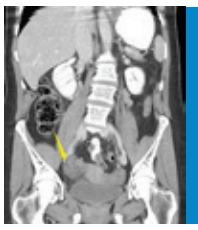
POLICY Rx

Prehospital Bias

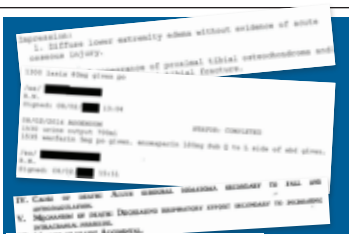
SEE PAGE 24



OVARIAN TORSION

Dispelling 5 Ovarian Torsion Myths

SEE PAGE 14



MEDICOLEGAL MIND

Bounceback Blowback

SEE PAGE 25

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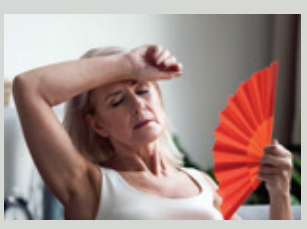
PLUS

PATIENT SATISFACTION

GRATITUDE AND COVID-19

SEE PAGE 16



HEAT ILLNESS

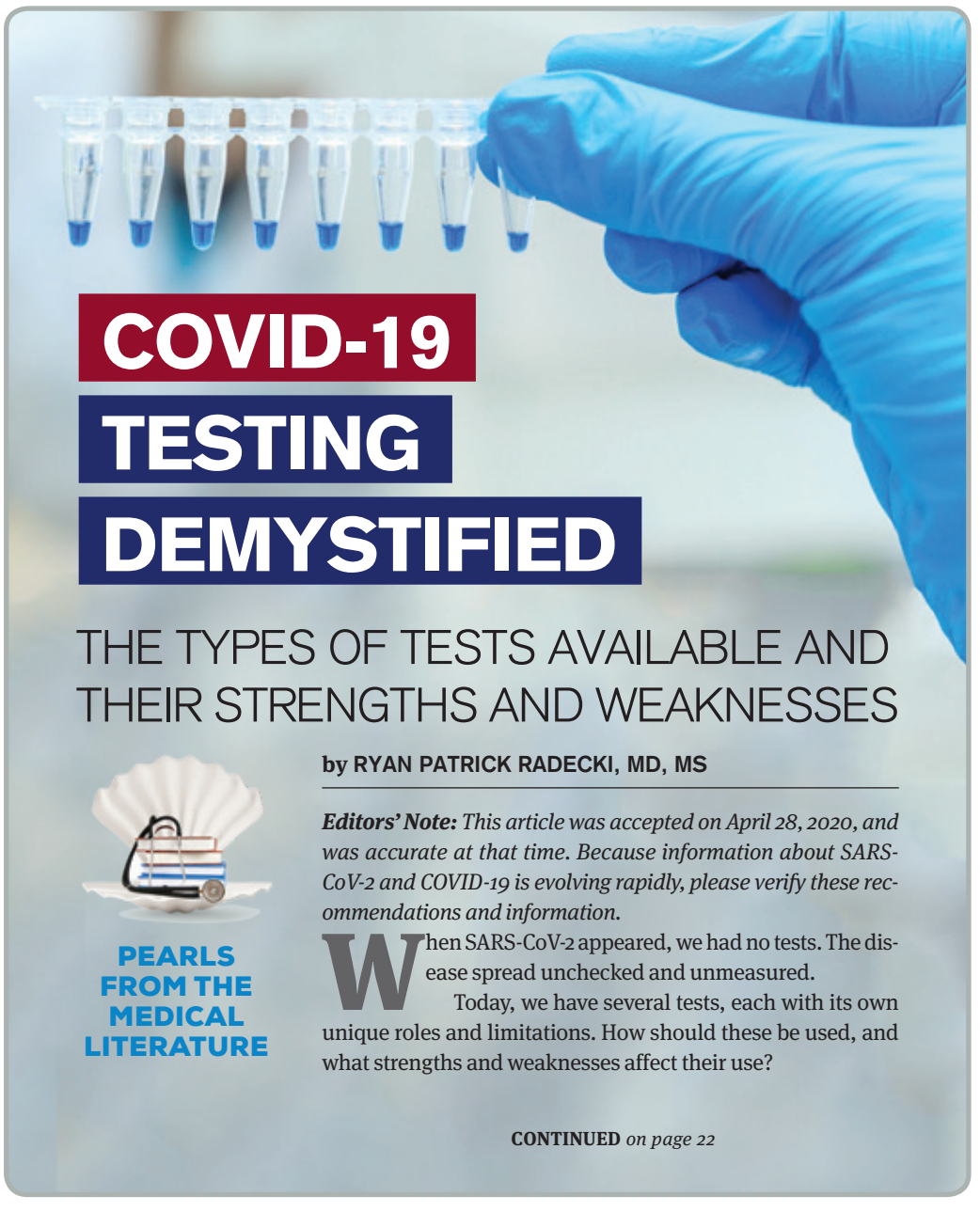
THERE'S MORE TO IT THAN HEATSTROKE

SEE PAGE 19

FIND IT ONLINE

For more clinical stories and practice trends, plus commentary and opinion pieces, go to:

www.acepnow.com



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THE TYPES OF TESTS AVAILABLE AND THEIR STRENGTHS AND WEAKNESSES

PEARLS FROM THE MEDICAL LITERATURE

by RYAN PATRICK RADECKI, MD, MS

Editors' Note: *This article was accepted on April 28, 2020, and was accurate at that time. Because information about SARS-CoV-2 and COVID-19 is evolving rapidly, please verify these recommendations and information.*

When SARS-CoV-2 appeared, we had no tests. The disease spread unchecked and unmeasured.

Today, we have several tests, each with its own unique roles and limitations. How should these be used, and what strengths and weaknesses affect their use?

CONTINUED *on page 22*

ALISTER MARTIN

Waiting room voter registration kiosk.

GETTING PATIENTS REGISTERED TO VOTE

Emergency departments can play an active role

by JONATHAN KUSNER; LAURA DEAN, MD; AND ALISTER MARTIN, MD, MMP

Rates of electoral participation in the United States continue to rank in the bottom quartile among developed nations.[1] Resulting from a number of factors, poor voter turnout has characterized our democracy for decades.[2] Can emergency departments help? It might seem like an oddly arranged marriage, but it isn't.

A majority of U.S. voters consistently rank health care as their top policy priority. Simultaneously, voter rolls are shrinking. This suggests that a smaller and smaller group of people are having their voices heard on the direction of health policy.[3,4] This is especially troubling for communities of color, those living in poverty, and the young, who are often among the least politically active. COVID-19 has led to the closure of motor vehicle registration offices and other traditional voter

CONTINUED *on page 17*

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NEWS FROM THE COLLEGE

UPDATES AND ALERTS FROM ACEP

ACEP's New Executive Director to Start in July

As the next step in a career dedicated to improving health care, Susan Sedory, MA, CAE, will assume the role of ACEP's next Executive Director. Ms. Sedory will build on the foundation laid by Dean Wilkerson, JD, MBA, CAE, who will retire after 16 years as ACEP's Executive Director on July 31, 2020.

Ms. Sedory has been the Executive Director of the Society of Interventional Radiology since 2011, leading the association of more than 8,100 interventional radiology physicians, scientists, and clinical professionals in the shared goal to optimize minimally invasive patient care. Ms. Sedory will be ACEP's fourth executive director—and first woman in this position—in the College's more-than-50-year history.

"Sue has been successful throughout her career. She's a terrific person who I greatly respect," Mr. Wilkerson said. "I'm pleased ACEP will be in good hands after I retire."

To read more about Ms. Sedory and the selection process, visit www.acep.org/new-executive-director.

ACEP Helps Develop Due Process Bill

ACEP worked closely with the offices of U.S. Rep. Roger Marshall, MD (R-KS), and U.S. Rep. Raul Ruiz, MD (D-CA), on the development of H.R. 6910, a bill introduced in the House on May 15 that would ensure every emergency physician has medical staff due process protections. The legislation would require the secretary of the U.S. Department of Health and Human Services to issue regulations that would provide due process rights for physicians furnishing emergency medical services. Specifically, the regulations would ensure physicians who are employed by or under contract with a hospital to furnish emergency medical services have a fair hearing and appellate review through appropriate medical staff mechanisms before any termination or restriction of their professional activities could be instituted. These protections could not be denied through third-party contracts. Read ACEP's support letter at www.acep.org/globalassets/new-pdfs/advocacy/acep-support-letter-due-process-04-16-20.pdf.

Stigma Video, Accreditation Program, and Online Waiver Trainings Highlight Latest Opioid Resources

Though COVID-19 has been front and center, work has continued on ACEP's other important public health initiatives, including opioids. Here are some of the latest developments:

- ACEP newest accreditation program, Pain and Addiction Care in the ED (PACED), launched this spring. It's the nation's only specialty-specific program that allows emergency departments to improve pain and addiction care. Learn more at www.acep.org/paced.
- In May, more than 750 people participated in a Zoom version of waiver training hosted by Get Waivered, ACEP, and ED Bridge. On June 17, ACEP is hosting an EM-specific online X-waiver training. Due to the popularity of these initial offerings, we plan to offer more online waiver trainings in the near future.
- In January, ACEP convened the Addressing the Opioid Stigma in the Emergency Department summit, and a powerful 11-minute video from that event can be viewed at www.acep.org/stigma. Emergency physicians are encouraged to watch the video, reflect, and break down the stigmas that impair patient care by sharing this video far and wide.
- ACEP's COVID-19 Field Guide has a section focused on the management of patients with substance use disorders. View more at www.acep.org/covid19fieldguide.

The Joint Commission Supports Removal of Barriers to Mental Health Care for Clinicians

On May 12, The Joint Commission (TJC) released a statement (www.acep.org/TJC-mental-health-statement) that supports "the removal of any barriers that inhibit clinicians and health care staff from accessing mental health care services, including eliminating policies that reinforce stigma and fear about the professional consequences of seeking mental health treatment." The statement came after ACEP met with TJC to discuss physicians being penalized by state licensing boards and other entities for seeking mental health support.

This is just one of the ways ACEP is working to support your emotional well-being during this incredibly trying time. Turn to p. 12 to read about the wellness resources available for emergency physicians, from peer-to-peer forums to free crisis support and more.

COVID-19 Center Curates the Content You Need

To keep up with its growing library of resources, ACEP's COVID-19 website has been redesigned to make it easier to find what you need, when you need it. Visit www.acep.org/covid-19 for more than 400 clinical resources organized by topic, plus COVID-specific advocacy updates, webinars, discounts, and more. It's also home to our most popular resource, the Field Guide to management of COVID-19 in the emergency department, a living document that has grown to more than 300 pages and been translated into five languages.

ACEP20 Registration to Open in July

It is unknown how COVID-19 will affect the rest of this calendar year, but we continue to plan for the ACEP Scientific Assembly Oct. 26–29. We look forward to commemorating a memorable and hard year where your bravery and dedication have been on display. ACEP is exploring virtual options to make this a special event for the entire emergency medicine team, no matter where you are. Registration is scheduled to open July 1 at www.acep.org/acep20.

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(apixaban) tablets 5mg 2.5mg

In the emergency department, both safety and efficacy matter

For appropriate patients with DVT/PE, consider **ELIQUIS** at discharge

DVT=deep vein thrombosis; PE=pulmonary embolism.

INDICATION

ELIQUIS is indicated for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and to reduce the risk of recurrent DVT and PE following initial therapy.

IMPORTANT SAFETY INFORMATION

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

(A) Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

(B) Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- **use of indwelling epidural catheters**
- **concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants**
- **a history of traumatic or repeated epidural or spinal punctures**
- **a history of spinal deformity or spinal surgery**
- **optimal timing between the administration of ELIQUIS and neuraxial procedures is not known**

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated.

Please see additional Important Safety Information and Brief Summary of Full Prescribing Information, including **Boxed WARNINGS,** on adjacent pages.

AMPLIFY[1,2] Study Design

A randomized, double-blind, phase III trial to determine whether ELIQUIS was noninferior to enoxaparin/warfarin for the incidence of recurrent venous thromboembolism (VTE)* or VTE-related death in 5400 patients with objectively confirmed, symptomatic proximal DVT/PE. 2693 patients were randomized to ELIQUIS 10 mg orally twice daily for 7 days followed by 5 mg orally twice daily for 6 months, and 2707 patients were randomized to standard of care, which was initial enoxaparin 1 mg/kg twice daily subcutaneously for at least 5 days (until INR ≥2), followed by warfarin (target INR range: 2.0-3.0) orally for 6 months. The primary efficacy endpoint was recurrent VTE* or VTE-related death, and the primary safety endpoint was major bleeding.

