Jean Mantz, M.D., Ph.D., Editor

Perioperative Medicine

Serum potassium levels and mortality on acute myocardial infarction. JAMA 2012; 307:157–64

The optimum serum potassium levels associated with favorable outcome in patients with acute myocardial infarction is uncertain. This large, retrospective, multicenter cohort study examined the impact of serum potassium levels on in-hospital mortality in patients with biomarker-confirmed acute myocardial infarction. The lowest mortality rate was observed in patients with serum potassium levels between 3.5 and 4.5 mM in comparison with those who had lower or higher serum potassium levels postadmission (fig. 1). Despite the limitations inherent to a retrospective cohort study, this paper suggests that serum potassium levels more than 4.5 mM should probably avoided at the early stage of myocardial infarction.

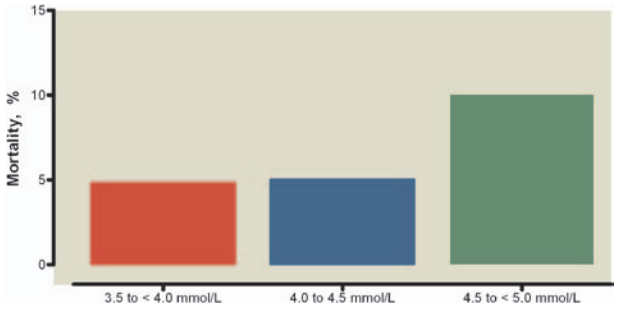

Fig. 1. Mortality was highest in patients with the highest serum potassium levels.

Interleukin-25 induces type 2 cytokine production in a steroid-resistant interleukin-17RB+ myeloid population that exacerbates asthmatic pathology. Nat Med 2012; 18:751–8

Asthmatics are a high-risk category of surgical patients. The limited efficacy of treatments such as inhaled corticosteroids supports the need for improving our understanding of the pathophysiology of asthma. In a murine model of chronic allergic asthma, interleukin-25 airway instillation induced the production of type 2 proinflammatory cytokines, interleukin-4 and interleukin-13, in a previously undescribed granulocytic population called T2M cells. Such a response was observed in peripheral blood of asthmatic subjects as well. High dose dexamethasone treatment did not reduce the interleukin-25-induced pulmonary response. These data provide insight into the mechanisms of steroid-resistant asthmatic manifestations and identify T2M cells as a new steroid-resistant cell population.

Magnesium for aneurysmal subarachnoid hemorrhage (MASH-2): A randomised placebo-controlled trial. Lancet 2012; 380:44–9

Magnesium has been advocated as a cerebroprotectant, but its efficacy in improving outcome after aneurysmal cerebral hemorrhage remains unproven. In this phase III, randomized, multicenter, placebo-controlled European-South American trial, patients in whom subarachnoid hemorrhage with a brain-imaging aneurysmal pattern was diagnosed within 4 days of hemorrhage were randomly allocated to receive either magnesium sulfate (64 mmol/day) or placebo. The primary outcome measure was poor outcome defined by a 4 to 5 modified Rankin Scale score 3 months after hemorrhage, or death. Of the 1,204 patients enrolled, 156 (26.2%) had a poor outcome in the magnesium group in comparison with 151 (25.3%) in the placebo group (risk ratio: 1.03, 95% CI: 0.85 to 1.25). These negative results were confirmed by an updated meta-analysis of seven randomized controlled trials including 2,047 patients (fig. 2). These data strongly support not to recommend magnesium suphate in aneurysmal subarachnoid hemorrhage.

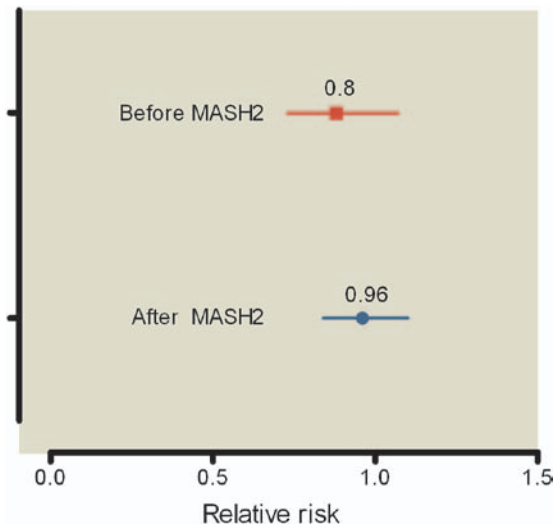

Fig. 2. Meta-analysis of effect of magnesium therapy after subarachnoid hemorrhage on poor outcome.

