Top Tips & Choosing Wisely XXXV

Recommendations from the American Academy of Pediatrics Section on Cardiology and Cardiac Surgery, American Society for Transplantation and Cellular Therapy, and Cell Therapy Transplant Canada

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This is my 35th article on Choosing Wisely from the Board of Internal Medicine Foundation. As previously noted, each specialty group is developing "Five or More Things that Physicians and Patients Should Know."

1. RECOMMENDATIONS ON PEDIATRIC CARDIOLOGY AND CARDIAC SURGERY

1. **Troponins should not be ordered for the routine evaluation of pediatric chest pain in the absence of a concerning history or abnormal electrocardiogram (ECG).**

Troponin-I levels are not as useful in the pediatric population, since the great majority of pediatric patients presenting with chest pain have normal troponin levels. They have also not been shown to be reliably correlated with severity or prognosis of many cardiac diseases known to cause chest pain in pediatric patients. Consideration of obtaining troponin levels is reasonable in those with a family history of very early cardiovascular disease, or a history suggestive of myocarditis/pericarditis.

2. A screening ECG should not be routinely ordered as part of a sports pre-participation examination in asymptomatic, otherwise healthy patients with no personal or family history of cardiac disease.

The American Heart Association is not currently recommending routine screening ECGs for pre-participation sports clearance. They do recommend 14-day screening guidelines, or the American Academy of Pediatrics' "Pre-participation Physical Evaluation" in conjunction with a targeted personal history, family history, and thorough physical examination. If there are warning signs that place certain athletes at risk of sudden cardiac death, these individuals should be referred for further evaluation to a pediatric cardiologist.

Routine ECG screening of healthy pediatric patients without a personal or family history of cardiac disease has demonstrated a high false-positive rate and has not been found to reduce mortality from sudden cardiac death. In those with a strong family history of conditions likely to cause sudden cardiac arrest or death, an ECG screening should be performed.[1]

3. An echocardiogram should not be ordered for the routine evaluation of pediatric chest pain in the absence of a concerning history or ECG abnormalities.

Chest pain is a common presenting symptom in pediatrics but is rarely life-threatening, and the vast majority of cases are not cardiac in origin. The addition of an echocardiogram increases the cost of care and adds minimally to the diagnostic value in very limited circumstances. Again, this could be something ordered by the pediatric cardiologist if there is exertional chest pain with an abnormal ECG or a family history of sudden or unexplained death or cardiomyopathy.

4. An echocardiogram should not be ordered for the routine evaluation of pediatric syncope in the absence of a concerning history or ECG abnormalities.

Syncope is a common complaint in pediatrics and is rarely caused by a cardiac problem in patients with a normal physical examination. If the episode is cardiac-related, it generally relates to a dysrhythmia, so the echocardiogram rarely adds diagnostic value, while increasing the cost of care. If syncope

occurs with an abnormal EKG, exertional syncope, unexplained post-exertional syncope, or syncope in the setting of a concerning family history, consultation with a pediatric cardiologist is recommended, and they can obtain an echocardiogram if needed.

5. A screening ECG should not be ordered prior to initiation of attention-deficit/hyperactivity disorder (ADHD) therapy in asymptomatic otherwise healthy pediatric patients with no personal or family cardiac disease.

Many ECGs are ordered before initiating stimulant therapy for ADHD out of fear of triggering an adverse cardiovascular event or worsening previously undiagnosed cardiovascular disease. The probability that such screening will lead to the diagnosis of cardiac disease is low. Even if ECG abnormalities are identified, they rarely warrant a change in planned ADHD therapy. Obtaining the ECG in the primary care office just increases the cost and can increase stress for both the patient and the family.[2]

11. RECOMMENDATIONS ON TRANSPLANTATION AND CELLULAR THERAPY

1. Peripheral blood stem cells for patients with aplastic anemia should not be routinely used when a suitable bone marrow donor is available, due to a higher risk of graft-versus-host disease.

In patients with aplastic anemia, engraftment is faster with filgrastim-mobilized peripheral blood stem cells than with bone marrow, and results in quicker recovery of peripheral blood counts, but the higher rate of graft-versus-host disease may be detrimental.

2. More than 2 mg/kg/day of methylprednisolone (or equivalent) should not be used for the initial treatment of graft-versus-host disease.