≈90% of patients in the AMPLIFY trial had an unprovoked DVT/PE at baseline.[1]

- The 10% of patients with a provoked DVT/PE were required to have an additional ongoing risk factor in order to be randomized†

*Recurrent symptomatic VTE (nonfatal DVT or nonfatal PE).
†Risk factors included previous episode of DVT/PE, immobilization, history of cancer, active cancer, and known prothrombotic genotype.

IMPORTANT SAFETY INFORMATION (CONT'D)

CONTRAINDICATIONS

- Active pathological bleeding
- Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions)

WARNINGS AND PRECAUTIONS

- **Increased Risk of Thrombotic Events after Premature Discontinuation:** Premature discontinuation of any oral anticoagulant, including ELIQUIS, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.
- **Bleeding Risk:** ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding.
  - Concomitant use of drugs affecting hemostasis increases the risk of bleeding, including aspirin and other antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, SSRIs, SNRIs, and NSAIDs.
  - Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage.
  - The anticoagulant effect of apixaban can be expected to persist for at least 24 hours after the last dose (i.e., about two half-lives). An agent to reverse the anti-factor Xa activity of apixaban is available. Please visit www.andexxa.com for more information on availability of a reversal agent.
- **Spinal/Epidural Anesthesia or Puncture:** Patients treated with ELIQUIS undergoing spinal/epidural anesthesia or puncture may develop an epidural or spinal hematoma which can result in long-term or permanent paralysis.

  The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic puncture occurs, delay the administration of ELIQUIS for 48 hours.

  Monitor patients frequently and if neurological compromise is noted, urgent diagnosis and treatment is necessary. Physicians should consider the potential benefit versus the risk of neuraxial intervention in ELIQUIS patients.
- **Prosthetic Heart Valves:** The safety and efficacy of ELIQUIS have not been studied in patients with prosthetic heart valves and is not recommended in these patients.
- **Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy:** Initiation of ELIQUIS is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.
- **Increased Risk of Thrombosis in Patients with Triple Positive Antiphospholipid Syndrome (APS):** Direct-acting oral anticoagulants (DOACs), including ELIQUIS, are not recommended for use in patients with triple-positive APS. For patients with APS (especially those who are triple positive [positive for lupus anticoagulant, anticardiolipin, and anti–beta 2-glycoprotein I antibodies]), treatment with DOACs has been associated with increased rates of recurrent thrombotic events compared with vitamin K antagonist therapy.

ADVERSE REACTIONS

- The most common and most serious adverse reactions reported with ELIQUIS were related to bleeding.

TEMPORARY INTERRUPTION FOR SURGERY AND OTHER INTERVENTIONS

- ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be noncritical in location and easily controlled. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established.

DRUG INTERACTIONS

- **Combined P-gp and Strong CYP3A4 Inhibitors:** Inhibitors of P-glycoprotein (P-gp) and cytochrome P450 3A4 (CYP3A4) increase exposure to apixaban and increase the risk of bleeding. For patients receiving ELIQUIS doses of 5 mg or 10 mg twice daily, reduce the dose of ELIQUIS by 50% when ELIQUIS is coadministered with drugs that are combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, or ritonavir). In patients already taking 2.5 mg twice daily, avoid coadministration of ELIQUIS with combined P-gp and strong CYP3A4 inhibitors.

  Clarithromycin
  Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS.

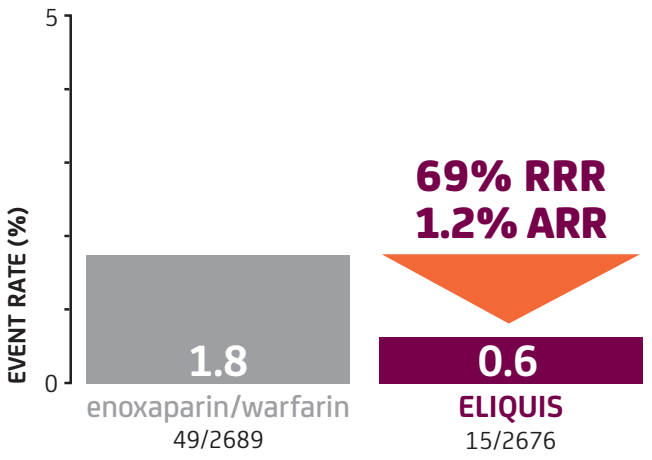
FOR THE TREATMENT OF DVT/PE

Only ELIQUIS demonstrated BOTH superiority in major bleeding events AND comparable efficacy vs enoxaparin/warfarin[1]

SUPERIOR

Major Bleeding‡

RR=0.31 (95% CI: 0.17–0.55); *P*<0.0001

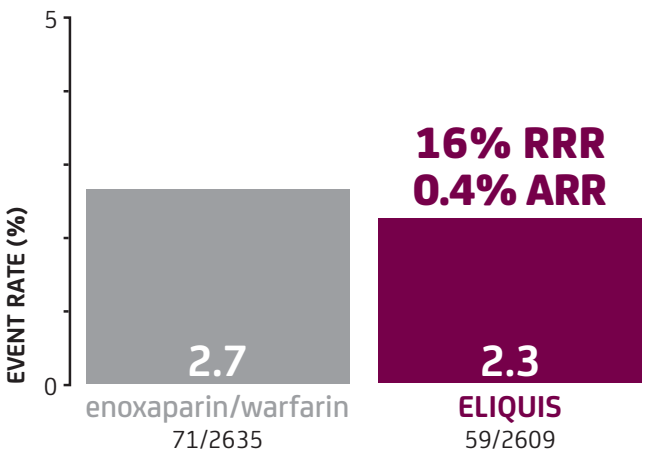


PRIMARY SAFETY ENDPOINT

COMPARABLE

in VTE*/VTE-related death

RR=0.84 (95% CI: 0.60–1.18); *P*<0.0001 for noninferiority



PRIMARY EFFICACY ENDPOINT

ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding[1]

- Discontinuation rate due to bleeding events: 0.7% in ELIQUIS-treated patients vs 1.7% with enoxaparin/warfarin[1]
- In AMPLIFY, the most commonly observed adverse reactions in ELIQUIS-treated patients (incidence ≥1%) were epistaxis, contusion, hematuria, menorrhagia, hematoma, hemoptysis, rectal hemorrhage, and gingival bleeding[1]

Major bleeding was defined as clinically overt bleeding accompanied by at least one of the following[2,3]:

1) A decrease in hemoglobin of ≥2 g/dL; 2) A transfusion of 2 or more units of packed red blood cells; 3) Bleeding that occurred in at least 1 of the following critical sites: intracranial, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, or retroperitoneal; 4) Fatal bleeding

ARR=absolute risk reduction; CI=confidence interval; HR=hazard ratio; INR=international normalized ratio; RR=relative risk; RRR=relative risk reduction.
‡Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

IMPORTANT SAFETY INFORMATION (CONT'D)

DRUG INTERACTIONS (cont'd)

- **Combined P-gp and Strong CYP3A4 Inducers:** Avoid concomitant use of ELIQUIS with combined P-gp and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban.
- **Anticoagulants and Antiplatelet Agents:** Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding. APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo.

PREGNANCY

- The limited available data on ELIQUIS use in pregnant women are insufficient to inform drug-associated risks of major birth defects, miscarriage, or adverse developmental outcomes.

  Treatment may increase the risk of bleeding during pregnancy and delivery, and in the fetus and neonate.
  - *Labor or delivery*: ELIQUIS use during labor or delivery in women who are receiving neuraxial anesthesia may result in epidural or spinal hematomas. Consider use of a shorter acting anticoagulant as delivery approaches.

LACTATION

- Breastfeeding is not recommended during treatment with ELIQUIS.

References: 1. Eliquis [package insert]. Bristol-Myers Squibb Company, Princeton, NJ, and Pfizer Inc, New York, NY. **2.** Agnelli G, Buller HR, Cohen A, et al; for AMPLIFY Investigators. Oral apixaban for the treatment of acute venous thromboembolism. *N Engl J Med*. 2013;369(9):799-808. Supplement available at http://www.nejm.org/doi/suppl/10.1056/NEJMoa1302507/suppl_file/nejmoa1302507_appendix.pdf. Accessed December 5, 2018. **3.** Agnelli G, Buller HR, Cohen A, et al. Apixaban for extended treatment of venous thromboembolism. *N Engl J Med*. 2013;368(8):699-708. Supplement available at http://www.nejm.org/doi/suppl/10.1056/NEJMoa1207541/suppl_file/nejmoa 1207541_appendix.pdf. Accessed December 18, 2018.

Please see Brief Summary of Full Prescribing Information, including **Boxed WARNINGS,** on adjacent pages.

Eliquis® (apixaban) tablets 5mg 2.5mg

Bristol Myers Squibb™ Pfizer

ELIQUIS® (apixaban) tablets, for oral use

℞ ONLY

Brief Summary of Prescribing Information. For complete prescribing information consult official package insert.

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS

(B) SPINAL/EPIDURAL HEMATOMA

(A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS

Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant *[see Dosage and Administration, Warnings and Precautions, and Clinical Studies (14.1) in full Prescribing Information]*.

(B) SPINAL/EPIDURAL HEMATOMA

Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- **use of indwelling epidural catheters**
- **concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants**
- **a history of traumatic or repeated epidural or spinal punctures**
- **a history of spinal deformity or spinal surgery**
- **optimal timing between the administration of ELIQUIS and neuraxial procedures is not known**

[see Warnings and Precautions]

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary *[see Warnings and Precautions]*.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated *[see Warnings and Precautions]*.

INDICATIONS AND USAGE

Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation— ELIQUIS is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery— ELIQUIS is indicated for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery.

Treatment of Deep Vein Thrombosis—ELIQUIS is indicated for the treatment of DVT.

Treatment of Pulmonary Embolism—ELIQUIS is indicated for the treatment of PE.

Reduction in the Risk of Recurrence of DVT and PE—ELIQUIS is indicated to reduce the risk of recurrent DVT and PE following initial therapy.

DOSAGE AND ADMINISTRATION (Selected information)

Temporary Interruption for Surgery and Other Interventions

ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding *[see Warnings and Precautions]*. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be non-critical in location and easily controlled. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established. (For complete *Dosage and Administration* section, see full Prescribing Information.)

CONTRAINDICATIONS

ELIQUIS is contraindicated in patients with the following conditions:

- Active pathological bleeding *[see Warnings and Precautions and Adverse Reactions]*
- Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions) *[see Adverse Reactions]*

WARNINGS AND PRECAUTIONS

Increased Risk of Thrombotic Events after Premature Discontinuation

Premature discontinuation of any oral anticoagulant, including ELIQUIS, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant *[see Dosage and Administration (2.4) and Clinical Studies (14.1) in full Prescribing Information]*.

Bleeding

ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding *[see Dosage and Administration (2.1) in full Prescribing Information and Adverse Reactions]*.

Concomitant use of drugs affecting hemostasis increases the risk of bleeding. These include aspirin and other antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, and nonsteroidal anti-inflammatory drugs (NSAIDs) *[see Drug Interactions]*.

Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage.

Reversal of Anticoagulant Effect

An agent to reverse the anti-factor Xa activity of apixaban is available. The pharmacodynamic effect of ELIQUIS can be expected to persist for at least 24 hours after the last dose, i.e., for about two drug half-lives. Prothrombin complex concentrate (PCC), activated prothrombin complex concentrate or recombinant factor VIIa may be considered, but have not been evaluated in clinical studies *[see Clinical Pharmacology (12.2) in full Prescribing Information]*. When PCCs are used, monitoring for the anticoagulation effect of apixaban using a clotting test (PT, INR, or aPTT) or anti-factor Xa (FXa) activity is not useful and is not recommended. Activated oral charcoal reduces absorption of apixaban, thereby lowering apixaban plasma concentration *[see Overdosage]*.

Hemodialysis does not appear to have a substantial impact on apixaban exposure *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. Protamine sulfate and vitamin K are not expected to affect the anticoagulant activity of apixaban. There is no experience with antifibrinolytic agents (tranexamic acid, aminocaproic acid) in individuals receiving apixaban. There is no experience with systemic hemostatics (desmopressin) in individuals receiving ELIQUIS, and they are not expected to be effective as a reversal agent.

Spinal/Epidural Anesthesia or Puncture

When neuraxial anesthesia (spinal/epidural anesthesia) or spinal/epidural puncture is employed, patients treated with antithrombotic agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma which can result in long-term or permanent paralysis.

The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic puncture occurs, delay the administration of ELIQUIS for 48 hours.

