July 2019 Featured Articles, Volume 229

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Article 1: Endocrinology, Thyroid, Parathyroid; General Surgery

Influence of adrenal venous sampling on management in patients with primary aldosteronism independent of lateralization on cross-sectional imaging. Campbell RA, Young DS, Shaver CN, et al. J Am Coll Surg 2019;229:116–124

Article 2: Burn, Trauma, Critical Care; General Surgery

Persistently elevated glucagon-like peptide-1 levels among critically ill surgical patients after sepsis and development of chronic critical illness and dismal long-term outcomes. Brakenridge SC, Moore FA, Mercier NR, et al. J Am Coll Surg 2019;229:58–67

Objectives: After reading the featured articles published in this issue of the *Journal of the American College of Surgeons* (JACS), participants in this journal-based CME activity should be able to demonstrate increased understanding of the material specific to the article featured and be able to apply relevant information to clinical practice.

A score of 75% is required to receive CME and Self-Assessment credit. The JACS Editor-in-Chief does not assign a manuscript for review to any person who discloses a conflict of interest with the content of the manuscript. Two articles are available each month in the print version, and usually **4 are available online for each monthly issue, going back 24 months.**

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Article 3: Breast; General Surgery

Competing risk of death in elderly patients with newly diagnosed stage I breast cancer. Wasif N, Neville M, Gray R, et al. J Am Coll Surg 2019;229:30–36

ARTICLE 1

(Please consider how the content of this article may be applied to your practice.)

Influence of adrenal venous sampling on management in patients with primary aldosteronism independent of lateralization on cross-sectional imaging

Campbell RA, Young DS, Shaver CN, et al
J Am Coll Surg 2019;229:116–124

Learning Objectives: After study of this article, surgeons should be able to evaluate which patients would benefit from adrenal venous sampling (AVS) and understand how AVS can affect the choice of therapy.

Question 1

Selective adrenal venous sampling (AVS) would be most useful in the diagnostic evaluation and treatment planning for which patient below?

a) An 88-year-old female with hypertension that is poorly controlled despite multiple medications, normal potassium, and with a normal left adrenal and a 1.3-cm right adrenal mass with imaging characteristics consistent with an adrenocortical adenoma. She is not interested in pursuing surgical intervention for hyperaldosteronism, if necessary.
b) A 21-year-old male with a family history of multiple endocrine neoplasia type 2, elevated urine metanephrine and normetanephrine, and bilateral adrenal masses.
c) A 50-year-old male with marked hypertension, potassium 2.9 mEq/L, plasma aldosterone 33 ng/dL, plasma renin activity 0.1 ng/mL/h. Adrenal CT demonstrates a 1.5-cm left adrenal mass consistent with adenoma, and nodular thickening of the right adrenal gland.

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d) A 63-year-old normotensive female with a CT scan that demonstrates an 8.0-cm right adrenal mass with macroscopic fat, and a normal left adrenal gland.
e) A 28-year old female with severe hypertension that is poorly controlled despite multiple antihypertensive medications, hypokalemia of 2.8 mEq/L, and a CT scan with a normal right adrenal gland, and a 1.8-cm left adrenal mass consistent with adrenocortical adenoma.

Critique: AVS plays a role in patients with primary aldosteronism (PA). Patients with PA may have unilateral or bilateral disease. CT scan and MRI are useful initially. Cross-sectional imaging may lateralize an adrenal nodule, but this is not always an accurate representation of the laterality of hyperaldosteronism. AVS can be used to determine laterality of hypersecretion of aldosterone. AVS is not useful in patients who are not surgical candidates, or in patients who are younger than 35 years old with obvious hypertension, hypokalemia, and a unilateral lesion on cross-sectional imaging.

Question 2

A 45-year-old male with confirmed primary aldosteronism has an MRI of the abdomen without contrast that shows prominence of the right adrenal gland. What is the next best step in management?

a) CT of the abdomen and pelvis
b) Laparoscopic right adrenalectomy
c) Start medical management with spironolactone
d) Adrenal venous sampling
e) MRI with contrast

Critique: MRI or CT scan are useful modalities to identify structural adrenal abnormalities. Adrenal venous sampling (AVS) is useful in identifying the laterality for hypersecretion of aldosterone, and AVS can confirm bilateral aldosterone hypersecretion in some patients with an apparent unilateral adrenal abnormality on imaging, and therefore, avoid a noncurative and unnecessary adrenalectomy. On imaging, patients with bilateral adrenal hyperplasia may have adrenal glands that appear normal or slightly thickened due to micro- or macrohyperplasia. Adrenalectomy is the treatment of choice for patients with a clear unilateral source of aldosterone hypersecretion. Mineralocorticoid antagonists are used to treat patients with hyperaldosteronism from a bilateral source.

