Should Asymptomatic Patients Be Advised to Undergo Electrocardiographic Stress Tests?

Moderated by **Joseph Alpert, MD**[1]

Discussants: **Ezra A. Amsterdam, MD**[2]**; Robert Harrington, MD**[3]

DR. ALPERT: Hello, I'm Joseph Alpert. I'm Professor of Medicine at the University of Arizona College of Medicine and Editor-in-Chief of *The American Journal of Medicine*. I'm here with two of the most distinguished clinical and investigative cardiologists in the United States today: Dr. Ezra Amsterdam and Dr. Robert Harrington. I'm going to let them introduce themselves, and then we're going to talk about a question that comes up every single day in clinical practice: Do we need to perform exercise stress tests—either routine electrocardiogram (ECG) or the more complex ones with imaging—in patients who are asymptomatic?

Dr. Amsterdam, why don't we start with you?

DR. AMSTERDAM: I'm Professor of Internal Medicine at University of California—Davis and Associate Chief (Academic Affairs) of the Division of Cardiovascular Medicine, and currently Chair of the writing committee for full revision of the American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the management of patients with non-ST-elevation acute coronary syndrome.

DR. HARRINGTON: I'm Bob Harrington. I'm Professor of Medicine at Stanford University and the Chairman of the Department of Medicine. I am also an interventional cardiologist.

DR. ALPERT: We are here today to talk about exercise testing or stress testing, as it's often called, in patients who are asymptomatic. I participated a few years ago in preparing the ACC/AHA guidelines[1] on the evaluation of patients with asymptomatic coronary disease; routine exercise testing in the asymptomatic patient was thought to be a class III indication. In other words, you don't do it, because the information you get is going to be more confusing and may result in unnecessary further testing that could lead to complications. I always say, as per Alpert's rule, that a least indicated test is more likely to be complicated and will, in some way, hurt the patient and make both of you feel terrible.

Do both of you agree that one shouldn't perform routine exercise testing on asymptomatic patients with few, mild, or moderate coronary risk factors?

DR. HARRINGTON: The guidelines tell us that the routine use of an exercise test is not recommended. In fact, as you say, it's a class III recommendation, which means it's something we should not do; I agree with that. This recommendation is based on the evidence as it exists today, and I don't understand why we would promote it in routine clinical practice.

ABSTRACT

The discussion focused primarily on: 1) The existing recommendations on the use of electrocardiographic stress testing in asymptomatic patients; 2) exceptions/qualifiers in the non-use of stress testing in asymptomatic patients; 3) how to assess an asymptomatic state; and 4) the role of stress imaging in asymptomatic patients.

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We must consider this when the information garnered from an exercise test is helpful in defining how to approach that patient and what the patient would like to do with their activities?

DR. ALPERT: It's not an absolute "no"; instead, it's a "no" with a possible qualified "yes," depending on circumstances.

DR. AMSTERDAM: I would agree completely with both of you, and I would also say that the answer is "no," but it's a qualified "no." I think that probably even with those qualifications, the emphasis still has to be on class III, because as with many cardiac tests, more are being performed than are actually needed.

Even though there may be an indication, we have to carefully consider what we are going to do with the information and how it will help the patient.

DR. HARRINGTON: I'm an interventional cardiologist, so I see these patients when they're referred to the catheterization laboratory after an exercise study for diagnostic coronary angiography. I think Dr. Amsterdam said something that is really important: you need to think about what you're going to do with the information, because now you're going down a road that leads to decision-making that might have been unnecessary to begin with, and I think we need to keep that in mind.

DR. ALPERT: These are excellent points, and it reminds me of my earlier years when I was a resident. The old-time clinicians used to tell us not to order a test unless we were going to do something about the result. A lot of that attitude has died out today, partly because of defensive medicine and partly because we are now aware that we need to be fully thorough. But, when we start picking up abnormal findings, for example, on routine computed tomography (CT) scans, we start going down a path that we probably don't want to take, since in most instances, the findings are irrelevant, and it results in a lot of unnecessary testing, which is sometimes harmful to the patient.

> ***"According to the ACC/AHA guidelines, routine exercise testing in the asymptomatic patient is a class III indication and therefore not recommended because the information you get is going to be more confusing and may lead to unnecessary further testing that could lead to complications."***
>
> **Joseph Alpert**

DR. AMSTERDAM: I completely agree and I underscore the issue of the use of this information, which leads to the problem of a positive test. We have to be careful that a positive exercise treadmill test is not an automatic indication for cardiac catheterization for asymptomatic or even symptomatic patients.