Monitor patients frequently for signs and symptoms of neurological impairment (e.g., numbness or weakness of the legs, or bowel or bladder dysfunction). If neurological compromise is noted, urgent diagnosis and treatment is necessary. Prior to neuraxial intervention the physician should consider the potential benefit versus the risk in anticoagulated patients or in patients to be anticoagulated for thromboprophylaxis.

Patients with Prosthetic Heart Valves

The safety and efficacy of ELIQUIS have not been studied in patients with prosthetic heart valves. Therefore, use of ELIQUIS is not recommended in these patients.

Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy

Initiation of ELIQUIS (apixaban) is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.

Increased Risk of Thrombosis in Patients with Triple Positive Antiphospholipid Syndrome

Direct-acting oral anticoagulants (DOACs), including ELIQUIS, are not recommended for use in patients with triple-positive antiphospholipid syndrome (APS). For patients with APS (especially those who are triple positive [positive for lupus anticoagulant, anticardiolipin, and anti–beta 2-glycoprotein I antibodies]), treatment with DOACs has been associated with increased rates of recurrent thrombotic events compared with vitamin K antagonist therapy.

ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in greater detail in other sections of the prescribing information.

- Increased Risk of Thrombotic Events After Premature Discontinuation *[see Warnings and Precautions]*
- Bleeding *[see Warnings and Precautions]*
- Spinal/Epidural Anesthesia or Puncture *[see Warnings and Precautions]*

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Reduction of Risk of Stroke and Systemic Embolism in Patients with Nonvalvular Atrial Fibrillation

The safety of ELIQUIS was evaluated in the ARISTOTLE and AVERROES studies *[see Clinical Studies (14) in full Prescribing Information]*, including 11,284 patients exposed to ELIQUIS 5 mg twice daily and 602 patients exposed to ELIQUIS 2.5 mg twice daily. The duration of ELIQUIS exposure was ≥12 months for 9375 patients and ≥24 months for 3369 patients in the two studies. In ARISTOTLE, the mean duration of exposure was 89 weeks (>15,000 patient-years). In AVERROES, the mean duration of exposure was approximately 59 weeks (>3000 patient-years).

The most common reason for treatment discontinuation in both studies was for bleeding-related adverse reactions; in ARISTOTLE this occurred in 1.7% and 2.5% of patients treated with ELIQUIS and warfarin, respectively, and in AVERROES, in 1.5% and 1.3% on ELIQUIS and aspirin, respectively.

Bleeding in Patients with Nonvalvular Atrial Fibrillation in ARISTOTLE and AVERROES

Tables 1 and 2 show the number of patients experiencing major bleeding during the treatment period and the bleeding rate (percentage of subjects with at least one bleeding event per 100 patient-years) in ARISTOTLE and AVERROES.

Table 1: Bleeding Events in Patients with Nonvalvular Atrial Fibrillation in ARISTOTLE*

	ELIQUIS N=9088 n (per 100 pt-year)	Warfarin N=9052 n (per 100 pt-year)	Hazard Ratio (95% CI)	P-value
Major†	327 (2.13)	462 (3.09)	0.69 (0.60, 0.80)	<0.0001
Intracranial (ICH)‡	52 (0.33)	125 (0.82)	0.41 (0.30, 0.57)	-
Hemorrhagic stroke§	38 (0.24)	74 (0.49)	0.51 (0.34, 0.75)	-
Other ICH	15 (0.10)	51 (0.34)	0.29 (0.16, 0.51)	-
Gastrointestinal (GI)¶	128 (0.83)	141 (0.93)	0.89 (0.70, 1.14)	-
Fatal**	10 (0.06)	37 (0.24)	0.27 (0.13, 0.53)	-
Intracranial	4 (0.03)	30 (0.20)	0.13 (0.05, 0.37)	-
Non-intracranial	6 (0.04)	7 (0.05)	0.84 (0.28, 2.15)	-

* Bleeding events within each subcategory were counted once per subject, but subjects may have contributed events to multiple endpoints. Bleeding events were counted during treatment or within 2 days of stopping study treatment (on-treatment period).
† Defined as clinically overt bleeding accompanied by one or more of the following: a decrease in hemoglobin of ≥2 g/dL, a transfusion of 2 or more units of packed red blood cells, bleeding at a critical site: intracranial, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, retroperitoneal or with fatal outcome.
‡ Intracranial bleed includes intracerebral, intraventricular, subdural, and subarachnoid bleeding. Any type of hemorrhagic stroke was adjudicated and counted as an intracranial major bleed.
§ On-treatment analysis based on the safety population, compared to ITT analysis presented in Section 14 in the full Prescribing Information.
¶ GI bleed includes upper GI, lower GI, and rectal bleeding.
** Fatal bleeding is an adjudicated death with the primary cause of death as intracranial bleeding or non-intracranial bleeding during the on-treatment period.

In ARISTOTLE, the results for major bleeding were generally consistent across most major subgroups including age, weight, $CHADS_2$ score (a scale from 0 to 6 used to estimate risk of stroke, with higher scores predicting greater risk), prior warfarin use, geographic region, and aspirin use at randomization (Figure 1). Subjects treated with ELIQUIS with diabetes bled more (3% per year) than did subjects without diabetes (1.9% per year).

Table 2: Bleeding Events in Patients with Nonvalvular Atrial Fibrillation in AVERROES

	ELIQUIS (apixaban) N=2798 n (%/year)	Aspirin N=2780 n (%/year)	Hazard Ratio (95% CI)	P-value
Major	45 (1.41)	29 (0.92)	1.54 (0.96, 2.45)	0.07
Fatal	5 (0.16)	5 (0.16)	0.99 (0.23, 4.29)	-
Intracranial	11 (0.34)	11 (0.35)	0.99 (0.39, 2.51)	-

Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

Other Adverse Reactions

Hypersensitivity reactions (including drug hypersensitivity, such as skin rash, and anaphylactic reactions, such as allergic edema) and syncope were reported in <1% of patients receiving ELIQUIS.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery

The safety of ELIQUIS has been evaluated in 1 Phase II and 3 Phase III studies including 5924 patients exposed to ELIQUIS 2.5 mg twice daily undergoing major orthopedic surgery of the lower limbs (elective hip replacement or elective knee replacement) treated for up to 38 days.

In total, 11% of the patients treated with ELIQUIS 2.5 mg twice daily experienced adverse reactions.

Bleeding results during the treatment period in the Phase III studies are shown in Table 3. Bleeding was assessed in each study beginning with the first dose of double-blind study drug.

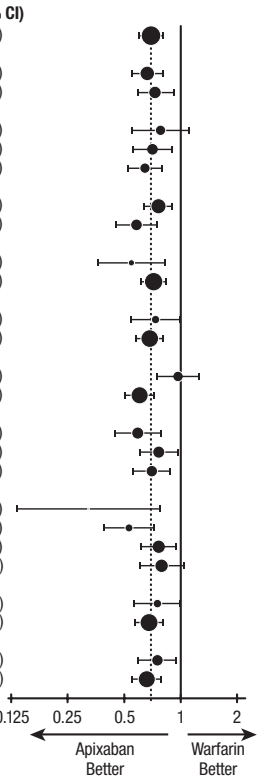
Table 3: Bleeding During the Treatment Period in Patients Undergoing Elective Hip or Knee Replacement Surgery

Bleeding Endpoint*	ADVANCE-3 Hip Replacement Surgery		ADVANCE-2 Knee Replacement Surgery		ADVANCE-1 Knee Replacement Surgery	
	ELIQUIS 2.5 mg po bid 35±3 days	Enoxaparin 40 mg sc qd 35±3 days	ELIQUIS 2.5 mg po bid 12±2 days	Enoxaparin 40 mg sc qd 12±2 days	ELIQUIS 2.5 mg po bid 12±2 days	Enoxaparin 30 mg sc q12h 12±2 days
	First dose 12 to 24 hours post surgery	First dose 9 to 15 hours prior to surgery	First dose 12 to 24 hours post surgery	First dose 9 to 15 hours prior to surgery	First dose 12 to 24 hours post surgery	First dose 12 to 24 hours post surgery
All treated	N=2673	N=2659	N=1501	N=1508	N=1596	N=1588
Major (including surgical site)	22 (0.82%)†	18 (0.68%)	9 (0.60%)‡	14 (0.93%)	11 (0.69%)	22 (1.39%)
Fatal	0	0	0	0	0	1 (0.06%)
Hgb decrease ≥2 g/dL	13 (0.49%)	10 (0.38%)	8 (0.53%)	9 (0.60%)	10 (0.63%)	16 (1.01%)
Transfusion of ≥2 units RBC	16 (0.60%)	14 (0.53%)	5 (0.33%)	9 (0.60%)	9 (0.56%)	18 (1.13%)
Bleed at critical site§	1 (0.04%)	1 (0.04%)	1 (0.07%)	2 (0.13%)	1 (0.06%)	4 (0.25%)
Major + CRNM¶	129 (4.83%)	134 (5.04%)	53 (3.53%)	72 (4.77%)	46 (2.88%)	68 (4.28%)
All	313 (11.71%)	334 (12.56%)	104 (6.93%)	126 (8.36%)	85 (5.33%)	108 (6.80%)

* All bleeding criteria included surgical site bleeding.
† Includes 13 subjects with major bleeding events that occurred before the first dose of ELIQUIS (administered 12 to 24 hours post-surgery).
‡ Includes 5 subjects with major bleeding events that occurred before the first dose of ELIQUIS (administered 12 to 24 hours post-surgery).
§ Intracranial, intraspinal, intraocular, pericardial, an operated joint requiring re-operation or intervention, intramuscular with compartment syndrome, or retroperitoneal. Bleeding into an operated joint requiring re-operation or intervention was present in all patients with this category of bleeding. Events and event rates include one enoxaparin-treated patient in ADVANCE-1 who also had intracranial hemorrhage.
¶ CRNM = clinically relevant nonmajor.

Figure 1: Major Bleeding Hazard Ratios by Baseline Characteristics – ARISTOTLE Study

Subgroup	n of Events / N of Patients (% per year) Apixaban	Warfarin	Hazard Ratio (95% CI)
All Patients	327 / 9088 (2.1)	462 / 9052 (3.1)	0.69 (0.60, 0.80)
Prior Warfarin/VKA Status			
Experienced (57%)	185 / 5196 (2.1)	274 / 5180 (3.2)	0.66 (0.55, 0.80)
Naive (43%)	142 / 3892 (2.2)	188 / 3872 (3.0)	0.73 (0.59, 0.91)
Age			
<65 (30%)	56 / 2723 (1.2)	72 / 2732 (1.5)	0.78 (0.55, 1.11)
≥65 and <75 (39%)	120 / 3529 (2.0)	166 / 3501 (2.8)	0.71 (0.56, 0.89)
≥75 (31%)	151 / 2836 (3.3)	224 / 2819 (5.2)	0.64 (0.52, 0.79)
Sex			
Male (65%)	225 / 5868 (2.3)	294 / 5879 (3.0)	0.76 (0.64, 0.90)
Female (35%)	102 / 3220 (1.9)	168 / 3173 (3.3)	0.58 (0.45, 0.74)
Weight			
≤60 kg (11%)	36 / 1013 (2.3)	62 / 965 (4.3)	0.55 (0.36, 0.83)
>60 kg (89%)	290 / 8043 (2.1)	398 / 8059 (3.0)	0.72 (0.62, 0.83)
Prior Stroke or TIA			
Yes (19%)	77 / 1687 (2.8)	106 / 1735 (3.9)	0.73 (0.54, 0.98)
No (81%)	250 / 7401 (2.0)	356 / 7317 (2.9)	0.68 (0.58, 0.80)
Diabetes Mellitus			
Yes (25%)	112 / 2276 (3.0)	114 / 2250 (3.1)	0.96 (0.74, 1.25)
No (75%)	215 / 6812 (1.9)	348 / 6802 (3.1)	0.60 (0.51, 0.71)
$CHADS_2$ Score			
≤1 (34%)	76 / 3093 (1.4)	126 / 3076 (2.3)	0.59 (0.44, 0.78)
2 (36%)	125 / 3246 (2.3)	163 / 3246 (3.0)	0.76 (0.60, 0.96)
≥3 (30%)	126 / 2749 (2.9)	173 / 2730 (4.1)	0.70 (0.56, 0.88)
Creatinine Clearance			
<30 mL/min (1%)	7 / 136 (3.7)	19 / 132 (11.9)	0.32 (0.13, 0.78)
30-50 mL/min (15%)	66 / 1357 (3.2)	123 / 1380 (6.0)	0.53 (0.39, 0.71)
>50-80 mL/min (42%)	157 / 3807 (2.5)	199 / 3758 (3.2)	0.76 (0.62, 0.94)
>80 mL/min (41%)	96 / 3750 (1.5)	119 / 3746 (1.8)	0.79 (0.61, 1.04)
Geographic Region			
US (19%)	83 / 1716 (2.8)	109 / 1693 (3.8)	0.75 (0.56, 1.00)
Non-US (81%)	244 / 7372 (2.0)	353 / 7359 (2.9)	0.68 (0.57, 0.80)
Aspirin at Randomization			
Yes (31%)	129 / 2846 (2.7)	164 / 2762 (3.7)	0.75 (0.60, 0.95)
No (69%)	198 / 6242 (1.9)	298 / 6290 (2.8)	0.66 (0.55, 0.79)



Note: The figure above presents effects in various subgroups, all of which are baseline characteristics and all of which were prespecified, if not the groupings. The 95% confidence limits that are shown do not take into account how many comparisons were made, nor do they reflect the effect of a particular factor after adjustment for all other factors. Apparent homogeneity or heterogeneity among groups should not be over-interpreted.