Question 3

In what way does adrenal venous sampling affect the choice of therapy?

a) By determining between bilateral adrenal hyperplasia and unilateral primary aldosteronism
b) By identifying patients with primary aldosteronism
c) By identifying patients with adrenal abnormalities
d) By determining laterality of adrenal nodules
e) By determining which patients will respond well to mineralocorticoid antagonists

Critique: Adrenal venous sampling is useful in determining laterality of the oversecretion of aldosterone in patients who have already been diagnosed with primary aldosteronism. Either CT or MRI is useful in identifying structural abnormalities of the adrenal gland. Patients with unilateral source of hyperaldosteronism can be treated surgically; patients with bilateral sources of hyperaldosteronism are treated with mineralocorticoid antagonists.

Question 4

Which one of the following ratios indicates unilateral aldosterone hypersecretion in a patient undergoing adrenal venous sampling with continuous cosyntropin infusion?

a) 1:1
b) 2:1
c) 3:1
d) 3:2
e) 4:1

Critique: The criteria used to determine the lateralization of aldosterone hypersecretion depend on whether the sampling is done under cosyntropin administration. Use of cosyntropin in continuous infusion helps to minimize fluctuations in aldosterone secretion, aids in confirming successful sampling of the adrenal vein, and maximizes the secretion of aldosterone from an aldosterone-producing adenoma. Dividing the right and left adrenal veins' aldosterone concentrations by their respective cortisol concentrations corrects for dilutional effects of the inferior phrenic vein joining the left adrenal vein, and potentially, inferior vena cava sampling effects from the right adrenal vein and are

known as "cortisol-corrected aldosterone ratios." With continuous cosyntropin, a cutoff of the cortisol-corrected aldosterone ratio from the high side to low side of greater than 4:1 indicates hypersecretion from a unilateral source. Lateralization ratios between 3:1 and 4:1 should be interpreted with caution and in combination with other clinical data. In the absence of cosyntropin administration, a cortisol-corrected aldosterone lateralization high-side to low-side ratio of more than 2:1 may be considered consistent with unilateral source of aldosterone production.

ARTICLE 2

(Please consider how the content of this article may be applied to your practice.)

Persistently elevated glucagon-like peptide 1 levels among critically ill surgical patients after sepsis and development of chronic critical illness and dismal long-term outcomes

Brakenridge SC, Moore FA, Mercier NR, et al
J Am Coll Surg 2019;229:58–67

Learning Objectives: After study of this article, surgeons should be able to identify patients at risk of developing poor outcomes after sepsis and understand the potential predictive and mechanistic role of persistently elevated glucagon-like peptide 1 levels in critically ill surgical sepsis patients.

Question 1

In this study, the incidence of early death (within 14 days) after sepsis onset among critically ill surgical patients was _____, while incidence of mortality at 6 months was significantly _____. Choose the most appropriate 2 words that correctly reflect the data:

a) Low; lower
b) Low; higher
c) High; higher
d) High; lower
e) High; the same

Critique: Historically, inpatient mortality rates after sepsis exceeded 30% to 50%. The development and implementation of evidenced-based critical care has significantly improved inpatient mortality rates after sepsis among surgical patients. These components of care include the implementation of the core tenets of the Surviving Sepsis Campaign (sepsis screening, early antibiotics, targeted resuscitation) and advanced organ support therapies such as advanced respiratory support and renal replacement therapy. Although more patients are surviving the initial septic insult, an increasing proportion of patients survive with persistent, but manageable, organ dysfunction. Long-term outcomes of these chronic critically ill patients remain incompletely described. However, functional outcomes at 6 months are poor, and mortality approaches 50%. In this study, both early death (<14 days; n = 4, 2.9%) and overall inpatient mortality were low (n = 12, 7.6%). However, post-discharge 6-month mortality was nearly 3-fold higher (19.7%).