DR. HARRINGTON: Yes, it's a really interesting dilemma, isn't it, Dr. Amsterdam? Here, you see people who are referred for a coronary angiography who have had a positive stress test. As we all know, the positive stress test indicates anything between a low risk to a very high risk. I do think that the caveats brought up by you and Dr. Alpert are the important ones for our audience to consider. You really need to know what you will do with this information.

As I make rounds with the fellows and the house officers, I always ask them to think through their decision-making analysis; if you get a positive result, what are you going to do? If you get a negative test, what are you going to do? Do this before you order further tests. There's too much of an emphasis on ordering tests, and in many ways, the electronic medical systems have made that easier. You check the box and things happen.

DR. AMSTERDAM: I am a strong advocate of the treadmill test. I think it has important indications and uses. My caveats here are not because I don't believe in the value of treadmill testing. I believe that, when appropriate and indicated, we should be doing more treadmill tests and fewer stress imaging studies. I think we do too many of the latter tests.

DR. HARRINGTON: We really could be talking about whether we should perform routine stress testing in asymptomatic individuals, but maybe there are some qualifiers.

If we decide that a person needs an exercise or a stress test, what method should we use to decide upon it? I agree with you that we

underutilize ECG stress testing, by far, and all that we can learn from it. The default practice in many ways is to directly opt for stress imaging, and I suspect we will discuss that as well.

DR. ALPERT: One of the things I want to point out is that in decision analysis and Bayesian thinking, the less common the illness in the population being tested, the more likely is the possibility of false positives than true positives or an equal number of true and false positives. And, so, in an asymptomatic population that doesn't have a very high incidence of the disease, one will consequently see a high number of false positives, and many patients will have a cardiac catheterization that they might not have needed.

Admittedly, cardiac catheterization is quite safe, but I remember a case at the University of Massachusetts with Dr. Harrington, when we catheterized the brother-in-law of a staff member, who kept coming to the emergency room with atypical chest pain despite negative exercise tests. During the procedure, a small atheroma traveled to his brain; it led to internuclear ophthalmoplegia, and he couldn't work for 6 months.

We all were at such a loss, because although the patient did go on to have normal coronaries, we shouldn't have performed a coronary angiography. So, I think that, each time we order a test, we should ask ourselves "what are we going to do if the outcome is such and such versus something else?" just as Dr. Harrington said.

Well, let's talk about some special subsets. Let's first talk about routine patients following angioplasty or bypass surgery, 6 or 8 months down the road. Do you think they ought to have an exercise test done to see how adequate the intervention has been?

DR. HARRINGTON: We know the answer to that one, Dr. Alpert, because there have been randomized clinical trials,[2] and the answer is a resounding "no." In the absence of symptoms, after a revascularization procedure, one should not routinely perform exercise tests, because the added information is not helpful.[3]

DR. ALPERT: Do you agree, Dr. Amsterdam?

DR. AMSTERDAM: I agree. I know of an individual who had bypass surgery about 10 years ago. He plays tennis, works full-time, is asymptomatic, and undergoes yearly stress myocardial perfusion testing. This abuse of testing is not rare.

DR. ALPERT: Here, in Arizona, there are a lot of snowbirds. Many of my patients see me once during their 4 or 5 months in Arizona. They come in and say, "Okay, my doctor said I could have my annual stress test here this year." Then we have to have a conversation in which I say, "I don't do routine stress tests every year." Then I explain to them that if they're vigorous and active and they're not having symptoms, it's very unlikely that the information will help us in any way, and it may actually end up leading to some harm.

Now, let's talk about the definition of asymptomatic. Do we believe he/she is asymptomatic if the patient says "I never have symptoms" or do we have to dig further?

DR. AMSTERDAM: Aortic stenosis (AS) is a very good example. I think of where we've come from years ago, when we didn't do stress testing in patients with critical AS. But, with echocardiography, we can identify critical AS in patients who, by history, are asymptomatic. But, sometimes we can't be sure about their level of activity or inactivity. In those cases, a supervised treadmill test is appropriate, safe, and informative, and may uncover symptoms at low exertion levels, inadequate rise in blood pressure, or ischemic ST segment changes, and these findings play an important role in the decision of whether or not to consider intervention for the AS.

