Clinical pathology selected abstracts

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Alternatives to prostate-specific antigen tests for detecting clinically significant prostate cancer

August 2022—Prostate cancer is the second leading cause of cancer death in men, following lung cancer. It is necessary to balance efforts to identify prostate cancer in the early stages against complications and harms from overtreatment and overdiagnosis. Even though the large-scale European Randomized Study of Screening for Prostate Cancer showed that prostate-specific antigen (PSA) screening reduces prostate cancer mortality, it is still necessary to evaluate new tests for their ability to better predict aggressive prostate cancer and prevent overdiagnosis of slower-growing insignificant forms of the disease. Among several free-PSA subforms that have been studied, proPSA was shown to have higher values in prostate cancer. Of the circulating forms of proPSA identified in serum, [-2]proPSA has greater stability, and Beckman Coulter has developed an automated immunoassay to detect it. The authors conducted a study to evaluate the clinical utility of [-2]proPSA derivatives in detecting clinically significant prostate cancer (csPCa) and define acceptable cutoffs. They also sought to compare the diagnostic accuracy of [-2]proPSA to PSA and percentage of free PSA (%fPSA). The authors enrolled in the study 237 men with a PSA value between 2 and 10 ng/mL who were scheduled for a prostate biopsy. Blood was collected for PSA, free PSA (fPSA), and [-2]proPSA on the day of the biopsy but before the procedure. The investigators applied parametric and nonparametric tests, receiver operating characteristic curves, and logistic regression analysis to show the outcomes for csPCa and prostate cancer overall. The results showed that 118 (49.8 percent) of the 237 patients had prostate cancer, including 100 (42.2 percent) who had csPCa. The [-2]proPSA derivatives were significantly higher in csPCa and prostate cancer as a whole ($P<0.001$). The areas under the curve for predicting csPCa were higher for the percentage of [-2]proPSA (%[-2]proPSA; 0.781) and the Prostate Health Index (PHI; 0.814) than for PSA (0.651) and %fPSA (0.724). Of interest, there was an 11 percent gain in diagnostic accuracy when %[-2]proPSA or the PHI was added to the base algorithm of PSA and %fPSA. The data showed that 25 to 29 percent of biopsies could have been spared using %[-2]proPSA and the PHI in the testing algorithm, missing only 10 percent of csPCa. The authors obtained the same results using [-2]proPSA as a reflex test when %fPSA was 25 percent or less. The authors concluded that [-2]proPSA derivatives could improve the diagnostic accuracy of csPCa when PSA values were between 2 and 10 ng/mL. This would prevent unnecessary biopsies and identify patients needing active surveillance. The authors noted that the use of [-2]proPSA as a reflex test based on the %fPSA values can be a cost-effective testing approach for csPCA while reducing the potential harm from unnecessary biopsies.

Garrido MM, Marta JC, Bernardino RM, et al. The percentage of [-2]pro-prostate-specific antigen and the Prostate Health Index outperform prostate-specific antigen and the percentage of free prostate-specific antigen in the detection of clinically significant prostate cancer and can be used as reflex tests. *Arch Pathol Lab Med*. 2022;146:691–700.

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How a potassium-based quality-of-service metric reduces phlebotomy errors

Preanalytical errors in laboratory testing are a frequent cause of inaccurate clinical lab results and can occur at any time—from test ordering, to sample collection, to specimen transport and handling. Data about preanalytical errors are often collected, and monitoring helps identify areas in which such errors are more likely to occur. Preanalytical errors often occur during sample-collection steps and can involve tourniquet time, tube type, order of draw, and filling, mixing, and transporting specimens to prevent hemolysis. If performed incorrectly, these process steps can

cause changes in concentrations of critical serum and plasma analytes, including potassium. Because true hyperkalemia is a life-threatening panic value, it is important to address phlebotomy steps that may lead to spurious potassium results. The authors described herein the institutionwide implementation of a continuous quality management program focused on a potassium phlebotomy metric that supports continuous feedback, intervention, and retraining. This quality-of-service phlebotomy metric involves systematically evaluating plasma potassium concentrations per phlebotomist to detect preanalytical biases caused by variations in sample collection and handling that do not lead to frank hemolysis. The authors monitored potassium and retrained 26 full-time phlebotomists as part of their quality-of-service intervention pilot program. They periodically downloaded potassium values, measured between January 2013 and December 2020, from the electronic health record system. The name of the person performing the phlebotomy and the collection location, time, and date were recorded. The potassium threshold selected for hyperkalemia was more than 5.2 mmol/L and for hypokalemia was up to 3.5 mmol/L. The authors assessed how variations in potassium concentrations affected resource utilization. Laboratory-associated costs were calculated based on turnaround time, processing/procedure-related times and expenses, and the average hourly salaries of lab personnel, including phlebotomists. The authors developed an algorithm for monitoring data and providing feedback on a per phlebotomist basis. Their project was divided into three phases: Phase one involved investigating phlebotomy techniques and procedures; phase two involved implementing monthly surveillance on a per phlebotomist basis and monitoring potassium values for their effects on resource utilization; and phase three involved institutionwide use of the aforementioned quality-of-service metric. The results showed that intervention and retraining reinforced compliance with phlebotomy techniques and reduced the percentage of venipunctures with potassium results above the threshold. This resulted in an average savings of 13 to 100 percent for each high-volume phlebotomist and reduced the number of repeat blood draws needed to confirm hyperkalemia. Supervisors initially met with each phlebotomist monthly to review the data but, eventually, met only with those who had more than two percent of draws with potassium values above the 5.2 mmol/L threshold, to help reinforce compliance with techniques. The authors concluded that the ability to provide feedback and retraining on a per phlebotomist basis reduced erroneous hyperkalemia events and critical value alerts and led to significant cost savings. The simplicity and impact of this quality-of-service metric may help reduce preanalytical errors from phlebotomy techniques at other institutions as well.

Lucas F, Mata DA, Greenblatt MB, et al. A potassium-based quality-of-service metric reduces phlebotomy errors, resulting in improved patient safety and decreased cost. *Am J Clin Pathol*. 2022;157:789–798.

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