Question 2

Hyperglycemia among critically ill surgical patients after trauma or sepsis is associated with:

a) A lower incidence of inpatient mortality
b) A decreased incidence of surgical site infection
c) An increase in overall nosocomial infection rates
d) Has no effect on post-surgical outcomes
e) Is best treated with strict targeting of low glucose control targets (ie 80 to 110 mg/dL)

Critique: Hyperglycemia is common among critically ill patients and is associated with multiple inpatient complications including death, increased risk of hospital-associated infections, and high inpatient resource use. While glycemic control clearly helps decrease the risk of many of these outcomes, randomized controlled trials have shown that the implementation of "tight" glucose control (80 to 100 mg/dL) among critically ill patients offers no benefit and higher risks over more modest glucose control targets (ie <180 mg/dL).

Question 3

The primary physiologic effects of glucagon-like peptide 1 (GLP-1) are:

a) Increased pancreatic insulin secretion
b) Decreased cellular glucose uptake
c) Increased appetite and food intake
d) Cannot be reliably stimulated by available GLP-1 agonist agents
e) Not significantly evoked by oral nutritional intake

Critique: Incretins (eg GLP-1) are a group of metabolic hormones that stimulate a decrease in blood glucose levels. Incretins are released after eating and augment the secretion of insulin released from pancreatic beta cells by a blood glucose-dependent mechanism. GLP-1 also inhibits glucagon release from the alpha cells of the islets of Langerhans. In addition, they slow the rate of absorption of nutrients into the blood stream by reducing gastric emptying and may directly reduce food intake. The 2 main candidate

molecules that fulfill criteria for an incretin are the intestinal peptides GLP-1 and gastric inhibitory peptide (glucose-dependent insulinotropic polypeptide; GIP). Medications based on incretin agonists are used in the treatment of diabetes mellitus type 2.

Question 4

Glucagon-like peptide 1 (GLP-1) levels after surgical sepsis:

a) Are strictly linked to and dependent upon severity of systemic inflammation
b) When elevated early after sepsis onset, are not associated with a prolonged ICU course or persistent organ dysfunction
c) Are strictly linked to and dependent upon peak glucose levels and/or insulin dose requirements
d) Are not significantly correlated with severity of sepsis-associated organ dysfunction
e) When persistently elevated at 14 days after sepsis, are associated with death or severe disability at 6 months

Critique: In this study, we have shown that circulating GLP-1 levels are elevated among surgical patients with sepsis. High levels of GLP-1 detected within 24 hours of ICU treatment initiation were noted in patients who had an ICU course longer that 14 days and persistent organ dysfunction. Surgical sepsis patients with elevated GLP-1 levels at 2 weeks after sepsis onset had significantly higher risks of being bedbound or dead at 6 months. The association of GLP-1 with these outcomes appears to be independent of systemic inflammation and glucose dysregulation. It is possible that persistently elevated GLP-1 after sepsis reflects ongoing metabolic dysregulation (such as cellular anaerobic glycolysis) associated with ongoing organ dysfunction and underlying comorbidities, but these possible mechanisms need further study.

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ANSWERS

Article 1	Article 2
Question 1 _____	Question 1 _____
Question 2 _____	Question 2 _____
Question 3 _____	Question 3 _____
Question 4 _____	Question 4 _____

Evaluation Form

Article 1	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
1. Topics and content were consistent with learning objectives.	○	○	○	○	○
2. Content was relevant to my educational needs.	○	○	○	○	○
3. I will seek additional information on this subject.	○	○	○	○	○
4. The article and questions were relevant to my practice.	○	○	○	○	○
5. Content was fair, objective, and unbiased.	○	○	○	○	○
(Please explain any specific instance[s] of bias or conflict of interest.)					
Article 2					
1. Topics and content were consistent with learning objectives.	○	○	○	○	○
2. Content was relevant to my educational needs.	○	○	○	○	○
3. I will seek additional information on this subject.	○	○	○	○	○
4. The article and questions were relevant to my practice.	○	○	○	○	○
5. Content was fair, objective, and unbiased.	○	○	○	○	○
(Please explain any specific instance[s] of bias or conflict of interest.)					

Questions? Call 312-202-5316. Email: jacscme@facs.org.