The Impact of Future Technology on Patient Safety

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Nanocrystals: immunologically inert “eggshells” capable of carrying materials such as drugs, gases, or antigens; can be signaled by marker recognition (eg, when nanocrystal reaches tumor site, tumor antibodies attach to antigens on nanocrystal surface and open shell; this permits site-specific drug delivery, with less toxicity; magnets may also be placed on nanocrystal exterior and pulled to tumor site with magnetic resonance imaging; ultrasonic energy then “cracks open” eggshell)

Appendicitis: nanocrystals can be filled with bleach, given to patient in oral solution, and pulled magnetically into appendix via cecum; bleach sterilizes appendix and evokes intense inflammatory response, which leads to fibrosis and scarring (obliterates appendix)

Other uses: crystals made of carbon; can be spun into nanotubes and made into clothing fibers that conduct electricity—can play indispensable role in success of health care system

Image-guided applications of external power: ultrasonic energy — can be concentrated at focal point to generate heat to “spot weld” or burn, eg, tumors; has been used to treat uterine fibroids, breast tumors, and osteosarcomas

Improved radiation therapies: linear accelerators — currently used to treat tumors at some hospitals; employ energy generated by electrons; small size of electrons makes dose calculation difficult and results in collateral damage to healthy tissue; mediastinal tumors of particular concern to anesthesiologists due to potential for tracheal compression; after presurgical shrinkage with linear accelerator, patients often experience side effects such as esophagitis; dose calculation and focusing of beam simpler with protons (have much larger mass); with less risk for collateral damage; drawbacks — proton beam generators huge; cost $250 million apiece; too many currently being built

Educational Objectives

The goals of this program are to increase use of new technologies that improve patient outcomes and to improve management of acute kidney injury. After hearing and assimilating this program, the clinician will be better able to:

1. Recognize clinical applications for new technologies such as nanocrystals and minimally invasive surgical techniques.
2. Describe the anesthesiologist’s role in the surgical home model.
3. Define acute kidney injury (AKI) according to currently recognized criteria.
4. Consider advantages and disadvantages of using serum creatinine as a marker for AKI.

Conclusions: anesthesiologists will be increasingly performing tasks outside of operating room; surgical home model — surgeon or proceduralist determines course of treatment; anesthesiologist then takes patient through preoperative assessment and management, intraoperative and postoperative management, pain management, intensive care, and discharge; anesthesiologists also may determine need for hospice care; speaker suggests that anesthesia providers must acquire skills beyond delivery of anesthesia to maintain share of revenue; by assuming management of surgical home (with increases in efficiency and prevention of expensive complications), anesthesiologists can play indispensable role in success of health care system

5. Cite evidence on biomarkers that show promise as tools for early detection of AKI.

Faculty Disclosure

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Cardiac Surgery and Acute Kidney Injury: Why Doesn’t Anything Seem to Help?

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Acute kidney injury (AKI): term proposed 10 yr ago by international group of nephrologists; developed in response to growing recognition of need for consistent diagnostic criteria for renal injury, and that even minor increases in serum creatinine (SCR) associated with important and clinically relevant adverse outcomes

Definition of AKI: proposed in 2004 by Acute Dialysis Quality Initiative Group; criteria include risk, injury, failure, loss, and end-stage disease (RIFLE); diagnoses AKI on basis of increasing SCR or periods of oliguria; risk defined as 50% increase in SCR over 7 days, or urine output <0.5 mL/kg per hour for >6 hr; in 2007, Acute Kidney Injury Network (AKIN) proposed similar criteria, but added absolute increase in SCR by ≥0.3 mg/dL over 48 hr to define and diagnose stage 1 AKI

Significance of relatively minor kidney injury: may promote multiorgan dysfunction by upregulating inflammatory response in distant organs; probably mediated through cytokines, chemokines, and neurohumoral mechanisms; AKI consistently associated with increased length of stay in intensive care unit and hospital, with corresponding cost increases; perioperative AKI associated with increased mortality; in analysis of patients undergoing cardiac or thoracic aortic surgery, any postoperative increase in SCR associated with significant increase in 30-day mortality; conclusions — even small increases in perioperative SCR cannot be considered insignificant; regardless of criteria used, clinical setting, or degree or renal injury, AKI consistently associated with 2- to 6-fold increase in perioperative mortality; even patients who survive AKI have markedly increased risk of progressing to chronic kidney disease (CKD); Hobson and colleagues showed that, among survivors of AKI after cardiac surgery, mortality remains elevated ≤10 yr postoperatively