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Ezra A. Amsterdam

DR. ALPERT: Dr. Harrington, do you agree?

DR. HARRINGTON: There's a whole body of literature on the regurgitant lesions,[4] including reports on patients with stenotic lesions that Dr. Amsterdam specifically talked about. Stress testing is used as a way to understand the pathobiology of the valve and whether or not it's time to think about intervention for that valve. That gets us into a complex area regarding how one utilizes the results of stress testing to guide the management of patients with valve disease.

But I think more broadly, Dr. Alpert, that your initial question is "How do we assess an asymptomatic state, and are there various degrees of asymptomatic states?" I think the answer to that resides in a careful history and physical examination. If, for example, our physical examination uncovers a very sedentary lifestyle for somebody who now wants to embark upon an active exercise program, and this person has multiple cardiac risk factors, which are perhaps not well managed, an exercise test as a prelude to exercise, or an exercise prescription, might well be a reasonable way ahead. That would be an example of an asymptomatic patient that would need to be evaluated further.

Dr. Amsterdam has mentioned the valve disease patient that we might manage with stress tests. I would add that we consider patients as asymptomatic until we start taking their histories. Then, we begin uncovering facts that might lead us to investigate the patient and even look for symptomatic coronary disease. So, I do think it's not something to use routinely. We should rely on our history and physical examination, and there are indications for which we might want to pursue stress testing in selected individuals.

DR. AMSTERDAM: We can certainly do better at history taking, but, as you said, exercise or stress testing is an extension of the history and physical examination that can fine-tune our clinical assessment. For example, exercise testing quantifies patients' functional capacity, and it is not uncommon to find a considerable disparity between a patient's history of physical examinations and what he is actually able to do on testing, with the latter being commonly far less.

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>
> **Robert Harrington**

DR. ALPERT: As I was sitting here, I was thinking about my days as a student, resident and fellow. Lewis Dexter, who, of course, is one of the great pioneer cardiologists of the 20th century, was my teacher and professor. He would often talk about patients with mitral stenosis. In those days, we had so many of them because Dwight Harken was at the Brigham performing 2 or 3 mitral valvuloplasties a day.

In those patients, Dexter always emphasized that it was important to have the spouse or friend there with the patient, because you would ask questions like "Have you had any shortness of breath when you exert yourself or when you're doing housework?" The patient would say "no," and the spouse would say, "No, they're not doing anything, they've stopped all exertion. They've stopped making the beds in the morning. They're not vacuuming. They're basically just sitting around all day." Of course, mitral stenosis was mostly seen in women.

I remember Dexter would often say to the patient, "Okay, let's go out and walk down a flight of stairs and up a flight of stairs." And when the patient would get down 3 or 4 stairs and had to stop because of dyspnea, you knew that the story was very different from what the patient was saying. So, it often helps to have corroboration. Again, when you think that the patient may not be giving you the true story, I think that's an indication for an exercise test as well.

DR. HARRINGTON: I think that Dr. Amsterdam's comment that it can be an extension of our history taking and physical examination is an important comment. I think of it with regard to patients who are referred to us and want to begin an exercise program. Many of us, when we reach middle age, decide that we need

to improve our exercise habits. As you start to uncover things from a history, which might concern you a bit, or if you want to lay out the exercise prescription safely for a middle-aged person with important risk factors, I think it can be an important addition to our history and physical findings.

In that case, you're absolutely taking full advantage of everything the exercise test offers: How far do they go? What happened to their heart rate? What happened to their blood pressure? Do they have any symptoms that limit them? What did their ECG look like? There's a lot of information to gain from the exercise test that is often not considered.

DR. ALPERT: I think that is so crucial, Dr. Harrington. The assessment of the treadmill exercise ECG, based on the ST segment alone, is really obsolete, and we don't emphasize much on that. I see that in many places. The exercise ECG, all the factors that you talked about, the hemodynamic factors, arrhythmia, the heart rate, the functional capacity, and the heart rate recovery, all are extremely important.

If those factors are actually looked at in a careful way by using the Duke treadmill score or some integrated score, when you compare that score to the nuclear or exercise echo, which I also am an advocate of, and if you use all the exercise treadmill test information, then the stress imaging tests are nearly as accurate as the standard ECG exercise stress test when you look at all the exercise data alongside the ST segment. Examples include total exercise time, maximum heart rate achieved, symptoms during or after exercise, blood pressure, and heart rate response.