No advantage has been shown using equivalent doses higher than 2 mg/kg/day in acute graft-versus-host disease. Higher doses increase the risk of corticosteroid related toxicity. In patients with grade I-II acute graft-versus-host disease, initial therapy with lower dose corticosteroids equivalent to 1 mg/kg/day may be adequate.[3]

3. When a single unit of adequate size is available for standard umbilical cord blood transplantation, it should be used routinely over 2 cord blood units, recognizing that higher cell doses are preferred when using units with greater HLA mismatch.

Randomized trials demonstrate similar clinical outcomes after single-unit and double-unit umbilical cord blood transplantation, including comparable rates of relapse, engraftment failure, overall survival, and transplantation related mortality. Moreover, graft-versus-host disease may be more frequent after double-cord blood transplantation.

4. When a suitable bone marrow donor is available it is not routinely recommended to use peripheral blood stem cells from matched unrelated donor transplantation using myeloablative conditioning and standard graft-versus-host disease prevention regimens.

Patients undergoing myeloablative matched unrelated donor hematopoietic cell transplantation with a peripheral blood stem cell graft and standard graft-versus-host disease prophylaxis (calcineurin inhibitor and methotrexate), experience more symptomatic chronic graft-versus-host disease than those receiving bone marrow, without affecting relapse rates or overall survival. Peripheral blood stem cells may be considered in cases with substantial recipient/donor size discrepancy, donor preference, and for malignant diseases with high risk for graft failure.

5. Immunoglobulin replacement should not be routinely given to adult hematopoietic cell transplantation recipients in the absence of recurrent infections regardless of the IgG level.

Meta-analyses of controlled trials conclude that immunoglobulin replacement offers no advantage for infection prevention and overall survival, and may predispose to a higher risk of hepatic sinusoidal obstruction syndrome and venous thromboembolism, and impairs the efficacy of post-transplant vaccinations. Prophylactic immunoglobulin replacement may be considered, such as in umbilical cord blood transplant recipients, in children undergoing transplantation for inherited or acquired disorders

associated with B-cell deficiency, and in chronic graft-versus-host disease patients with recurrent sino-pulmonary infections.[4]

Top Tips

POEMS CONSISTENT WITH THE PRINCIPLES OF CHOOSING WISELY [5]

POEMs (Patient-Oriented Evidence that Matters) of 2019 that were judged to be the most consistent with the principles of Choosing Wisely have been gathered in an international effort to reduce unnecessary medical tests, treatments, and procedures.

In deference to the respiratory disease outbreak that we are now suffering, here are four of the POEM titles that should remind you of clinical actions I have discussed in previous Choosing Wisely articles in this Journal:

- Shorter courses of antibiotics for community-acquired pneumonia are at least as good as longer courses. Choosing Wisely has stated that community-acquired pneumonia should be treated with antibiotics until the patient is clinically stable (i.e. normal vital signs, able to eat, and normal mentation) but for a minimum of 5 days.

- POEM states that excess treatment with antibiotics for pneumonia is common and may lead to harm. Choosing Wisely states we should not routinely prescribe an additional 5-10 days of antibiotics on hospital discharge if not indicated by guidelines.

- The third POEM stated there is more evidence now against using antibiotics for exacerbations of acute asthma. Choosing Wisely says that antibiotics should not be used for patients with exacerbations of acute asthma in the absence of a clear indication.

- POEM says that guidance with C-reactive protein levels safely reduces antibiotic use in patients with acute exacerbations of chronic obstructive lung disease, with the number needed to treat equal to 5. Choosing Wisely also states that C-reactive protein levels should be guiding decisions about use of antibiotics in patients with exacerbations of chronic obstructive disease.

UPDATED MANAGEMENT OF LYME DISEASE [6]

This is a summary update to the 2006 Infectious Diseases Society of America and 2007 American Academy of Neurology guidelines on the management of Lyme disease.

Key recommendations include:

- For patients with symptoms suggesting Lyme arthritis, serologic studies should be done, followed by polymerase chain reaction (PCR) studies of synovial fluid or tissue.

- After appropriate antibiotic therapy for Lyme disease, do not use additional antibiotic therapy for patients who have persistent non-specific symptoms without objective findings.

- Treat patients with erythema migrans following Ixodes scapularis tick bites. No recommendation is made for or against antibiotic therapy for a rash following lone star tick bites.

- As before, doxycycline is recommended for antibiotic prophylaxis after high-risk tick bites.

- Use intravenous ceftriaxone, cefotaxime or penicillin, or oral doxycycline for acute neurological manifestations without parenchymal involvement of the brain or spinal cord. Use IV therapy for patients with parenchymal or spinal cord involvement as determined by MRI or objective focal findings on neurological examination.