Incidence of AKI: 20% after cardiac surgery

Prevention and interventions: prevention difficult; interventions include attempts to increase renal blood flow (clinical studies have not supported use of dopamine; fenoldopam currently under investigation); goal-directed therapy promising in recent meta-analysis, but goals and interventions used varied widely among studies (does not permit conclusions about specific interventions); neither furosemide nor mannitol shown to be renoprotective (quality of studies questionable; furosemide now being studied in Canadian patients with early AKI); results of studies on a-type and b-natriuretic peptides conflict; blocking upregulation of inflammatory pathways associated with cardiac surgery shows little success; data supporting avoidance of cardiopulmonary bypass “arguable”

Major study limitations: renal injury usually assessed as secondary outcome; studies often underpowered to detect treatment benefits for milder degrees of kidney injury

Interventions currently under study: remote ischemic preconditioning; perioperative alkalinization of plasma and urine; perioperative administration of statins; preoperative administration of erythropoietin (for anti-inflammatory and anti-apoptotic effects, not correction of anemia); advanced transfusion of red blood cells for patients with preoperative anemia undergoing elective cardiac surgery

Obstacles to progress: complexity of mechanisms and pathways — AKI associated with cardiac surgery represents end result of interplay among multiple mechanisms and overlapping pathways; predominant mechanism probably varies among individuals; thus, no single treatment alone likely to have major impact in typically heterogeneous adult cardiac surgery population; lack of study power — may cause small treatment effects in clinical trials to be missed; use of oversimplified animal models — no intervention effective in animals has ever proven effective in humans; histologic injury patterns seen in animals differ from those in humans due to mechanisms used to produce experimental injuries; animal models characterized by proximal tubular injury (severity correlates well with functional impairment); human injuries typically more limited and focal (mosty affect distal tubules, ascending limbs, and collecting ducts); if injury model does not mimic clinical situation, likelihood of developing successful interventions remains low

Lack of consensus on definition of significant renal injury: over last 10 to 15 yr, >30 definitions of AKI used in various studies; uncertain definitions associated with problems in understanding epidemiology of AKI and difficulties comparing effects of similar interventions across different studies; RIFLE and AKIN criteria developed to improve consistency in research, but significant variation remains in application of criteria and use of oliguric component; despite variations, large body of evidence shows that even small postsurgical increases in SCR associated with increased morbidity and mortality

Use of SCR as diagnostic tool: diminished glomerular filtration rate (GFR) associated with slowing of rise in SCR; AKI may not be detectable until postoperative day 2 or beyond; SCR passive and nonlinear marker of GFR (not renal injury); significant injury and reduction of GFR may occur with little rise in SCR, “rendering SCR a crude and relatively insensitive tool for diagnosis”; frequently declines within 24 hr after cardiac surgery; animal studies suggest window of opportunity for effective intervention probably limited to short period around time of injury; early recognition of evolving AKI necessary for effective intervention; exact role of SCR questionable; roles of intravascular filling pressure and urine output should be explored; SCR identifies patients who have already suffered significant renal insult, but does not provide early warning of impending problem

Intravascular filling pressure: overt uncorrected hypovolemia potential contributor to AKI; limited evidence supports use of specific interventions

Urine output and oliguria: standalone diagnostic criterion for AKI according to AKIN and RIFLE definitions; oliguria is early warning that kidneys under stress, but oliguric component of consensus definitions more difficult to validate than SCR component; definitions require exclusion of hypovolemia as cause of oliguria before using oliguria to diagnose AKI (may be difficult); data for utility of oliguria as monitor of AKI currently mixed; may vary with population under study; oliguria within first 48 hr after cardiopulmonary bypass and cardiac surgery may be relatively ubiquitous and benign occurrence

Biomarkers for early detection of AKI: ideal biomarker — should be evident early and correlate reliably with degree of injury; should be sensitive and specific for AKI; also should be specific for etiology of injury; should be cost effective; levels must provide prognostic information about clinically relevant adverse outcomes

Caveats: due to complexity of AKI pathophysiology, no single marker will serve as comprehensive independent diagnostic tool; panel of biomarkers should be developed to provide temporal and etiologic specificity to guide risk stratification and therapy

Candidates under investigation: neutrophil gelatinase-associated lipocalin (NGAL) — small glycoprotein produced by tubular epithelial cells; gene maximally amplified within 2 hr of ischemic reperfusion injury; true marker of renal injury, rather than passive marker of function (like SCR); thus far, clinical studies show mixed results; in recent meta-analyses in which patients experienced rise in NGAL but...
not SCR after cardiac surgery or stay in intensive care unit, increased NGAL associated with significantly increased risk for adverse outcomes; authors concluded NGAL valid and important marker of AKI; in study of >1200 adults undergoing cardiac surgery, Parikh and colleagues found that NGAL provided limited standalone diagnostic utility for creatinine-based diagnosis of AKI, but elevated NGAL associated with composite outcome of hospital mortality or dialysis and increased length of stay; cistatin-c — proteinase inhibitor; typically measured in plasma; passive marker of glomerular filtration; short half-life (2 hr) believed to permit earlier detection of AKI (short half-life implies rapid initial rise), but diagnostic performance varied in clinical studies, compared to SCR; interleukin-18 — small cytokine produced by renal proximal tubule cells, monocytes, and macrophages; upregulated in response to renal reperfusion injury; diagnostic performance varies widely in clinical studies; has shown promise as marker of AKI and predictor of mortality, need for dialysis, and longer length of stay; kidney injury molecule (KIM)-1 — glycoprotein believed to be produced by regenerating proximal tubular epithelial cells; diagnostic value for AKI variable

