Article:
Karen A. Moser.
D-dimer: Common Assay, Challenges Abound, Caution Advised.
J Appl Lab Med 2019;3:756-59.
http://jalm.aaccjnls.org/content/3/5/756

Guest: Dr. Karen Moser is an Assistant Professor of Pathology at the University of Utah and the Medical Director of the Hemostasis/Thrombosis Laboratory at ARUP Laboratories.

Randye Kaye: Hello, and welcome to this edition of "JALM Talk," from *The Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

Venous thromboembolism, or VTE, is a serious medical condition characterized by a blood clot in a vein, also known as deep vein thrombosis. If the clot breaks free from the vein, it can cause a life-threatening pulmonary embolism by blocking blood supply to the lungs. Over 100,000 Americans may die from VTE per year. If recognized quickly, VTE may be effectively treated with anticoagulant therapy; however, it can be difficult to detect when VTE is occurring and when treatment is warranted, thus the clinical laboratory plays an important role in performing diagnostic tests for VTE.

One such test that is commonly used in this context is D-dimer. The March 2019 issue of *The Journal of Applied Laboratory Medicine* includes a Review article by Drs. Rugvedita Parakh and Daniel Sabath, entitled "Venous Thromboembolism: Role of the Clinical Laboratory in Diagnoses and Management." In the same issue is an Editorial by Dr. Karen Moser titled, "D-dimer: Common Assay, Challenges Abound, Caution Advised." Dr. Moser is our guest on this podcast.

Dr. Moser is an Assistant Professor of Pathology at the University of Utah and the Medical Director of the Hemostasis/Thrombosis Laboratory at ARUP Laboratories. Her research interests included hemostasis and thrombosis testing and pathology education. She is a current member of the College of American Pathologists, Hemostasis and Thrombosis Committee. Welcome Dr. Moser. So, what is D-dimer and when is testing for it clinically useful?

Karen Moser: D-dimer is a fibrin degradation product that's formed when cross linked fibrin is degraded by plasmin. It contains two fibrin D domains, hence the name D-dimer. We measure D-dimer in a clinical laboratory using immunologic assays such enzyme immunoassays or latex immunoassays. D-dimer is

clinically useful in evaluation of both VTE and disseminated intravascular coagulation, or DIC.

Randye Kaye: I see. So, are there tools, additional tools, that can help physicians decide if D-dimer testing is appropriate for a given patient?

Karen Moser: Yes, there are validated clinical decision rules, such as the Wells score of the Geneva score, that can help physicians determine if patient's pretest probability of VTE or pulmonary embolism. Experienced physicians can also use their clinical judgment to assess pretest probability which appears to be comparable to the performance of the decision rule. In patients with low pretest probability, D-dimer testing with an assay cleared for VTE exclusion can rule out VTE if the result is negative without any further testing.

In patients with intermediate or high pretest probability, imaging studies are required to definitively rule VTE in or out. It's also important to keep in mind that that the diagnostic algorithms combining pretest probability, D-dimer and imaging for VTE diagnosis were developed in non-pregnant adults. So, they may not apply to pregnant women or children.

Randye Kaye: Are there factors that laboratories should consider when they are reporting the D-dimer result?

Karen Moser: There are several important considerations for D-dimer reporting and I will focus on two key points now.

Randye Kaye: Okay.

Karen Moser: First, laboratories should consider whether their D-dimer assay is cleared for exclusion of VTE or as an aid in diagnosis of VTE. These are designations made on the basis of data submitted by the assay manufacturer to the FDA for review and this information will be clearly stated in the package insert. It is important to include this information in laboratory reports as well so that only D-dimer assays cleared for exclusion of VTE are used to rule out VTE along with low pretest probability.

Second, laboratories need to be aware of which unit type their D-dimer results are reported in. Currently, D-dimer assays can be reported in either D-dimer units, abbreviated DDU, or fibrinogen equivalent units, abbreviated FEU.

The unitized differ by a factor of approximately two, that is to say, 1 ng/mL DDU is equal to 2 ng/mL FEU. Reporting D-dimer results in the unit type specified by the manufacturer is considered a best practice. It's also not recommended to

convert mathematically between unit types to eliminate the conversion as a potential source of error.

Randye Kaye: Okay, thank you so much. Can you clear something up for me, what is it mean for assays to be standardized, and why aren't D-dimer assays standardized?

Karen Moser: I have that question too. One would expect a standardized test to be reported in the same units between laboratories and also to be calibrated with a calibrator traceable to a standard. Neither of these considerations are true for D-dimer. The differing units as well as different monoclonal antibodies specificity for D-dimer between kits reflect the differences between the many commercially available assays developed by different manufactures. There's also not an international standard available for D-dimer assay calibration. Efforts to develop a standard in the past have been unsuccessful possibly due to this differing antibody specificity between kits that we mentioned earlier. There have been several calls for standardization of D-dimer assays in the recent literature and this is an effort where our continued effort is required.

Randye Kaye: Thank you, very interesting. Now, last question, how can laboratories apply these important considerations for D-dimer testing into clinical practice?

Karen Moser: I have three pearls for laboratories to consider when they're performing D-dimer tests. One, be aware of whether your D-dimer assay is cleared for exclusion of VTE or as an aid and diagnosis of VTE. Two, know which unit type your D-dimer assay is reported in, and make sure that matches the manufacturer's recommendation, and that the unit type is clearly stated on your report.

Three, when you are reviewing literature about the clinical utility of D-dimer testing, make sure that you clearly identify which D-dimer assays were used in the study and that you know which units the D-dimer results are reported in. Because of the variability between D-dimer assays, it is so important to know this information to understand whether the claims made in the paper including any stated cutoff, can apply to your D-dimer result.

Randye Kaye: Thank you so much, very interesting. Thank you for joining us today Dr. Moser.

Karen Moser: Thank you.

Randye Kaye: That was Dr. Karen Moser from the University of Utah and ARUP Laboratories discussing her editorial on the challenges and considerations for D-dimer testing in venous thromboembolism from the March 2019 issue of JALM.

Thanks for tuning in to this episode of "JALM Talk." See you next time and don't forget to submit something for us to talk.