The new recommendations have changed in that specific neurological symptoms should prompt testing for Lyme neuroborreliosis; these include meningitis, painful radiculoneuritis, mononeuropathy multiplex, acute cranial neuropathies, and spinal cord or brain inflammation in the setting of likely exposure to Borrelia burgdorferi. Diagnosis can be made on the basis of serologic studies, alone or with cerebrospinal fluid serologic studies,

and not on the basis of PCR or culture.

The update also includes more detailed discussion of all aspects of Lyme carditis. Finally, oral antibiotic therapy is still recommended for initial management of Lyme arthritis, and IV antibiotic therapy is reserved for individuals who have no or minimal response to initial treatment.

MICROHEMATURIA GUIDELINES [7]

These guidelines provide a clinical framework for the diagnosis, evaluation, and follow-up of microhematuria (MH). Clinicians should define MH as ≥ three red blood cells per high-power field on microscopic evaluation of a single, properly collected urine specimen. MH should not be defined by positive dipstick testing alone; rather, a positive dipstick test (trace blood or greater) should prompt a formal microscopic evaluation of the urine.

Initial evaluation should include a history and physical examination to assess risk factors for genitourinary malignancy, medical renal disease, gynecological, and non-malignant genitourinary causes of MH. The same evaluation should be done for patients with MH who are taking antiplatelet agents or anticoagulants.

In patients with findings suggestive of a gynecological or non-malignant urological etiology, clinicians should evaluate the patients with appropriate physical examination techniques and tests to identify such an etiology. In patients diagnosed with such an etiology, a urinalysis should be repeated following the resolution of the gynecological or non-malignant genitourinary cause. If MH persists or the etiology cannot be identified, clinicians should perform a risk-based urological evaluation.

In patients with hematuria attributed to a urinary tract infection, clinicians should obtain a urinalysis with a microscopic evaluation following treatment to ensure resolution of the hematuria. Patients with MH should be referred for a renal evaluation if medical renal disease is suspected; however, a risk-based urological evaluation should still be performed.

The guidelines then discuss risk stratification, and review the recommendations for low-risk, intermediate-risk, or high-risk for genitourinary malignancy.

Urine cytology or urine-based tumor markers should not be used in the initial evaluation of patients with MH. The guidelines conclude with follow-up recommendations based on the initial evaluation.

Most of the clinical framework was based on multiple publications. If sufficient evidence existed, the body of evidence for a particular modality was assigned strength of rating A (high), B (moderate), or C (low), and evidence-based clinical recommendations of Strong, Moderate, or Conditional were developed.

2020 AMERICAN COLLEGE OF RHEUMATOLOGY GUIDELINES FOR MANAGEMENT OF GOUT [8]

Allopurinol is now the sole recommended first-line treatment for managing gout, according to the updated 2020 guidelines from the American College of Rheumatology. Major reasons were treatment costs and cardiovascular concerns about febuxostat. Allopurinol is strongly recommended for all patients, including those with stage III and higher chronic kidney disease (CKD). The guidelines recommend using a low starting dose of Allopurinol (≤100 mg/day and lower) in chronic kidney disease.

A treat-to-target management strategy is recommended, with urate-lowering therapy guided by serial serum urate measurements, and a serum urate target of <6 mg/dl. When initiating therapy, concomitant anti-inflammatory prophylaxis therapy for at least 3-6 months was strongly recommended. For management of gout flares, colchicine, nonsteroidal anti-inflammatory drugs, or glucocorticoids (oral, intraarticular, or intramuscular) were strongly recommended.

Febuxostat was recommended as first line therapy in 2012, but now patients with a new cardiovascular disease (CVD) event or a history of CVD events should consider switching from febuxostat.

DO NOT CHECK AMMONIA LEVELS IN PATIENTS WITH HEPATIC ENCEPHALOPATHY [9]

Despite their poor diagnostic accuracy, ammonia levels still are commonly ordered for patients with suspected hepatic encephalopathy (HE), but HE remains a clinical diagnosis.

Investigators reviewed records of 1,200 consecutive adult patients with cirrhosis and a diagnosis of HE who were admitted to a South Carolina Medical Center from 2005 to 2015. Ammonia levels were determined in 46% of the patients, and were elevated in 60% of tested patients. The amount of lactulose given in the first 48 hours of HE management was similar in the tested and untested groups. There were no correlations between lactulose dose and ammonia level.

In a propensity-matched analysis, conducted to address possible confounders (e.g. age, severity of liver disease), there were no significant differences between tested and untested patients in mortality, length of stay, and time to clinical improvement.

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