Adverse reactions occurring in ≥1% of patients undergoing hip or knee replacement surgery in the 1 Phase II study and the 3 Phase III studies are listed in Table 4.

Table 4: Adverse Reactions Occurring in ≥1% of Patients in Either Group Undergoing Hip or Knee Replacement Surgery

	ELIQUIS (apixaban), n (%) 2.5 mg po bid N=5924	Enoxaparin, n (%) 40 mg sc qd or 30 mg sc q12h N=5904
Nausea	153 (2.6)	159 (2.7)
Anemia (including postoperative and hemorrhagic anemia, and respective laboratory parameters)	153 (2.6)	178 (3.0)
Contusion	83 (1.4)	115 (1.9)
Hemorrhage (including hematoma, and vaginal and urethral hemorrhage)	67 (1.1)	81 (1.4)
Postprocedural hemorrhage (including postprocedural hematoma, wound hemorrhage, vessel puncture-site hematoma and catheter-site hemorrhage)	54 (0.9)	60 (1.0)
Transaminases increased (including alanine aminotransferase increased and alanine aminotransferase abnormal)	50 (0.8)	71 (1.2)
Aspartate aminotransferase increased	47 (0.8)	69 (1.2)
Gamma-glutamyltransferase increased	38 (0.6)	65 (1.1)

Less common adverse reactions in ELIQUIS-treated patients undergoing hip or knee replacement surgery occurring at a frequency of ≥0.1% to <1%:

Blood and lymphatic system disorders: thrombocytopenia (including platelet count decreases)

Vascular disorders: hypotension (including procedural hypotension)

Respiratory, thoracic, and mediastinal disorders: epistaxis

Gastrointestinal disorders: gastrointestinal hemorrhage (including hematemesis and melena), hematochezia

Hepatobiliary disorders: liver function test abnormal, blood alkaline phosphatase increased, blood bilirubin increased

Renal and urinary disorders: hematuria (including respective laboratory parameters)

Injury, poisoning, and procedural complications: wound secretion, incision-site hemorrhage (including incision-site hematoma), operative hemorrhage

Less common adverse reactions in ELIQUIS-treated patients undergoing hip or knee replacement surgery occurring at a frequency of <0.1%:

Gingival bleeding, hemoptysis, hypersensitivity, muscle hemorrhage, ocular hemorrhage (including conjunctival hemorrhage), rectal hemorrhage

Treatment of DVT and PE and Reduction in the Risk of Recurrence of DVT or PE

The safety of ELIQUIS has been evaluated in the AMPLIFY and AMPLIFY-EXT studies, including 2676 patients exposed to ELIQUIS 10 mg twice daily, 3359 patients exposed to ELIQUIS 5 mg twice daily, and 840 patients exposed to ELIQUIS 2.5 mg twice daily.

Common adverse reactions (≥1%) were gingival bleeding, epistaxis, contusion, hematuria, rectal hemorrhage, hematoma, menorrhagia, and hemoptysis.

AMPLIFY Study

The mean duration of exposure to ELIQUIS was 154 days and to enoxaparin/warfarin was 152 days in the AMPLIFY study. Adverse reactions related to bleeding occurred in 417 (15.6%) ELIQUIS-treated patients compared to 661 (24.6%) enoxaparin/warfarin-treated patients. The discontinuation rate due to bleeding events was 0.7% in the ELIQUIS-treated patients compared to 1.7% in enoxaparin/warfarin-treated patients in the AMPLIFY study.

In the AMPLIFY study, ELIQUIS was statistically superior to enoxaparin/warfarin in the primary safety endpoint of major bleeding (relative risk 0.31, 95% CI [0.17, 0.55], P-value <0.0001).

Bleeding results from the AMPLIFY study are summarized in Table 5.

Table 5: Bleeding Results in the AMPLIFY Study

	ELIQUIS N=2676 n (%)	Enoxaparin/Warfarin N=2689 n (%)	Relative Risk (95% CI)
Major	15 (0.6)	49 (1.8)	0.31 (0.17, 0.55) p<0.0001
CRNM*	103 (3.9)	215 (8.0)	
Major + CRNM	115 (4.3)	261 (9.7)	
Minor	313 (11.7)	505 (18.8)	
All	402 (15.0)	676 (25.1)	

* CRNM = clinically relevant nonmajor bleeding.

Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

Adverse reactions occurring in ≥1% of patients in the AMPLIFY study are listed in Table 6.

Table 6: Adverse Reactions Occurring in ≥1% of Patients Treated for DVT and PE in the AMPLIFY Study

	ELIQUIS N=2676 n (%)	Enoxaparin/Warfarin N=2689 n (%)
Epistaxis	77 (2.9)	146 (5.4)
Contusion	49 (1.8)	97 (3.6)
Hematuria	46 (1.7)	102 (3.8)
Menorrhagia	38 (1.4)	30 (1.1)
Hematoma	35 (1.3)	76 (2.8)
Hemoptysis	32 (1.2)	31 (1.2)
Rectal hemorrhage	26 (1.0)	39 (1.5)
Gingival bleeding	26 (1.0)	50 (1.9)

AMPLIFY-EXT Study

The mean duration of exposure to ELIQUIS was approximately 330 days and to placebo was 312 days in the AMPLIFY-EXT study. Adverse reactions related to bleeding occurred in 219 (13.3%) ELIQUIS-treated patients compared to 72 (8.7%) placebo-treated patients. The discontinuation rate due to bleeding events was approximately 1% in the ELIQUIS-treated patients compared to 0.4% in those patients in the placebo group in the AMPLIFY-EXT study.

Bleeding results from the AMPLIFY-EXT study are summarized in Table 7.

Table 7: Bleeding Results in the AMPLIFY-EXT Study

	ELIQUIS 2.5 mg bid N=840 n (%)	ELIQUIS 5 mg bid N=811 n (%)	Placebo N=826 n (%)
Major	2 (0.2)	1 (0.1)	4 (0.5)
CRNM*	25 (3.0)	34 (4.2)	19 (2.3)
Major + CRNM	27 (3.2)	35 (4.3)	22 (2.7)
Minor	75 (8.9)	98 (12.1)	58 (7.0)
All	94 (11.2)	121 (14.9)	74 (9.0)

* CRNM = clinically relevant nonmajor bleeding.

Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

Adverse reactions occurring in ≥1% of patients in the AMPLIFY-EXT study are listed in Table 8.

Table 8: Adverse Reactions Occurring in ≥1% of Patients Undergoing Extended Treatment for DVT and PE in the AMPLIFY-EXT Study

	ELIQUIS (apixaban) 2.5 mg bid N=840 n (%)	ELIQUIS 5 mg bid N=811 n (%)	Placebo N=826 n (%)
Epistaxis	13 (1.5)	29 (3.6)	9 (1.1)
Hematuria	12 (1.4)	17 (2.1)	9 (1.1)
Hematoma	13 (1.5)	16 (2.0)	10 (1.2)
Contusion	18 (2.1)	18 (2.2)	18 (2.2)
Gingival bleeding	12 (1.4)	9 (1.1)	3 (0.4)

Other Adverse Reactions

Less common adverse reactions in ELIQUIS-treated patients in the AMPLIFY or AMPLIFY-EXT studies occurring at a frequency of ≥0.1% to <1%:

Blood and lymphatic system disorders: hemorrhagic anemia

Gastrointestinal disorders: hematochezia, hemorrhoidal hemorrhage, gastrointestinal hemorrhage, hematemesis, melena, anal hemorrhage

Injury, poisoning, and procedural complications: wound hemorrhage, postprocedural hemorrhage, traumatic hematoma, periorbital hematoma

Musculoskeletal and connective tissue disorders: muscle hemorrhage

Reproductive system and breast disorders: vaginal hemorrhage, metrorrhagia, menometrorrhagia, genital hemorrhage

Vascular disorders: hemorrhage

Skin and subcutaneous tissue disorders: ecchymosis, skin hemorrhage, petechiae

Eye disorders: conjunctival hemorrhage, retinal hemorrhage, eye hemorrhage

Investigations: blood urine present, occult blood positive, occult blood, red blood cells urine positive

General disorders and administration-site conditions: injection-site hematoma, vessel puncture-site hematoma

DRUG INTERACTIONS

Apixaban is a substrate of both CYP3A4 and P-gp. Inhibitors of CYP3A4 and P-gp increase exposure to apixaban and increase the risk of bleeding. Inducers of CYP3A4 and P-gp decrease exposure to apixaban and increase the risk of stroke and other thromboembolic events.

Combined P-gp and Strong CYP3A4 Inhibitors

For patients receiving ELIQUIS 5 mg or 10 mg twice daily, the dose of ELIQUIS should be decreased by 50% when coadministered with drugs that are combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir) *[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3) in full Prescribing Information]*.

For patients receiving ELIQUIS at a dose of 2.5 mg twice daily, avoid coadministration with combined P-gp and strong CYP3A4 inhibitors *[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3) in full Prescribing Information]*.

Clarithromycin

Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Combined P-gp and Strong CYP3A4 Inducers

Avoid concomitant use of ELIQUIS with combined P-gp and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Anticoagulants and Antiplatelet Agents

Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding.

APPRAISE-2, a placebo-controlled clinical trial of ELIQUIS in high-risk, post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with ELIQUIS compared to placebo. The rate of ISTH major bleeding was 2.8% per year with ELIQUIS versus 0.6% per year with placebo in patients receiving single antiplatelet therapy and was 5.9% per year with ELIQUIS versus 2.5% per year with placebo in those receiving dual antiplatelet therapy.

In ARISTOTLE, concomitant use of aspirin increased the bleeding risk on ELIQUIS from 1.8% per year to 3.4% per year and concomitant use of aspirin and warfarin increased the bleeding risk from 2.7% per year to 4.6% per year. In this clinical trial, there was limited (2.3%) use of dual antiplatelet therapy with ELIQUIS.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

The limited available data on ELIQUIS use in pregnant women are insufficient to inform drug-associated risks of major birth defects, miscarriage, or adverse developmental outcomes. Treatment may increase the risk of bleeding during pregnancy and delivery. In animal reproduction studies, no adverse developmental effects were seen when apixaban was administered to rats (orally), rabbits (intravenously) and mice (orally) during organogenesis at unbound apixaban exposure levels up to 4, 1 and 19 times, respectively, the human exposure based on area under plasma-concentration time curve (AUC) at the Maximum Recommended Human Dose (MRHD) of 5 mg twice daily.

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk

Pregnancy confers an increased risk of thromboembolism that is higher for women with underlying thromboembolic disease and certain high-risk pregnancy conditions. Published data describe that women with a previous history of venous thrombosis are at high risk for recurrence during pregnancy.

Fetal/Neonatal adverse reactions

Use of anticoagulants, including ELIQUIS, may increase the risk of bleeding in the fetus and neonate.

Labor or delivery

All patients receiving anticoagulants, including pregnant women, are at risk for bleeding. ELIQUIS use during labor or delivery in women who are receiving neuraxial anesthesia may result in epidural or spinal hematomas. Consider use of a shorter acting anticoagulant as delivery approaches *[see Warnings and Precautions]*.

Data

Animal Data

No developmental toxicities were observed when apixaban was administered during organogenesis to rats (orally), rabbits (intravenously) and mice (orally) at unbound apixaban exposure levels 4, 1, and 19 times, respectively, the human exposures at the MRHD. There was no evidence of fetal bleeding, although conceptus exposure was confirmed in rats and rabbits. Oral administration of apixaban to rat dams from gestation day 6 through lactation day 21 at maternal unbound apixaban exposures ranging from 1.4 to 5 times the human exposures at the MRHD was not associated with reduced maternal mortality or reduced conceptus/neonatal viability, although increased incidences of peri-vaginal bleeding were observed in dams at all doses. There was no evidence of neonatal bleeding.

