Clinical pathology selected abstracts

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Prostate cancer screening with PSA test: systematic review and meta-analysis

December 2018—Prostate cancer is the second most common cancer and the fifth leading cause of cancer-associated mortality among men worldwide. The use of serum prostate-specific antigen (PSA) to screen for prostate cancer is intended to detect the cancer at an early stage to reduce overall and disease-specific mortality. However, evidence that PSA screening for prostate cancer saves lives is somewhat lacking. Furthermore, there is concern about harm from overdiagnosis and complications from diagnosis and treatments for what may be an indolent disease. The U.S. Preventive Services Task Force recently updated its recommendation statement for PSA-based screening, changing it from a grade D recommendation, which advises against PSA-based screening for prostate cancer, to a grade C recommendation, which advocates for an individualized approach to screening. The authors performed a systematic review and meta-analysis of all available randomized trials that assessed PSA-based screening for prostate cancer in an effort to create trustworthy practice guidelines in a timely manner. They conducted the review in response to the recent Cluster Randomised Trial of PSA Testing for Prostate Cancer performed in the United Kingdom. The authors conducted an electronic search of databases up to April 2018, seeking randomized controlled trials comparing PSA screening with usual care in men without a diagnosis of prostate cancer. At least two reviewers screened studies, extracted data, and assessed the quality of eligible studies. A parallel guideline committee also provided input on the study design and selection of outcomes important to patients. The authors used a random-effects model to obtain an incidence rate ratio and conducted subgroup analysis when feasible. The quality of evidence was assessed by the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) approach. The authors found five randomized controlled trials enrolling 721,718 men. The studies varied with respect to screening frequency and intervals, PSA threshold for biopsy, and risk of bias. The results showed that screening probably has no effect on all-cause mortality and may have no effect on prostate-specific mortality. Sensitivity analysis at lower risk of bias also showed that PSA screening has no effect on all-cause mortality but may have a small effect on prostate-specific mortality. The authors noted that this results in one less death from prostate cancer per 1,000 men screened over 10 years. In summary, screening for prostate cancer can lead to a small reduction in disease-specific mortality over 10 years but does not impact overall mortality. The authors recommend that when clinicians and patients consider PSA-based screening, they weigh these benefits against the potential complications from biopsies and subsequent treatments as well as the risk of overdiagnosis and overtreatment.

Dragan I, Djulbegovic M, Jung J, et al. Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. *BMJ.* 2018;362. doi.org/10.1136/bmj.k3519.

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A combination lymphocyte apoptosis model to predict survival of sepsis patients

In the United States, about half of patients with severe sepsis are treated in the ICU, where sepsis is the leading cause of death. Sepsis is considered a complex clinical syndrome due to the ambiguity of clinical findings and the challenge of unclear risk stratification. The initial phase of sepsis is characterized by an inflammatory response, which is thought to be accompanied by downregulation of immune cell function, including that of lymphocytes, dendritic cells, and neutrophils, which could lead to further immunosuppression and worsening outcomes. Studies have shown that lymphocyte apoptosis plays a role in this immunosuppressive state, which suggests that lymphocyte apoptosis may be a potential prognostic predictor for sepsis patients. To identify possible prognostic

markers in sepsis, the authors designed a lymphocyte apoptosis model, which is a combination of parameters measuring lymphocyte apoptosis (lymphocyte apoptotic percentage, lymphocyte count, and cytochrome c level) and immune function (monocyte expression of HLA-DR, Th1/Th2 ratio, CD4+/CD8+ T cell ratio, and inflammatory cytokine levels). They then conducted a prospective observational study and enrolled sepsis patients without multiple organ dysfunction syndrome who were admitted to the ICU. They recorded progression of sepsis and outcomes at 28 days. The study showed that compared with survivors, nonsurvivors had significantly higher lymphocyte apoptotic percentages and plasma cytochrome c levels and significantly lower lymphocyte counts, Th1/Th2 ratios, and HLA-DR expression on day one of admission. Multivariate analysis indicated that cytochrome c levels, lymphocyte apoptotic percentage, lymphocyte count, and HLA-DR expression were independent predictors of 28-day mortality. A regression analysis also showed that these risk factors predicted 28-day mortality with greater accuracy than did the APACHE II score or any single biomarker. In summary, the lymphocyte apoptosis model may be useful for risk stratification and predicting the prognosis of sepsis patients. This suggests that patients with high scores should be started on therapy as quickly as possible to prevent further deterioration of their condition. The authors noted that further validation of the model is needed.

Jiang W, Zhong W, Deng Y, et al. Evaluation of a combination “lymphocyte apoptosis model” to predict survival of sepsis patients in an intensive care unit. *BMC Anesthesiol.* 2018;18. doi.org/10.1186/s12871-018-0535-3.

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