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Guest: Dr. Evangelos Giannitsis is an Assistant Professor of Medicine at the Department of Cardiology at the University of Heidelberg, Germany.

Bob Barrett: This is a podcast from *Clinical Chemistry* sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I'm Bob Barrett.

If acute pulmonary embolism is not diagnosed early and treated appropriately, it can be lethal. This is a common disease with a high fatality rate, as some 300,000 people in the United States die from acute pulmonary embolism each year. Once pulmonary embolism is confirmed, individuals are managed according to risk. A number of different algorithms and biomarkers are used for risk stratification.

The January 2017 issue of *Clinical Chemistry* includes a mini review of biomarkers for clinical decision making in the management of pulmonary embolism. In this podcast, we're joined by one of the authors, Dr. Evangelos Giannitsis. He is an Assistant Professor of Medicine at the Department of Cardiology at the University of Heidelberg, Germany. Dr. Giannitsis served on the program committee of the European Society of Cardiology and is a member of the organization's working group for cardiac biomarkers. So Dr. Giannitsis, what is the most important difference between the previous and the current ESG Guidelines regarding risk stratification?

Dr. Giannitis: Before, there was classification of risk into high risk, intermediate risk and low risk. And particularly, the patients in the intermediate risk group were considered for thrombolytic therapy because they were believed to have the highest risk for adverse outcomes and complications and death, particularly those who had signs of right ventricular dysfunction plus elevated biomarkers, but still normal circulation.

So this changed. In the new guidelines, the risk classification now is modified. We have still a low risk patient group. We have a high risk patient group. But the intermediate risk group is dichotomized into an intermediate low risk group and an intermediate high risk group. And the intention is not longer to identify the patient who should receive thrombolytic therapy, but to identify the candidate who might be a candidate for thrombolytic therapy if he

further deteriorates. So a patient who still qualifies for monitoring and observation and not discharged home, but not automatically qualifies for thrombolytic therapy.

On the other hand, the patient with a low risk, he is somebody who could be considered for early discharge home and home treatment. So this is totally a new concept of risk stratification and patient management.

Bob Barrett: How did the PEITHO study influence risk stratification concepts?

Dr. Giannitis: The PEITHO study was randomized trial on 1,005 patients with hemodynamically stable pulmonary embolism, especially the group of interest in whom risk stratification could show beneficial effects of thrombolytic therapy. So in this group, patients were randomized to receive thrombolytic therapy if they fulfilled the criteria of having right ventricular dysfunction by imaging, or an elevated biomarker of myocardial injury and in that study, troponin was selected as the marker of choice for this.

Unfortunately, the results of the PEITHO trial were not as expected. So on the one hand, there was a benefit of thrombolytic therapy among patients who had elevated biomarkers plus the right ventricular dysfunction, but these patients also suffered significantly more major bleedings. So the concept of directing a patient with high-risk features to thrombolytic therapy was not confirmed by this trial, and the whole concept of risk stratification and allocation to therapy was reconsidered. And after that, several new risk stratification scores were developed and validated in order to have more precise individualized risk stratification and management options for patients with hemodynamically stable pulmonary embolism.

Bob Barrett: What role do biomarkers play in the management of pulmonary embolism?

Dr. Giannitis: Biomarkers are very important tools. They give us information on myocardial injury or pressure and stress overload to the heart, particularly to the right ventricle.

And they were used to risk estimate the patient into intermediate risk patient requiring thrombolytic therapy, or not. Nowadays, the biomarker information is important in order to give adjunctive information to clinical scores, and if a patient has an intermediate risk and has both evidence of right ventricular dysfunction by imaging and a positive biomarker result, then he is classified as an intermediate high risk patient, and again, these patients need monitoring to detect the compensation earlier or to detect the need of rescue reperfusion therapy.

Otherwise, if a patient at intermediate risk, as classified by the PESI (Pulmonary Embolism Severity Index) or Simplified PESI score who has only one indicator positive, means imaging evidence of right ventricular dysfunction or biomarker evidence of injury or fluid or pressure overload or both negative, then this patient is classified as an intermediate low risk patient.

And in these patients, hospitalization is required and in hospital treatment of pulmonary embolism, but they do not need monitoring as close as patients with the intermediate high risk classification.

Bob Barrett: Finally doctor, you spoke of patients who could go home early. Who are suitable candidates for early discharge and home treatment after confirmation of pulmonary embolism?

Dr. Giannitis: These are patients that have been classified as low risk patients, and low risk is either identified by a PESI score, this is one of the at least two scores that are available for this risk classification. So if a patient has a PESI class of two or lower, or a Simplified PESI class of zero, he is estimated as being low risk patient. This patient can be considered for early discharge and outpatient treatment.

Bob Barrett: Dr. Evangelos Giannitsis is an Assistant Professor of Medicine at the Department of Cardiology at the University of Heidelberg, Germany. He's been our guest in this podcast from *Clinical Chemistry*. I'm Bob Barrett. Thanks for listening.