Lactation

Risk Summary

There are no data on the presence of apixaban or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Apixaban and/or its metabolites were present in the milk of rats (see Data). Because human exposure through milk is unknown, breastfeeding is not recommended during treatment with ELIQUIS (apixaban).

Data

Animal Data

Maximal plasma concentrations were observed after 30 minutes following a single oral administration of a 5 mg dose to lactating rats. Maximal milk concentrations were observed 6 hours after dosing. The milk to plasma AUC (0-24) ratio is 30:1 indicating that apixaban can accumulate in milk. The concentrations of apixaban in animal milk does not necessarily predict the concentration of drug in human milk.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Of the total subjects in the ARISTOTLE and AVERROES clinical studies, >69% were 65 years of age and older, and >31% were 75 years of age and older. In the ADVANCE-1, ADVANCE-2, and ADVANCE-3 clinical studies, 50% of subjects were 65 years of age and older, while 16% were 75 years of age and older. In the AMPLIFY and AMPLIFY-EXT clinical studies, >32% of subjects were 65 years of age and older and >13% were 75 years of age and older. No clinically significant differences in safety or effectiveness were observed when comparing subjects in different age groups.

Renal Impairment

Reduction of Risk of Stroke and Systemic Embolism in Patients with Nonvalvular Atrial Fibrillation

The recommended dose is 2.5 mg twice daily in patients with at least two of the following characteristics *[see Dosage and Administration (2.1) in full Prescribing Information]*:

- age greater than or equal to 80 years
- body weight less than or equal to 60 kg
- serum creatinine greater than or equal to 1.5 mg/dL

Patients with End-Stage Renal Disease on Dialysis

Clinical efficacy and safety studies with ELIQUIS did not enroll patients with end-stage renal disease (ESRD) on dialysis. In patients with ESRD maintained on intermittent hemodialysis, administration of ELIQUIS at the usually recommended dose *[see Dosage and Administration (2.1) in full Prescribing Information]* will result in concentrations of apixaban and pharmacodynamic activity similar to those observed in the ARISTOTLE study *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. It is not known whether these concentrations will lead to similar stroke reduction and bleeding risk in patients with ESRD on dialysis as was seen in ARISTOTLE.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery, and Treatment of DVT and PE and Reduction in the Risk of Recurrence of DVT and PE

No dose adjustment is recommended for patients with renal impairment, including those with ESRD on dialysis *[see Dosage and Administration (2.1) in full Prescribing Information]*. Clinical efficacy and safety studies with ELIQUIS did not enroll patients with ESRD on dialysis or patients with a CrCl <15 mL/min; therefore, dosing recommendations are based on pharmacokinetic and pharmacodynamic (anti-FXa activity) data in subjects with ESRD maintained on dialysis *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Hepatic Impairment

No dose adjustment is required in patients with mild hepatic impairment (Child-Pugh class A). Because patients with moderate hepatic impairment (Child-Pugh class B) may have intrinsic coagulation abnormalities and there is limited clinical experience with ELIQUIS in these patients, dosing recommendations cannot be provided *[see Clinical Pharmacology (12.2) in full Prescribing Information]*. ELIQUIS is not recommended in patients with severe hepatic impairment (Child-Pugh class C) *[see Clinical Pharmacology (12.2) in full Prescribing Information]*.

OVERDOSAGE

Overdose of ELIQUIS increases the risk of bleeding *[see Warnings and Precautions]*.

In controlled clinical trials, orally administered apixaban in healthy subjects at doses up to 50 mg daily for 3 to 7 days (25 mg twice daily for 7 days or 50 mg once daily for 3 days) had no clinically relevant adverse effects.

In healthy subjects, administration of activated charcoal 2 and 6 hours after ingestion of a 20-mg dose of apixaban reduced mean apixaban AUC by 50% and 27%, respectively. Thus, administration of activated charcoal may be useful in the management of ELIQUIS overdose or accidental ingestion. An agent to reverse the anti-factor Xa activity of apixaban is available.

PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Medication Guide).

Advise patients of the following:

- Not to discontinue ELIQUIS without talking to their physician first.
- That it might take longer than usual for bleeding to stop, and they may bruise or bleed more easily when treated with ELIQUIS. Advise patients about how to recognize bleeding or symptoms of hypovolemia and of the urgent need to report any unusual bleeding to their physician.
- To tell their physicians and dentists they are taking ELIQUIS, and/or any other product known to affect bleeding (including nonprescription products, such as aspirin or NSAIDs), before any surgery or medical or dental procedure is scheduled and before any new drug is taken.
- If the patient is having neuraxial anesthesia or spinal puncture, inform the patient to watch for signs and symptoms of spinal or epidural hematomas *[see Warnings and Precautions]*. If any of these symptoms occur, advise the patient to seek emergent medical attention.
- To tell their physicians if they are pregnant or plan to become pregnant or are breastfeeding or intend to breastfeed during treatment with ELIQUIS *[see Use in Specific Populations]*.
- How to take ELIQUIS if they cannot swallow, or require a nasogastric tube *[see Dosage and Administration (2.6) in full Prescribing Information]*.
- What to do if a dose is missed *[see Dosage and Administration (2.2) in full Prescribing Information]*.

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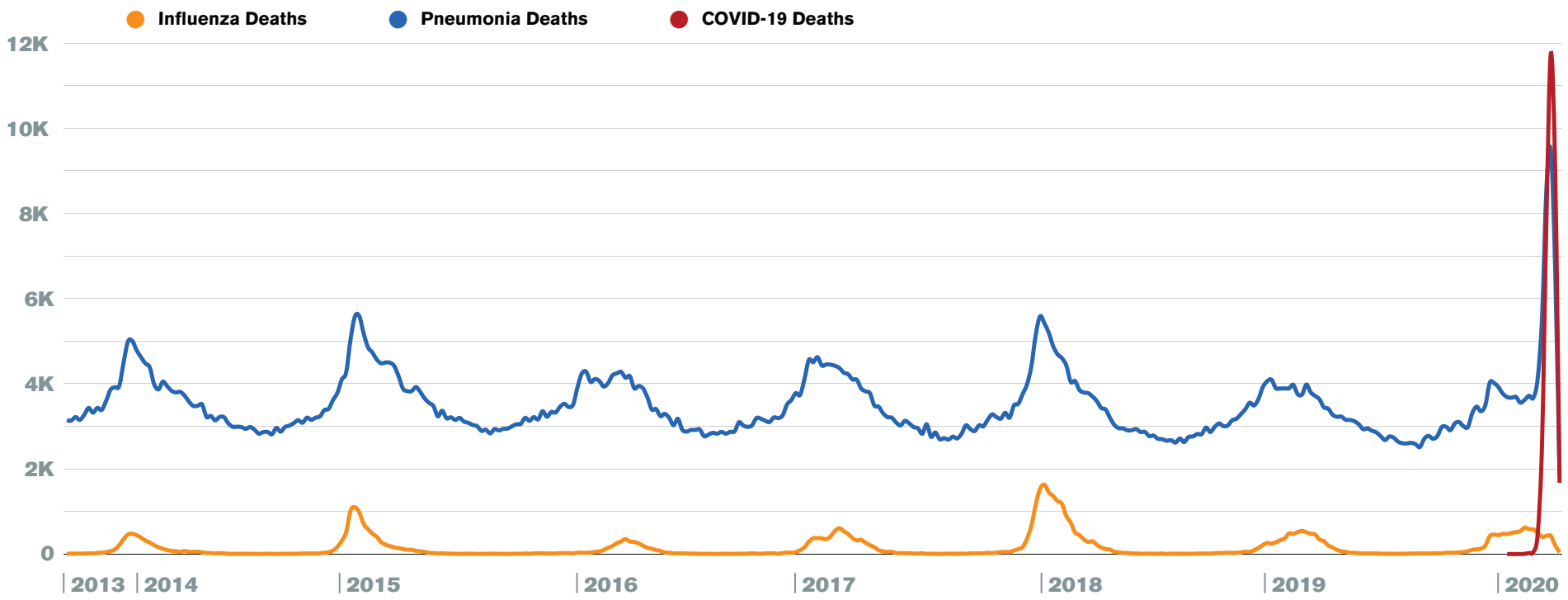
Data Snapshots
QUICK STATS FROM THE ED

U.S. Influenza and Pneumonia Deaths 2013–2020



A seasonal pattern of influenza and pneumonia deaths is seen annually. In 2020, there is a large increase in pneumonia deaths accompanying COVID-19.

SOURCE: CDC

by **SAM ASHOO, MD, FACEP**, founder and CEO of Admin EM. More at admin-em.com.

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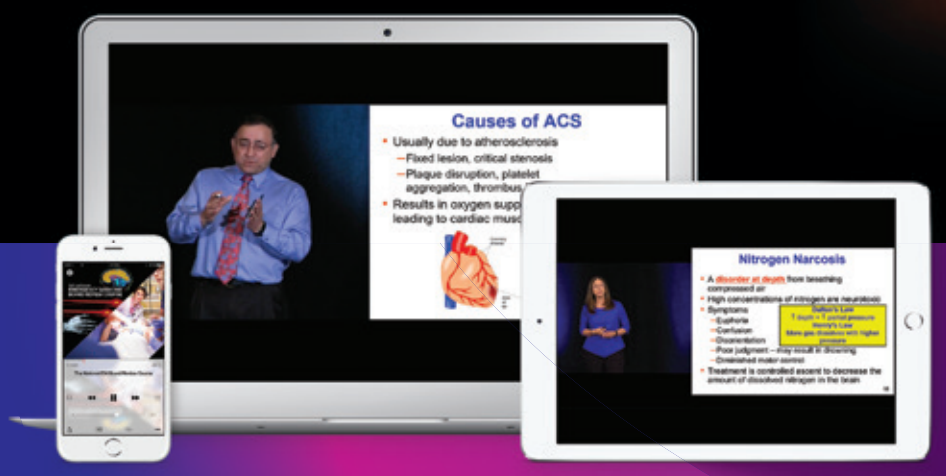

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END OF THE RAINBOW

by JAMES M. DAHLE, MD, FACEP

INVESTING LESSONS FROM THE CORONABEAR

There are at least six lessons that can be drawn from this collective economic experience.

1. Stocks Are Risky

For many physicians, especially those younger than 40, the recent market downturn was their first experience losing a large amount of real money. At its nadir, the stock market was down 35 percent. A physician with a $2 million portfolio composed of 80 percent stock would have lost over half a million dollars. That might represent twice the cost of their education, more than the value of their house, or a decade worth of retirement account contributions. This is not a mere academic financial experience but an emotional and behavioral one. You likely learned a lot about your risk tolerance and can now adjust your investing plan going forward accordingly. If you did not have a written investing plan, you likely learned the value of having one. You also learned the value of having less-risky assets like bonds in a portfolio.

Read the other lessons at ACEPNow.com.

ADVOCACY

by L. ANTHONY CIRILLO, MD, FACEP

ACEP VIRTUAL DAY ON THE HILL: ADVOCATING FROM THE FRONT LINE

On April 28, ACEP hosted a highly successful, first-of-its-kind "Virtual Hill Day." This virtual event provided ACEP members the opportunity to talk with members of Congress (MOCs) and Capitol Hill staffers about the personal, professional, and financial challenges that emergency physicians are facing during the COVID-19 pandemic. These would normally have been in-person visits as part of the annual ACEP Leadership & Advocacy Conference, but there is clearly nothing normal about the world we are living in today. Although different—and not as much fun as being in Washington, D.C., together—the virtual Hill visits were incredibly valuable as we shared our first-hand, front-line experiences in responding to the COVID-19 pandemic.

The success of this program is evident in the numbers. A total of 474 ACEP members from 45 states participated in 306 virtual Hill visits. These numbers are not far off from our usual, in-person meetings. More impressively the percentage of visits with Members of Congress was almost 50 percent, which is higher than ever!

Visit ACEPNow.com for Dr. Cirillo's full report on Virtual Hill Day, as well as impressions from first-time attendee Robyn Levine, MD.

SPECIAL OPS

by SHARI WELCH, MD, FACEP; AND JAMES J. AUGUSTINE, MD, FACEP

OPTIMIZE ED FLOW AND PREVENT SPREAD OF SARS-COV-2 DURING THE COVID-19 PANDEMIC

As we come to grips with the COVID-19 pandemic and how it's changed the way we practice, it's important to employ optimum strategies for staff and patient flow. There is no one-size-fits-all approach, however, because the coronavirus has impacted states and municipalities in vastly different ways. The disease's prevalence, hospital and resource capacity, and testing capabilities result in different problems and solutions. However, several core concepts can help each emergency department and its leaders determine new strategies for practicing post COVID-19.

