV disease or those at risk for CV disease.[16]

Case Continues

Within the availability of your region and healthcare system, it is important to incorporate your healthcare team and other specialists in the care of patients with heart failure. The primary care provider, at times with the help of a CV specialist, is in the best place to treat CV risk factors and incorporate newer agents into routine clinical practice. Clinicians can now choose from several therapies that have positive CV benefits in addition to their effects on blood glucose.[17]

These therapies have improved clinical outcomes for those with heart failure with or without comorbid diabetes and should be actively considered in each appropriate patient. The choice of therapy should always be discussed proactively with the patient to meet each patient's needs. The patient's clinical profile and safety/tolerance considerations will aid treatment decisions and thus, providers and patients should weigh the risks and benefits of therapies.

Clinicians should remember dosing and usage considerations in patients with renal impairment. SGLT-2 inhibitors require dose adjustments with reduced estimated glomerular filtration rates. Guidelines also indicate that caution should be taken when initiating or increasing SGLT-2 inhibitors' dosage because of acute kidney injury risk.[18] As well, for patients taking sacubitril/valsartan, clinicians should monitor for impaired renal function and increasing potassium levels.[8]

You order a repeat echocardiogram to re-stratify her heart failure, given her increased weight and pulmonary symptoms of fluid overload.

This brings us to our final clinical question.

Question #5

Based on Sherryl's clinical history and preferences, which of the following changes to her treatment regimen would be most appropriate to reduce her risk of heart failure events based on current evidence?

- A. Add an SGLT-2 inhibitor and discontinue her beta-blocker
- **B. Add an SGLT-2 inhibitor to her existing regimen**
- C. Discontinue her beta-blocker
- D. Add ivabradine to her existing regimen

As discussed earlier, recent trial data show that SGLT-2 inhibitors positively impact HF hospitalization rates and mortality. Taking SGLT-2 inhibitors and beta-blockers together is not contraindicated. More importantly, beta-blockers prevent cardiac remodeling associated with heart failure, *providing a mortality benefit in heart failure patients*, as such they should be continued.[19] Given that she requires further treatment for heart failure, adding an SGLT-2 inhibitor is a reasonable option. Ivabradine is indicated in patients with heart failure. However, it is specifically indicated in patients with heart failure with reduced ejection fraction, with a heart rate ≥70 beats per minute who are in sinus rhythm.[7] This patient has atrial fibrillation and has an irregularly irregular heart beat on examination so this medication is not appropriate for her. This indicates the correct answer is B.

Other considerations include adding a mineralocorticoid receptor antagonist (e.g., spironolactone and eplerenone). These agents are associated with improved survival in patients with HF with reduced ejection fraction. Specifically, in the RALES trial, spironolactone showed a significant mortality benefit in patients with NYHA class III or IV HF and EF ≤35 percent.[20,21] The EMPHASIS-HF trial showed the benefit of eplerenone on reduced overall and cardiovascular mortality in patients with NYHA class II HF and either an EF ≤30 percent or LVEF >30 and ≤35 percent and QRS duration >130 ms.[22]

Case Continues

You and Sherryl discuss the potential advantages and limitations of both classes of agents. You both decide that the SGLT2 inhibitor, empagliflozin, is a reasonable option given its favorable efficacy and safety profile and proven HF, CV, and CKD benefits. She continues using her previous medications (including furosemide 40 mg PO QD, valsartan 160 mg PO BID, and carvedilol 12.5 mg PO BID) and begins taking empagliflozin 10 mg once daily.

With pharmacological interventions, you also help support lifestyle changes to improve her heart health. These interventions include weight-loss counseling, which may include the Dietary Approaches to Stop Hypertension (DASH) diet, and increasing omega-3 fatty acids, plant intake, and physical activity.[23–25]

In 3 months, Sherryl returns to the office and her breathing and lower limb edema have improved. Functionally, she has not quite returned to her previous exercise capacity, but is much improved. She can now climb one set of stairs without impairment. Her hemoglobin A1C has decreased slightly to 5.4%, and she reports no notable adverse effects since starting empagliflozin. You continue to monitor her renal function and note that a drop in eGFR to below 45 mL/min/1.73 m^2 would warrant discontinuation.[26]

Conclusions

HF is a serious condition with potentially devastating consequences. Its outcomes have remained relatively stagnant over the past years; however, new treatment options have emerged, showing promise. Still, PAs face knowledge gaps in the diagnosis and treatment of this condition. To treat HF effectively, it must first be diagnosed through effective history-taking and physical examination. Guideline updates have highlighted the use of investigational and newer biomarkers for diagnosis and disease stratification.

Evidence-based guidelines provide clinicians with a roadmap for providing patients with the best possible treatment. The implementation of these recommendations is crucial for maximizing the benefits of HF therapy in clinical practice. Similarly, type 2 diabetes is frequently comorbid with HF, so both conditions require effective co-management. SGLT-2 inhibitors have new evidence for their benefit in patients with heart failure, both with and without diabetes. Greater attention to all these concerns will help patients derive maximum benefits from HF management and experience an improved quality of life.

CLINICAL PEARL

We hope you have enjoyed this *eCase Challenge* and that you have increased your knowledge and confidence in diagnosing and managing patients with chronic heart failure. Chronic heart failure can be tricky to diagnose in its early stages.