Statins and the risk of cancer after heart transplantation. Circulation 2012; 126:440–7

Despite improved tolerance to immunosuppressive therapies after heart transplantation, cancer remains the leading cause of death in these circumstances. This Swiss retrospective trial

 Anesthesiology 2012; 117:1130–2

evaluated the rate of malignancy in 255 patients alive 1 yr after heart transplantation. Cancer was diagnosed in 108 (42%) patients during follow-up. In a Cox regression model adjusted for a significant number of cofounders, the use of statins was significantly associated with a decrease in the occurrence of malignancies (by 67%, hazard ratio: 0.33, 95% CI: 0.21 to 0.51, $P < 0.0001$) and improved survival. These promising data need to be confirmed in prospective trials.

Critical Care Medicine

Effect of empirical treatment with moxifloxacin and meropenem *versus* meropenem on sepsis-related organ dysfunction in patients with severe sepsis: A randomized trial. JAMA 2012; 307:2390–9

Accurate identification of causative microorganisms of sepsis in critically ill patients may not be possible in as many as 50% of septic patients. Therefore, several antibiotics are frequently given simultaneously to increase the likelihood of effective empiric coverage, but there are few studies comparing multi- with monotherapy in this situation. A randomized, open-label, multicenter, parallel-group trial was conducted to compare the effects of moxifloxacin and meropenem with meropenem alone on sepsis-related organ dysfunction. No statistically significant differences were observed between groups in the primary outcome measure of degree of organ failure over 14 days as evaluated by the mean sequential organ failure assessment score, or in secondary outcomes of 28-day and 90-day mortality rates, secondary infections, or clinical and microbiologic responses to treatment (fig. 3). Nevertheless, although these results show that the specific combination of moxifloxacin and meropenem may not be of greater benefit than meropenem alone in this population of patients, these results may not apply to other groups with different microbiologic patterns or to different antibiotic combinations. Moreover, the use of a quinolone for empiric therapy may not represent the best choice, because resistance rates are relatively high.

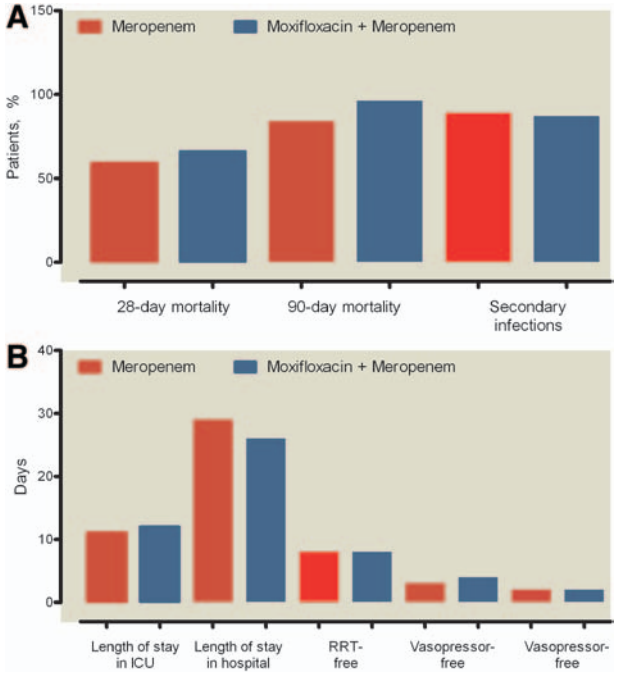

Fig. 3. No significant differences in primary or secondary outcomes were observed between the two groups. Mean Sequential Organ Failure Assessment scores were 7.9 and 8.3 in the meropenem and the moxifloxacin plus meropenem groups, respectively. Mortality and infection rates were similar (*A*) and days spent in the intensive care unit (ICU) or intervention-free were similar (*B*). RRT = renal replacement therapy.