Read more about modifying patient and staff flow in your hospital at ACEPNow.com.

FORENSIC FACTS

by RALPH J. RIVIELLO, MD, FACEP; AND HEATHER V. ROZZI, MD, FACEP

GENDER-BASED VIOLENCE DURING A PANDEMIC

Gender-based violence (GBV) does not take a break during times of crisis, disaster, or pandemic. In fact, it increases. Several countries have seen an increase in calls to domestic and sexual violence hotlines during disasters, and the COVID-19 pandemic is no exception. Stay-at-home orders place a victim and perpetrator in proximity for longer periods of time than normal. In addition, financial stressors, a loss of job/income, and fear of the virus can all contribute to an increased risk of GBV. Staying at home also increases the risk of sexual violence.

In addition, disaster and pandemic situations create several unique challenges to providing care to victims of GBV. It is imperative that patients have access to victim-centered, trauma-informed care during a crisis, disaster, or pandemic. Careful planning is needed to allow these patients to access care and start their healing process. How that care is provided may look different than it does under normal conditions.

Visit ACEPNow.com for advice on treating victims of GBV during the COVID-19 pandemic.

TOXICOLOGY

by JASON HACK, MD, FACEP, FACMT

MIGHT BE HELPFUL, BUT BE CAREFUL

Question: What saintly flower has been investigated as a treatment for depression?

Visit ACEPNow.com for the answer.

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ACEP4U: Find the Right Support During COVID Crisis

FROM PEER SUPPORT TO PROFESSIONAL COUNSELING, ACEP'S WELLNESS HUB CAN HELP

by JORDAN GRANTHAM

There is no such thing as a one-size-fits-all way to cope with a global pandemic. We're complicated people; what we need often changes by the day. This virus has ripple effects that extend to your family, your finances, and your career. Because every day is a new challenge, ACEP has created a new Wellness Hub (acep.org/wellness-hub) to help you find the support you need, when you need it. Here's a peek:

Support Pathways

Not sure what assistance would be best? The Wellness Hub is organized into support pathways that make it simple to parse your options, from peer forums and support to a list of companies offering free crisis support for frontline health care workers.

Peer Support

Sometimes you just need to talk to someone who "gets it," and no one really understands what you're going through like fellow emergency physicians.

- **Let's Talk** is a member-only online forum that aims to create a safe space where members can discuss ongoing challenges within their roles, emergency departments, and life in general. We understand some topics are difficult to discuss, so this is the only EngagED forum that allows anonymous posting—even the moderator can't see identifying information.
- ACEP is developing a **peer support program** that launched with an introductory webinar on June 11. "**Who's Got Your Back? Psychiatric Awareness & Team Support"** focused on the value of peer support and how emergency physicians can support one another during times of crisis. The program is based on the concept that peer support provides a sense of belonging through shared experiences. When you can express frustrations, share coping strategies, and have honest conversations about your experiences, you can build a common foundation and deeper relationships.
- **COVID Captures** is ACEP's new platform created to record COVID-19 history as it happens. Research shows that keeping a diary—written or recorded—can help a person process their experiences. The mission of COVID Captures is twofold: 1) make it simple for emergency physicians to record firsthand accounts of pandemic response that can informfuture generations; and 2) give ACEP members a place to record video diaries as a way of processing the COVID-19 experience alongside their peers.

Crisis and Wellness Support

When ACEP released a joint statement supporting the removal of barriers to clinician mental health care (see "Advocating for Physician Wellness and Breaking Down Stigmas" at right), ACEP President Bill Jaquis, MD, FACEP, emphasized: "A physician's choice to address his or her mental health should be encouraged, not penalized."

To that end, the Wellness Hub provides a full list of free counseling and wellness coaching options available to ACEP members. Whether you prefer in-person sessions or

you'd rather text with a professional counselor, you can find an option that works for you.

- **ACEP's Wellness & Assistance Program** offers members three free crisis support, counseling, or wellness sessions in partnership with Mines & Associates. Sessions are available 24-7 by phone, text, or online messaging, or you can schedule a face-to-face appointment near your office, home, or school. Sessions can cover COVID-19-related stress or everyday issues, including stress, anxiety, depression, family issues, drug and alcohol abuse, relationships, death and grief, and more. This program also includes wellness coaching sessions, 30-minute phone calls with National Board of Medical Examiners–certified wellness coaches who can help you set specific wellness goals and plan for progress checks along the way to help you reach your objectives. This program is strictly confidential.
- Many organizations are stepping up to provide **free crisis support to health care workers** during COVID-19. Whether you prefer to have a video chat or simply text back and forth with someone, there are many options available. We've gathered them all into a list so you can find the best fit for you.

Sources of Stress and Topical Tools

For those who want to start at the source, resources have been organized into some of the most common contributors to stress for emergency physicians: patient care, workplace, financial, personal, and litigation.

The concept of "physician wellness" is such a broad umbrella that encompasses many specific areas of research, so the Wellness Hub provides a topic-based section covering COVID-19, posttraumatic stress disorder, compassion fatigue, physician suicide, burnout, and diversity/equity issues.

We're in This Together

As we settle into the long-term stage of this pandemic, just remember that it's okay to not be okay. This isn't a Pixar movie; this real-life "hero work" is exhausting. Just like a marathon runner stops for hydration and energy bars along the route, you may need to check in with your peers or a crisis counselor to keep yourself in the race. Find the support you need at www.acep.org/wellness-hub.

MS. GRANTHAM is ACEP's communications manager.

ADVOCATING FOR PHYSICIAN WELLNESS AND BREAKING DOWN STIGMAS

Some physicians fear the professional consequences of seeking mental health care, wanting to avoid any reporting requirements for state licensure. ACEP has long advocated at the state and federal levels for the removal of barriers that stop emergency physicians from seeking the support they need.

Joining Forces to Address Barriers to Physician Mental Health Care

On June 2, ACEP and other leading medical associations released a joint statement outlining steps to support the mental health of emergency physicians and other clinicians during this pandemic. Developed by ACEP and the Coalition on Psychiatric Emergencies, the joint statement was signed by more than 40 supporting groups. It emphasizes that a clinician's history of mental illness or substance use disorder treatment should not be used as an indicator of their current or future ability to competently practice medicine. View the statement at www.acep.org/clinician-mental-health-joint-statement.

In late April, ACEP met with The Joint Commission (TJC) to discuss physicians being penalized by state licensing boards and other entities for seeking mental health support. On May 12, TJC released a statement that acknowledged the problem and spoke out against "barriers that inhibit clinicians and health care staff from accessing mental health care services, including eliminating policies that reinforce stigma and fear about the professional consequences of seeking mental health treatment." TJC does not require organizations to ask about a clinician's history of mental health treatment, and its statement encouraged organizations to "limit inquiries to conditions that *currently* impair the clinicians' ability to perform their job. It is critical that we ensure health care workers can feel free to access mental health resources."

Lobbying for Physician Mental Health

On the legislative front, ACEP has been working with the office of U.S. Rep. Raja Krishnamoorthi (D-IL) on mental health priorities, including research on the mental health impacts of the coronavirus pandemic on physicians and other health care providers (a provision that was included in the HEROES Act that passed the House of Representatives on May 16).

ACEP also supported Rep. Krishnamoorthi's bipartisan "Dear Colleague" letter about the mental health impacts and access to resources for health care workers responding to the pandemic. The letter had more than 90 cosigners.

RESIDENCY SPOTLIGHT

MOUNT SINAI-ELMHURST

Twitter:
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Location:
New York City (NYC)

Year founded:
1994

Current number of residents:
25 per class

Program length:
4-year program

MOUNT SINAI-ELMHURST

SECRET WEAPONS (MEDICAL)

Patients bring their pathology from all over the world to the cutting-edge Mount Sinai system and Elmhurst Hospital Center, which is in the most diverse immigrant neighborhood in the country. Resident shifts in dedicated critical care areas and a strong EM-critical care faculty presence at both Sinai and Elmhurst leave residents prepared to treat any condition. Our 4-year curriculum offers one of the best-developed scholarly track programs in the country, backed by an unusual amount of curriculum time, mentoring, and department resources devoted to career development. Our residents are very involved in every department initiative and on a national level in their areas of interest and often graduate into leadership positions.

SECRET WEAPONS (NON-MEDICAL)

Being among our big family in a vibrant city makes it easier to face the challenges of residency (even when you become the epicenter of the epicenter of a pandemic). There are endless ways to play in NYC and so many residents live near each other—in the same building or within a few blocks—that bonding is inevitable. See the results weekly at Tuesday Night Fun or any time you walk into our break rooms. Also, it's NYC so we get every imaginable kind of food delivered straight to the emergency department at all hours!

RECENT PUBLICATIONS OF NOTE:

- Giwa A, Desai A, Duca A. Novel 2019 coronavirus SARS-CoV-2 (COVID-19): an updated overview for emergency clinicians. *Emerg Med Pract*. 2020;22(5):1-28.
- Nickerson J, Webb T, Boehm L, et al. Difficult delivery and neonatal resuscitation: a novel simulation for emergency medicine residents. *West J Emerg Med*. 2020;21(1):102-107.
- Lin M, Rivette A, Carr B, et al. Effect of accountable care organizations on emergency medicine payment and care redesign: a quantitative study. *Ann Emerg Med*. 2020;75(5):597-608.

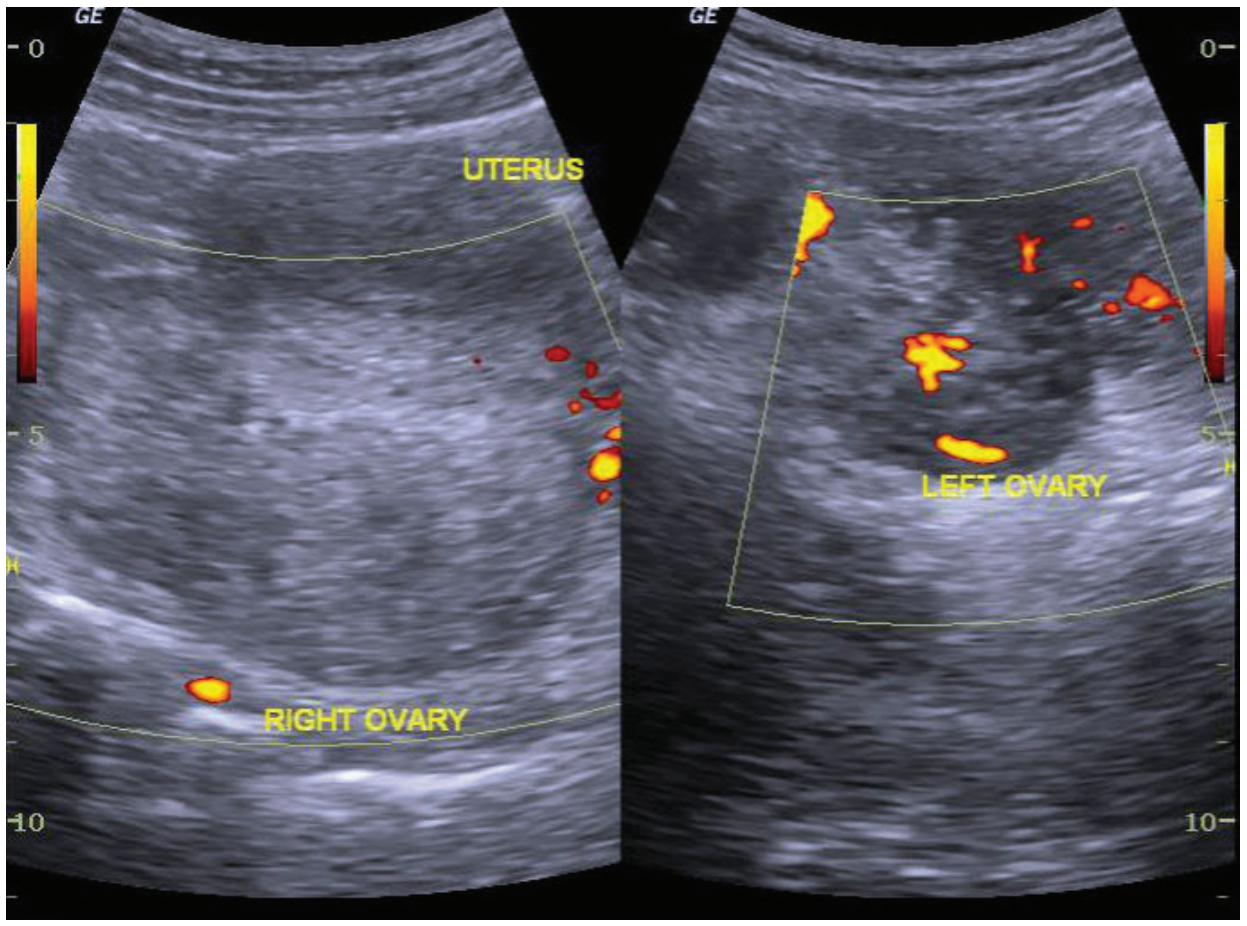
—Elaine Rabin, MD, FACEP, program director, residency in emergency medicine

TRIVIA

More than 130 languages are spoken in the Elmhurst Hospital neighborhood. Within three blocks of the hospital you can buy a sari, have some coffee from a Colombian coffee shop, and sweat in a Korean sauna.