There was the paper by Leslee Shaw and Nanette Wenger[5] that came out in late 2011, comparing myocardial perfusion stress imaging with exercise treadmill testing in low-risk women. This study showed that, in these women, there was very little or no significant difference in 2-year outcomes between the 2 tests, but the treadmill test was much less expensive. We don't teach that, and all the factors you just mentioned are neglected factors, Dr. Harrington.

DR. HARRINGTON: Yes, but in light of full disclosure, I introduced myself from Stanford, but I spent the 22 years before that at Duke and am well familiar with Dan Mark's work in developing the notion of the Duke treadmill score,[6,7] which again I think is underutilized. It's easy to order the imaging test. And as you say, Dr. Amsterdam, I think all 3 of us would agree there's an important role for imaging as an adjunct to exercise testing, but I think it's very easy to forget that you might not need it.

DR. AMSTERDAM: Absolutely, if you want to localize ischemia or estimate the extent of ischemia, those are appropriate indications. I want to note the role of stress testing in the patient who has been inactive and wants to undertake a vigorous exercise program, say, jogging or walk/jog. If such a patient has multiple risk factors, or is a male over 40 years of age or a postmenopausal woman, a stress test should be considered to provide a rational activity goal.

DR. ALPERT: Just to highlight something that you both said, because I think it's very important: so often, people just look at the ST segment and the heart rate and say that the patient didn't achieve a 95% heart rate, and therefore, the test doesn't give us the answer. But, in fact, the patient had a very excellent heart rate and blood pressure product, but perhaps didn't quite achieve 85% or 90% of the predicted maximum heart rate.

I see this all the time in the coronary care unit. A patient comes in with atypical chest pain, but only limited data can be obtained from his/her history on risk factors, etc, so you want to be a 100% certain before discharging him/her. So, we do a routine stress exercise test: an ECG test. The result shows that the patient maybe didn't quite achieve a 90% predicted maximum heart rate, but still had a very strong peak exercise heart rate-blood pressure product and no symptoms.

For me, that's all the information I need, because the patient came in with atypical rest pain. If the patient had unstable coronary disease, he/she would not be asymptomatic when I push the heart rate and blood pressure up to a reasonably good level, even if the patient didn't achieve the full diagnostic level that we normally like.

So again, I think you need to look at the whole test. You may also need to check whether there were arrhythmias. I've had a number of patients complain of palpitations. They say, "when I go for a walk in the morning, I get palpitations." Sometimes, I'll put them on the treadmill to see what are these palpitations, and often, as you both have seen numerous times, it turns out to be a small number of premature ventricular contractions or atrial premature beats. Then, you reassure the patient and you say, "We saw what it is and it's

nothing for you to worry about." So sometimes, the exercise test in that setting is actually therapeutic.

Let's talk a little bit about something that Dr. Amsterdam mentioned: the exercise prescription and screening of a person who is going to start an exercise program. Often, these are patients who have seen their primary care doctor. The primary care doctor points out that their lipids are abnormal and they have a diabetic tendency, some glucose intolerance, and slight hypertension. The patients are given a number of medicines, and then, the primary care doctor refers them to a cardiologist.

The patient, with a reasonable number of risk factors, is going to start a vigorous exercise program; let's say he/she has a positive family history of coronary disease developing in his/her relatives in their 50s. When you see such a patient with lots of risk factors who's going to start exercising, does it change your attitude about a routine exercise test?

DR. HARRINGTON: Yes, I actually send a lot of those patients for a stress test, in particular. As Dr. Amsterdam has already pointed out, for a man who is middle-aged or older or a woman who is postmenopausal, I do use the exercise test, but I spend a fair amount of time thinking about how active or inactive they really are and ask a lot of questions about what they do in their daily life while trying to gauge whether they are going to be pushing exercise more than I think they've been doing.

Most of these people who are thinking about embarking upon an exercise program are quite sedentary, and I find that the exercise test is helpful in many ways. It's obviously a screening tool for ischemia, but I do believe in its use for exercise prescription, because it helps set realistic goals.