An observational study fluid balance and patient outcomes in the Randomized Evaluation of Normal *versus* Augmented Level of Replacement Therapy Trial. Crit Care Med 2012; 40:1753–60

Rapid and sufficient fluid administration is considered a keystone of resuscitation therapies for patients with shock. However, determining how much fluid to give and when to stop fluid administration is not always clear. To examine associations between fluid balance and clinical outcomes in critically ill adult patients with acute kidney injury who required renal replacement therapy, an analysis of data from a large (n = 1,453), multicenter, randomized controlled trial of intensity of continuous RRT was conducted. During the intensive care unit stay, the mean daily (–234 ml/day *vs.* + 560 ml/day, $P = 0.0001$) and mean cumulative (–1,941 *vs.* 1,755 ml, $P = 0.0003$) fluid balances were significantly lower in survivors than in nonsurvivors (fig. 4). Using various statistical techniques, including multivariate analysis, propensity scoring, and Cox proportional hazards modeling, a negative mean daily fluid balance was shown to be consistently and independently associated with improved clinical outcomes, including survival and renal replacement therapy-free days, mechanical ventilation-free days, intensive care unit-free days, and hospital-free days. Although this

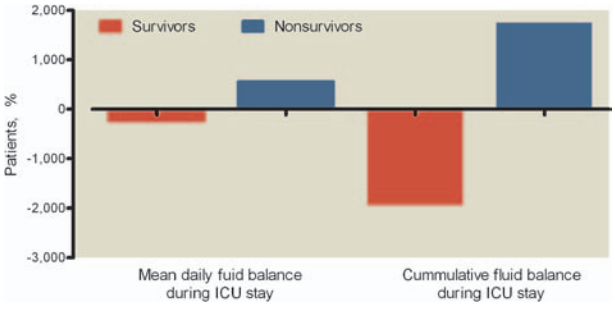

Fig. 4. Survivors had significantly lower daily and cumulative fluid balances than nonsurvivors ($P < 0.001$ for each). ICU = intensive care unit.

association does not necessarily indicate causality, these data do provide further evidence to support the need to carefully titrate fluids to individual patients, particularly those with or at risk of acute kidney injury.

Pain Medicine

Randomized control trial of topical clonidine for treatment of painful diabetic neuropathy. Pain 2012; 153:1815–23

Although preclinical, basic science studies suggest topical clonidine could be an analgesic drug, the clinical data are less convincing. This randomized, double-blind, placebo-controlled, parallel-group multicenter trial examined the analgesic effect of topical clonidine in patients with diabetic peripheral neuropathy. In all patients, topical clonidine provided modest pain relief (fig. 5). However, when patients were stratified based on the degree of cutaneous innervation, those patients with a positive cutaneous innervation phenotype had greater analgesia than those patients with a cutaneous denervation phenotype. Thus, within a disease state, diabetic neuropathy patients could be stratified to predict likelihood of response to topical clonidine.

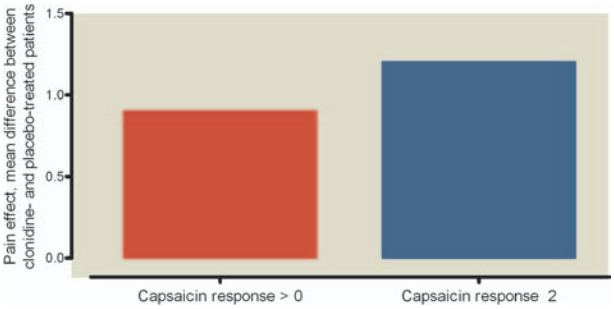

Fig. 5. Mean difference in pain response after treatment with clonidine or placebo. Only subjects with pain responses to capsaicin demonstrated a significant effect of clonidine ($P < 0.05$), and the magnitude of separation increased with increasing capsaicin ratings ($P < 0.01$).

The influence of children's pain memories on subsequent pain experience. Pain 2012; 153:1563–72

There is a lack of information regarding the long-term effects of repeated painful medical procedures, such as immunizations, on healthy children. This cohort study investigated laboratory pain ratings in 8- to 12-yr-old boys based on both their memories and expectancies of future pain. The results indicate that children who had a negative perception of their previous pain experience had developed greater pain expectancies and greater increases in pain scoring when facing future pain experience than those who had positively estimated pain memory. This study emphasizes the importance of pain memories on future pain experiences in healthy children.