Being mindful of careful history taking, especially regarding changing exercise ability and functional status, high-yield physical examination findings can include an S3 to rule in chronic heart failure, though it is an uncommon finding, and the absence of rales to rule out chronic heart failure. Echocardiography can help tease out the cause and type of heart failure, but heart failure remains a clinical diagnosis.

Upon diagnosis, the key is taking the initial time to explain what heart failure is, how the patient acquired it and how to manage it.

Remember to use your health care team to help in education. Treatments for chronic heart failure are evolving. Ivabradine is recommended for lowering hospitalization rates and worsening heart failure in patients, one, with stable symptomatic chronic heart failure with a left ventricular ejection fraction of 35% or less; two, who are in sinus rhythm with a heart rate of 70 bpm or more; and three, who are taking maximally tolerated doses of beta blockers or have contraindications to them.

Sacubitril/valsartan, an ARNI, has shown positive results in lowering cardiovascular death and hospitalizations in patients with New York Heart Association class II through IV heart failure with reduced ejection fraction of 40% or less.

More recently, SGLT-2 inhibitors have shown positive heart failure outcomes. Specifically, based on positive trial results, dapagliflozin was approved for reducing the risk of hospitalization for heart failure in patients with type 2 diabetes.

In 2020, dapagliflozin was also approved for the treatment of heart failure in patients with heart failure with reduced ejection fraction even in the absence of diabetes.

Canagliflozin has been approved for the reduction of risk of hospitalization for heart failure in patients with type 2 diabetes and diabetic kidney disease.

Empagliflozin is still in trials for treating heart failure.

But it is important not to forget the importance of lifestyle modification in helping patients with and at risk for heart failure. Key elements for counseling include smoking cessation, alcohol reduction, weight loss and perhaps sodium and fluid restriction.

Thank you again for your participation in this *eCase Challenge.*

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CME POST-TEST: Participants must: 1) read the educational objectives and faculty disclosures; 2) study the educational materials; 3) complete the post assessments in Learning Central. See page 2 for further information.

Question #1

Based on likelihood ratios, which of the following exam findings/investigations proved to be the most useful test to rule out heart failure (HF)?

A. Any EKG abnormality
B. Chest x-ray showing no evidence of cardiomegaly
C. Wheezes
D. Serum BNP < 100 pg/mL

Question #2

Which class of antihypertensives has NOT been shown to improve mortality in HF?

A. ACE inhibitors
B. Angiotensin II Receptor Blockers (ARBs)
C. Beta-blockers
D. Loop diuretics

Question #3

Which of the following exam findings/investigations is associated with hyperkalemia (elevated potassium levels)?

A. Elevated/peaked T waves
B. Flattened T waves
C. Slowing of heart rate
D. Spasms/tetany

Question #4

The 2017 ACC/AHA guidelines update recommend an angiotensin receptor-neprilysin inhibitor (ANRI) for which specific patient populations?

A. Chronic heart failure and left ventricular dysfunction
B. Chronic heart failure with reduced ejection fraction, NYHA Functional Class II-III, who are able to tolerate an ACEi or ARB
C. Heart failure in patients with type 2 diabetes (and established cardiovascular disease or multiple cardiovascular risk factors)
D. Symptomatic chronic heart failure, with ejection fraction ≤ 35%, in sinus rhythm, with HR ≥ 70 bpm, and already taking maximally tolerated doses of beta-blockers or contraindication to beta-blockers

Question #5

Which of the following is true about SGLT-2 inhibitors?

A. Certain agents have shown benefit in clinical trials for heart failure with reduced ejection fraction without diabetes
B. Common adverse events include hypertension and palpitations
C. Evidence for benefit in heart failure with preserved ejection fraction
D. No evidence for benefit in chronic kidney disease

Question #6

What consideration must be made when prescribing an ANRI?

A. Hypertension is a potential adverse effect
B. In patients taking an ACE inhibitor or ARB, they require a washout period of 36 hours prior to initiating an ARNI
C. In patients taking beta-blockers, the beta-blocker must be discontinued
D. Monitor BNP levels to assess therapeutic response

Question #7

When examining a patient and hearing an S3 heart sound, a primary care provider should always consider the possibility of which of the following?

A. Atrial fibrillation
B. Cardiomegaly
C. Hypertension
D. Volume overload

Question #8

Which of the following tools is considered "gold standard" for the diagnosis of HF?

A. Brain natriuretic peptide (BNP)
B. Cardiac CT scan
C. Echocardiogram
D. EKG

Question #9

A 56-year-old Caucasian man with a history of a large anterior wall myocardial infarction and an EF of 35% presents to your clinic. He notes shortness of breath after climbing two flights of stairs and after walking four or five blocks but denies PND or orthopnea. On examination he is in sinus rhythm with a resting heart rate of 95 beats per minute. He takes aspirin, atorvastatin, metoprolol, lisinopril and eplerenone. After diuresis, which of the following is the best step in managing his heart failure?

A. Start hydralazine and isosorbide dinitrate
B. Start digoxin
C. Start ivabradine
D. Hospitalization for intravenous dobutamine infusion

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