Conclusions: reasons for variable diagnostic performance of new biomarkers unclear; may be influenced by patient factors such as age, renal function, or atherosclerotic disease; may also reflect heterogeneity of AKI etiology; SCR may be poor comparator; accumulating evidence supports NGAL as clinically valid marker of renal injury, despite highly varied relationship to SCR; confirmation will require more evidence on more heterogeneous patient populations; currently, increased SCR remains imperfect gold standard

Acknowledgements
Drs. Warner and McIlroy were recorded at 62nd Annual Postgraduate Symposium on Anesthesiology, held April 13-15, 2012, in Kansas City, MO, and sponsored by the Kansas University Medical Center, Department of Anesthesiology. Information on upcoming CME activities from this sponsor can be found at www.KUMC.edu/anes/, or on the Upcoming Meetings page of our website, www.Audio-Digest.org. The Audio-Digest Foundation thanks the speakers and the Kansas University Medical Center, Department of Anesthesiology, for their cooperation in the production of this program.

Suggested Reading

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FUTURE TECHNOLOGY/ACUTE KIDNEY INJURY

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To submit a test form by mail or fax, complete Pretest section before listening and Posttest section after listening.

1. Nanocrystals have been used in clinical practice to:
   (A) Provide site-specific transport of therapeutic agents
   (B) Avoid surgical appendectomy
   (C) Carry iodine to heart for use as angiographic dye
   (D) All the above **

2. Which of the following statements about proton beam generators used in radiation therapy is incorrect?
   (A) Extremely costly
   (B) Dose calculations simpler than those with use of electrons
   (C) Associated with increased risk for collateral damage to healthy tissue**
   (D) Extremely large in size

3. The transrectal approach is gaining popularity in natural orifice transluminal endoscopic surgery (NOTES).
   (A) True (B) False **

4. Which statement best describes care under the surgical home model?
   (A) Surgeon determines course of treatment; anesthesiologist oversees perioperative care
   (B) Surgeon and anesthesiologist jointly determine treatment; nurse practitioner oversees perioperative care
   (C) Surgeon determines course of treatment; hospitalist oversees perioperative care
   (D) Hospitalist determines course of treatment; surgeon and anesthesiologist provide perioperative care

5. Diagnostic criteria for acute kidney injury (AKI) include:
   1. Absolute increase in serum creatinine \( \geq 0.5 \) mg/dL over 48 hr
   2. 50% increase in serum creatinine over 7 days
   3. Urine output <0.5 mL/kg per hour for >6 hr
   (A) 1,2,3 (B) 1,3 (C) 1,2 (D) 2,3 **

6. A recent analysis suggests that serum creatinine must increase \( \geq 1 \) mg/dL over 48 hr after cardiac or thoracic surgery to have a significant impact on 30-day mortality.
   (A) True (B) False **

7. The evidence suggests that, among people who survive AKI following cardiac surgery, the risk for death remains elevated for ______ postoperatively.
   (A) \( \leq 2 \) yr (B) \( \leq 5 \) yr (C) \( \leq 10 \) yr (D) \( \leq 15 \) yr

8. Choose the incorrect statement about serum creatinine.
   (A) Provides early warning of impending renal problems **
   (B) Frequently declines 24 hr after cardiac surgery
   (C) Is a passive and nonlinear marker of glomerular filtration rate (GFR)
   (D) Significant reduction in GFR may occur with little rise in serum creatinine

9. Neutrophil gelatinase-associated lipocalin (NGAL) is:
   (A) A proteinase inhibitor
   (B) A passive marker of GFR
   (C) A small glycoprotein produced by tubular epithelial cells **
   (D) A small cytokine produced by renal proximal tubule cells, monocytes, and macrophages

10. Research on new biomarkers for AKI has found that they:
    (A) Are consistently superior to serum creatinine
    (B) Are too expensive to produce
    (C) Have insufficiently long half-lives
    (D) Yield widely varying results among different studies

Answers to Audio-Digest Anesthesiology Volume 54, Issue 12: 1-D, 2-C, 3-A, 4-A, 5-D, 6-B, 7-A, 8-B, 9-A, 10-B