When you've exerted many metabolic equivalent tasks, you can use that to start a conversation with the patient about what the goals for the exercise are going to be. Don't get discouraged starting out slow and building up, because the hardest thing with an exercise program is getting people to maintain it. So, I think the exercise test can be a good way of setting the baseline and allowing the patient to have some realistic expectations that are both safe and helpful from a psychological point of view.

STUDIES DISCUSSED:
PROMISE, WOMEN

DR. AMSTERDAM: I like that. I would add, Dr. Alpert, that we've been discussing patients who are sedentary and have multiple risk factors. The guidelines have discouraged, in most cases, exercise testing in the asymptomatic population, but they give a fair endorsement, a class IIa ("is reasonable") in the diabetic patient.

But again, what is to be done with the information? An ischemic response would urge intensive risk factor modification,

Clinical Implications

- A positive exercise treadmill test alone is not an indication for direct catheterization.
- The less common the illness in the population being tested, the more likely is the possibility of false positives than true positives or an equal number of true and false positives.
- In the absence of symptoms, after a revascularization procedure, one should not routinely perform exercise tests, because the added information is not helpful.
- Patient history has its limits, and careful stress testing can be used as an extension of the history because it provides further information.
- Stress testing is important in a patient with risk factors who has been inactive but wants to undertake an active, vigorous exercise program.
- In asymptomatic patients, there are some subsets of "asymptomatic" where exercise testing is a good idea, but not for the vast majority of patients.
- Laboratory investigations should only be ordered when the results will influence clinical decision making.

but diabetes is a coronary risk equivalent, and so we should already be engaging in intensive risk factor modification.

So, in general, in all patients, a positive stress test in an asymptomatic patient doesn't mean you go to the catheterization laboratory, but it does help convince the patient and the doctor to pursue more intensive risk factor modification if that's not already being done.

DR. ALPERT: It's interesting, Dr. Amsterdam, that you mention coronary calcification, because I was just going to say that I don't order a lot of coronary calcification CTs for somebody with a lot of risk factors, particularly someone who's diabetic, is young, has a family history of coronary artery disease, or has been quite sedentary, except in the setting we're just talking about. In some patients, I get the sense that they're not taking the whole issue seriously enough or it's the opposite: they're extremely nervous that they're going to have a heart attack at any minute.

I think the coronary CT is helpful in these settings. Now, if it's very positive, then I will often do a stress test on top of it—in other words, to try and determine the burden of ischemia. That's not a large number of patients, but it's a group with a large number of risk factors. In this group, you just have this sixth sense that there's a lot going on because of their long list of risk factors.

DR. AMSTERDAM: So, Dr. Alpert, will you do a coronary calcium CT without CT coronary angiography?

DR. ALPERT: Well, that's an evolution. We're part of the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) trial[8] right now that's making all those comparisons, so I will just recommend that the patient have a coronary calcium CT done first. Then, if there are a lot of risk factors for atherosclerosis, we talk about whether we're going to do a CT angiography or a stress test, and part of that will be answered in the PROMISE trial sometime in the next 18 months, when we'll see which test was the most useful.

My prejudice is that all these tests are going to give you equivalent information in terms of the diagnosis, and maybe, even just the Framingham Risk Score will give you almost as much information. But, that's why I don't do many coronary calcium CTs, maybe just 1 or 2 a year, except in a particular case where I feel like they're extremely anxious or they're not anxious enough and not taking it seriously. Otherwise, as you've talked about, I usually do exercise testing to help with exercise prescription.

DR. AMSTERDAM: We usually do CT coronary angiography with coronary artery calcium scoring.

DR. ALPERT: This may change depending upon the results of the trials that are coming.

I think we're almost out of time. This has really been a delight. It's always a pleasure talking with both of you because you're so knowledgeable and have so many excellent practical points. Maybe I could just summarize it by saying that the answer is that in asymptomatic patients, there are some subsets of "asymptomatic" where exercise testing is a good idea, but for the vast majority of patients, you don't need to do exercise testing, and certainly, routine yearly exercise testing ought to be prescribed.

Do each of you have any further comments?

DR. HARRINGTON: I think you've summarized it well, Dr. Alpert. It's not routine to test people who are asymptomatic, but there are things that can be learned through exercise testing, which can be applied to some patients who are asymptomatic and fall into special categories. So, a class III recommendation generally is a wise one, but there are some areas where equipoise still exists and the information may be helpful.

DR. ALPERT: Thank you very much, gentlemen.

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