Dispelling 5 Ovarian Torsion Myths

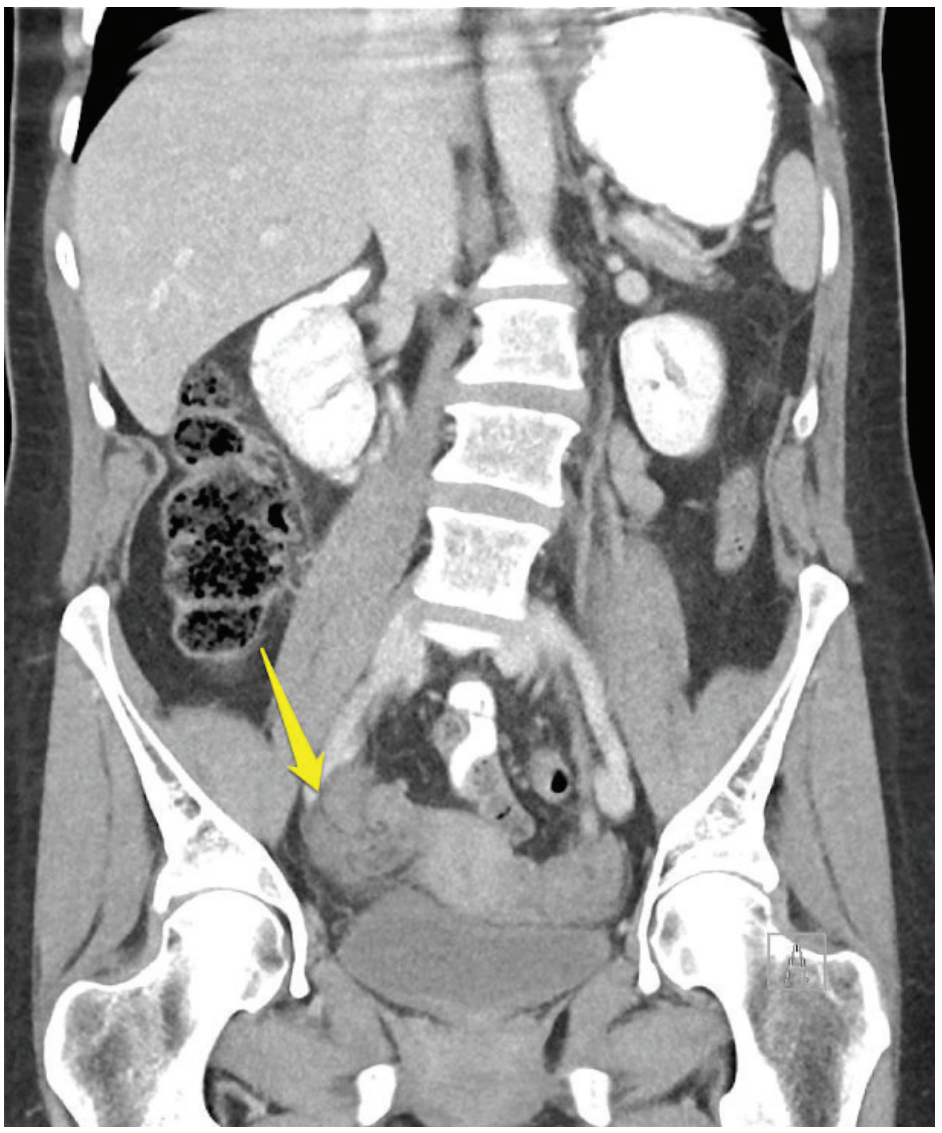
GET THE FACTS TO AVOID MAKING EVALUATION ERRORS



CASE COURTESY OF DR. MAULIK S. PATEL, RADIOPAEDIA.ORG, RID: 30458

Figure 1 (ABOVE)
Ovarian torsion on ultrasound with enlarged ovary and absent vascular flow.

Figure 2 (RIGHT)
CT depicting twisted follicle and enlarged ovary.



CASE COURTESY OF RMH CORE CONDITIONS, RADIOPAEDIA.ORG, RID: 28265.

by BRIT LONG, MD, FACEP; ALEX KOYFMAN, MD, FACEP, FAAEM; AND MICHAEL GOTTLIEB, MD, FAAEM

The Case

A 28-year-old female presents with severe lower right quadrant pain. Her intermittent pain started three days ago. She has had several episodes of non-bloody emesis, which usually occurs when the pain worsens, but she denies vaginal bleeding, vaginal discharge, urinary symptoms, fever, diarrhea, back pain, or other symptoms. She is significantly tender in the right lower quadrant, but a pelvic exam is unrevealing.

Abdominal and pelvic pain are common presentations in the emergency department, ranging from benign to serious. One important and dangerous condition not to miss is ovarian torsion.

Ovarian torsion occurs when the ovary completely or partially rotates on the ligamentous supports, resulting in necrosis and infertility if missed.[1–5] Here are five myths that can mislead the emergency physician.

Myth #1: Only Women of Reproductive Age Experience Ovarian Torsion

While ovarian torsion most commonly affects women of reproductive age, typically around 30 years old, the risk factor most strongly associated with torsion is an adnexal mass >5 cm, occurring in up to 80 percent of patients with torsion; underlying risks include polycystic ovarian syndrome, undergoing fertility therapies, history of previous torsion, and history of tubal ligation.[3–16]

Approximately 15 percent of ovarian torsion cases occur in pediatric patients, which is thought to occur due to an elongated utero-ovarian ligament.[3–5,11–13] Unlike other patient populations, more than half of pediatric patients with ovarian torsion have normal ovaries.[3–5,9–16] Postmenopausal patients account for another 15 percent of cases, although almost all of these patients have an enlarged ovary or mass within the pelvis. Pregnant patients are also at risk, accounting for 10 to 25 percent of all cases.[5,9,16–20] In fact, pregnancy is a significant risk factor for torsion, primarily due to progesterone increasing the risk of ovarian cyst formation.[16–20] Most patients with torsion during pregnancy experience it in the first 17 weeks (81 percent), and 73 percent of these patients have undergone fertility therapy.[4,18–20] Fertility treatments can result in ovarian hyperstimulation, further increasing the risk of ovarian cyst formation.[5,15]

Key Point: Consider ovarian torsion in female patients of all ages.

Myth #2: All Patients with Ovarian Torsion Present with Acute Severe Pain and Vomiting

Symptoms of ovarian torsion occur due to occlusion of vascular flow from torsion of the vascular pedicle. We classically associate this with abrupt, severe pain in the lower abdomen that radiates to the flank or inguinal area as well as nausea and vomiting.[4–7,10,21,22] However, sudden, severe pain only occurs in 50 percent of patients.[4–7,22] Some form of pain is present in up to 90 percent of patients, but the description of the pain varies.[4–7,22] Symptoms can be vague, lasting for days to months, and be constant *or* episodic due to intermittent torsion and detorsion of the

ovary.[23,24] Pain may resemble that of appendicitis, urolithiasis, ectopic pregnancy, and other conditions. Nausea and vomiting occurs in up to 70 percent of patients, and fever may also occur in 2 to 20 percent of patients, further complicating the diagnosis.[4,6,7,12,23,24] Diagnosing torsion in infants is extremely difficult, as these patients may present with irritability, fussiness, vomiting, or feeding intolerance.[5,11–13] Pediatric females can present with diffuse pain and fever, typically resulting in delayed diagnosis.[5,25,26]

Importantly, the critical ischemia time for the ovaries that results in necrosis is unknown. Patients may have symptoms for hours to days, and there is no specific time cutoff that reliably predicts irreversible necrosis.[4,5,27–29]

Key Point: Patients with ovarian torsion may present with constant, severe, abrupt, intermittent, or mild pain.

Myth #3: A Normal Physical Exam, Including Pelvic Exam, Can Rule Out Torsion

Up to one-third of patients have no tenderness on either an abdominal or pelvic exam.[4–7,10] One of the key risk factors is an ovarian mass or cyst, but unfortunately, exams are also unreliable in detecting the presence of adnexal tenderness or mass, with an inter-examiner reliability ranging from 23 to 32 percent.[5,30] Results are no better with a gynecologist-performed exam, with a sensitivity of detecting a mass >5 cm of 15 to 36 percent.[5,31] The exam's reliability further decreases in the setting of increased patient weight (defined as >200 pounds) and in patients older than age 55.[32]

Key Point: A normal abdominal or pelvic exam does not exclude ovarian torsion.

Myth #4: A Normal Ultrasound Can Rule Out Torsion

Transvaginal ultrasound (TVUS) with grayscale imaging and Doppler flow is usually the go-to imaging modality to evaluate for torsion. While TVUS has high specificity, it has poor sensitivity, ranging from 35 to 85 percent.[33–35] The most common finding is an enlarged ovary due to edema, often with a mass.[5,16,17,33–36] Other signs include an ovary displaced to the midline. The "string-of-pearls sign," in which an enlarged ovary is lined around the periphery by follicles, suggests torsion.[5,16,17,33–36] Grayscale may demonstrate a hypoechoic appearance of the ovary due to edema. Color Doppler may reveal decreased or absent intraovarian venous flow, which may be followed by absent arterial flow later in the disease (see Figure 1).[5,16,17,33–36] One major pitfall with TVUS use is reliance of normal arterial flow to exclude torsion, as the ovaries have dual blood flow from the ovarian and uterine arteries.[5,34] Torsion initially occurs with lymphatic and venous outflow obstruction. Arterial inflow is not compromised until later in the disease course.[35,36] Arterial flow is completely normal in more than 25 percent of patients with surgery-confirmed torsion, and more than half of patients will have detectable arterial flow.[16,17,35,36] Therefore, assessing venous flow is a better indicator. However, intermittent or partial torsion may also result in normal venous flow TVUS.

Literature suggests that combining ultrasound findings can improve sensitivity and specificity compared to only focusing on vascular flow.[5] Evaluating for free fluid within the pelvis, ovarian enlargement and edema, and vascular flow can improve sensitivity.[5] The whirlpool sign is strongly suggestive of torsion; it consists of a circular collection of blood vessels within an enlarged ovary or mass.[5,37,38]

Key Point: Do not rely on normal vascular flow to rule out ovarian torsion. A combination of TVUS findings such as ovarian enlargement and mass, free fluid in the pelvis, and vascular flow may improve your ability to diagnose ovarian torsion.

Myth #5: CT of the Abdomen and Pelvis Has No Role in Evaluating Ovarian Torsion

Patients with undifferentiated abdominal pain often undergo CT, but can CT assist in ruling in or out ovarian torsion? CT with IV contrast will often display findings suggestive of torsion.[5,16,33,39–42] Findings on CT with high specificity for ovarian torsion include a twisted vascular pedicle (see Figure 2), a thickened fallopian tube with target/beak-like appearance, absent or reduced ovarian enhancement with contrast, and an enlarged ovary with a follicular ovarian stroma and peripherally displaced follicles.[16,33,39–42] Features that are commonly found but not specific include an enlarged ovary, an adnexal mass, adnexal mass mural thickening, free pelvic fluid, fat stranding surrounding the ovary, uterine deviation toward the torsed ovary, and ovarian displacement toward the uterus.[16,33,39–42] CT with contrast demonstrates a high sensitivity for these secondary findings, approaching 100 percent.[16,33,39–42] If one of these secondary findings is present, TVUS and OB/GYN consultation should be expedited. If these findings are not present and the ovary is normal in size, TVUS may not be needed, depending on the any changes in the clinical course. If the ovary is abnormal on CT, then obtain TVUS.

Finally, if suspicious of torsion based on your history and exam, an ob-gyn consultation should be initiated prior to imaging. If an ob-gyn is unavailable, a general surgery consultation is warranted. Torsion is a time-sensitive condition; early involvement of specialists is paramount.

Key Point: A normal CT of the abdomen and pelvis with contrast that has no secondary findings displays high sensitivity for excluding ovarian torsion. If secondary findings such as an enlarged ovary are present, then obtain TVUS.

KEY POINTS

- Ovarian torsion can affect women of all ages.
- Pain in the setting of ovarian torsion can vary significantly; it may be abrupt, intermittent, or not present at all.
- The exam is unreliable. Do not use it to exclude ovarian torsion.
- Use a combination of factors on TVUS when evaluating torsion: Doppler flow, ovarian size, and free fluid within the pelvis.
- A completely normal CT of the abdomen/pelvis with contrast is sensitive for ovarian torsion. If there are secondary findings (eg, enlarged ovary), obtain a TVUS.
- Consult an ob-gyn early in the care of these patients.

Case Conclusion

The CT of the abdomen and pelvis reveals a normal appendix but an enlarged right ovary. A small amount of pelvic free fluid and fat stranding around the right ovary are observed. You consult the ob-gyn on call, who requests a TVUS. The TVUS reveals an enlarged ovary with decreased venous flow on Doppler. The ob-gyn evaluates the patient and takes her to the operating room, where detorsion is successful.

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GRATITUDE AND COVID-19

ED PATIENT SATISFACTION INCREASING DESPITE GLOBAL COVID-19 PANDEMIC

by JONATHAN LEGGETT, DO

The COVID-19 pandemic has changed life as we know it. A fluid situation, there has been great focus on COVID-19 case incidence rates, mortality rates, and possible treatments. There has also been a surge of public appreciation for frontline medical workers, including first responders, emergency physicians, nurses, physician assistants, and medical staff in general. That acknowledgement is correlating to better patient satisfaction scores during emergency department visits. In the Southeastern region (where I am an EM resident physician), there has been an upward trend in patient satisfaction scores for emergency department visits during the COVID-19 period.

Emergency departments ebb and flow in volume and acuity, even many times throughout a day. Before the start of the COVID-19 pandemic, emergency departments around the country were in what might be referred to as a season of bed-holds, which had its own challenges. Prolonged ED wait times, patients in hallway beds, crowded waiting rooms; all of these problems generally correlate to suboptimal care and lower patient satisfaction scores.

Did things change during the COVID-19 outbreak? To find out, emergency medicine program evaluated patient satisfaction, utilizing Press Ganey (PG) scores, at eight large teaching hospitals in the Southeastern region. These scores have several components for evaluating emergency physicians, including time to listen, courtesy, informative treatment, and concern for comfort. From Nov. 2019 through March 2020, 4,856 Press Ganey patient surveys were returned (3,994 Nov. 2019–Feb. 2020 pre-COVID and 862 March 2020 COVID era). During the pre-COVID time, PG surveys scored in the 25th percentile of all PGs in the country (63.8 percent "top-box," the highest rating score) as compared to scoring in the 40th percentile of all PGs (67.4 percent top-box) during the COVID-19 period. These data were statistically significant (chi-squared analysis with P=0.043, see Figure 1).

Patient satisfaction scores, as represented by the PG score, were significantly higher during the COVID-19 month compared to the pre-COVID months for eight teaching hospitals in the Southeastern region of the United States. During the pandemic, ED volumes have been lower in many parts of the country. This translates to fewer hallway beds, shorter waiting times, and more patient-physician time. While our patient volumes have decreased, there has also been a decrease in staffing as we adjust coverage schedules to lower censuses. Therefore, our increase in scores should not be solely attributed to more time and resources being available for each patient.

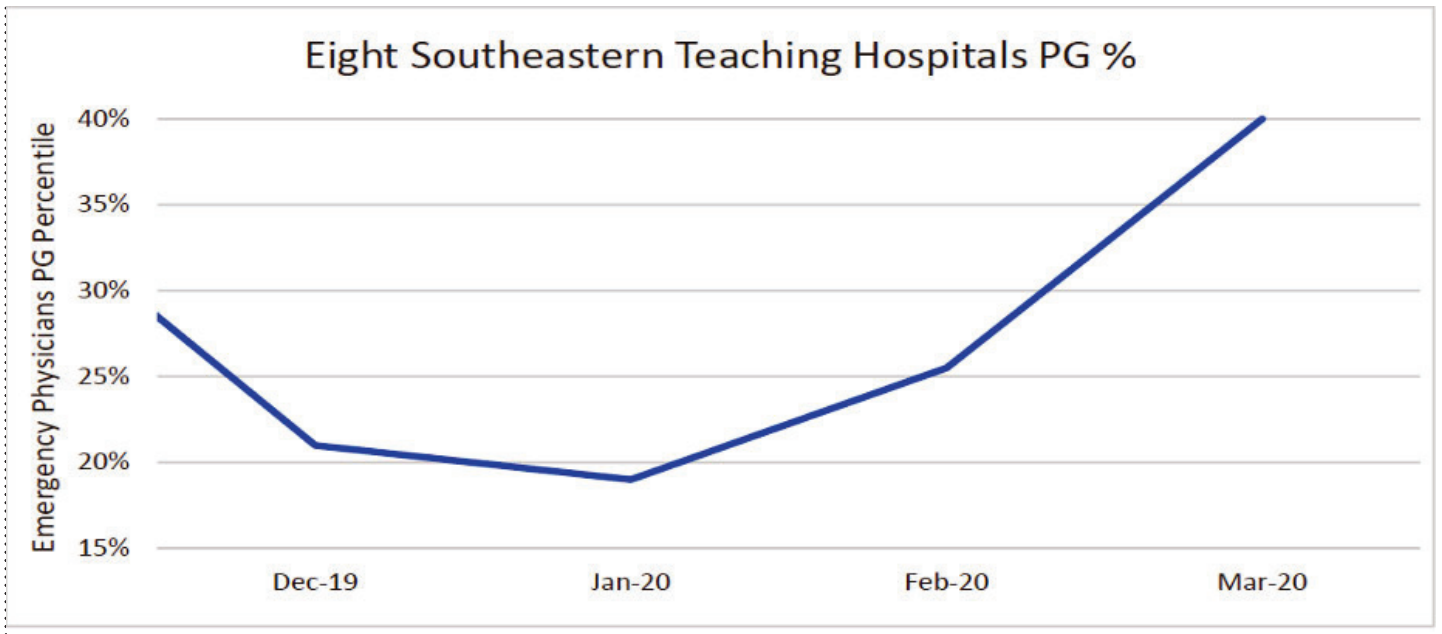

Figure 1: Press Ganey patient ssurvey ratings for eight Southeastern teaching hospitals, Nov. 2019–March 2020.

Outside of the emergency department, medical professionals have been recipient of widespread support and appreciation by local and national media, ranging from standing ovations recorded in Istanbul, London, Buenos Aires, and Tamil Nadu, India, to free smoothies, reduced-cost gas, and even parades. The rise in patient satisfaction scores seen in our corner of the United States further demonstrates the support and gratitude from within our own communities. As the *Washington Post* put it, "In the fight against coronavirus, the world gives medical heroes a standing ovation."

We are striving to learn how to treat this disease and adapt to our new reality. Our data, and the outpouring of public support, indicate that taking take the time to listen to our patients and continuing to provide courteous and informative treatment in these challenging times are being noticed.

Disclaimer: *This research was supported (in whole or in part) by HCA and/or an HCA-affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA or any of its affiliated entities.*

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VOTE | CONTINUED FROM PAGE 1

registration venues, resulting in plummeting rates of voter registration nationwide. We know that these marginalized patient populations use emergency departments at disproportionately higher rates than the average population because of a lack of access to traditional forms of health care.[5] The discrepancies in ED use along the lines of age, race, and socioeconomic demographics represent both a challenge and an opportunity for health care workers as the needs of these populations often extend beyond traditional health care boundaries.

Rising to the Challenge

Many health care professionals have risen to this challenge by broadening their scope of care, engaging more deeply with the social determinants of health, and administering programs that address larger societal issues affecting their patients such as housing, food insecurity, and opioid addiction.[6,7] Marginalized patient populations benefit most from these and larger structural changes needed to improve health care delivery systems. But they also have the lowest rates of voter registration.

For example, a disproportionately large share of eligible Americans who were not registered in the 2016 presidential election were low-income citizens and people of color.[8] Among eligible voters, 31 percent of African Americans, 43 percent of Hispanics, and just over 43 percent of low-income Americans were not registered to vote in that election.[9] Rates among the nation's young voters are not much better: Only 50 percent of millennials voted in the 2016 election compared to 69 percent of baby boomers and 63 percent of generation X.[10]

Regardless of party affiliation, policy endorsement, or stance on a given issue, we can all agree that to be pro-democracy we must be pro-participation. Further, most can agree that without claiming their role in our democracy, these groups will never achieve true equity in and risk being politically voiceless.

Previous Efforts

Health care-based nonpartisan voter registration has worked before. In 2008, the National Association of Community Health Centers ran a voter registration drive in health centers that resulted in more than 18,000 low- and middle-income citizens added to official rolls.[11] Another program, conducted in 2012 at two Federally Qualified Health Centers in the Bronx, New York, demonstrated that successful nonpartisan voter registration initiatives can be run out of community health centers without requiring significant physician effort, disrupting clinic workflows, or compromising the patient-doctor relationship.[11]

Patients have been extremely receptive to nonpartisan voter registration services, with one study finding that 89 percent of individuals approached in a health center waiting room expressed openness to registering to vote.[11] These models, specifically directed toward low-acuity patients, are readily adapted to hospital ED waiting rooms.

Another Initiative: VotER

Accordingly, emergency departments across the United States have already begun implementing such voter registration efforts. VotER is one such effort that was founded at Massachusetts General Hospital in Boston and has since been adopted at more than a dozen emergency departments across the United States. The program uses iPad-based kiosks and posters and discharge paperwork with QR codes in low-acuity emergency department waiting areas to offer patients a convenient, nonpartisan, and optional opportunity to register to vote or check their registration status while waiting.

The platform does not interrupt clinical care or rely on doctors, physician assistants, or nurses providing care to interact with the voter registration process. Patients are guided through the voter registration application on their phone or the iPad-based kiosk in 90 seconds or less. Emergency departments can play a critical role in encouraging patients to regis-

CONTINUED *on page 18*

Waiting room sign with a text message registration trigger.

ALISTER MARTIN

ter to vote without detracting from the delivery of care using platforms like VotER. Groups like VotER, Patient Voting, and Med Out The Vote are launching the first Civic Health Month in August 2020 to bring a renewed focus to helping patients get to the ballot box, particularly when COVID-19 has made voting in a safe and healthy way a public health issue.

Health care professionals must be concerned with our democracy's health and mindful of who gets to participate in it. The demographic overlap of patients who lack access to stable care—and therefore use the emergency department at higher rates—and those who historically have low civic engagement affords a natural opportunity to pilot and develop voter registration efforts in the emergency department.

ED-based nonpartisan voter registration via nonintrusive platforms such as VotER is an innovation that can improve our civic system and the well-being of the communities we serve. With an eye toward national elections later this year, emergency departments have the potential to elevate all patient voices in our national dialogue of how to deliver effective, affordable health care in the United States.

Visit www.vot-ER.org to learn more.

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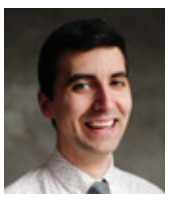

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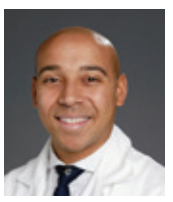

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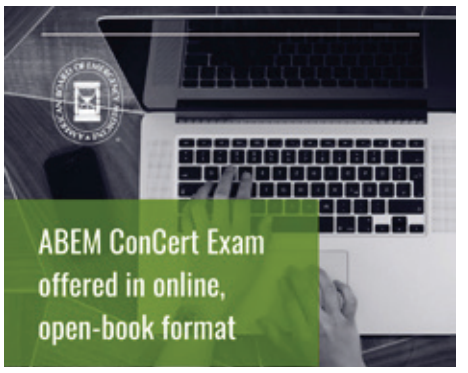

ABEM Changes ConCert Exam to Meet Challenge of Pandemic

Nationwide, emergency physicians are facing unprecedented circumstances related to COVID-19. The American Board of Emergency Medicine (ABEM) recognizes this and is making changes to the ConCert Exam effective immediately. The ConCert Exam will now be offered in an online, open-book format.

1. This exam will be offered as an open-book test in two three-week windows during 2020, 2021, and 2022 to eligible physicians.
2. There will be no additional costs associated with the move to an online, open-book exam.

Further details about the timing of the online exams are available on the ABEM website at www.abem.org/public/news-events/news/2020/04/21/abem-message-regarding-covid-19-monitoring. Please contact ABEM at 517-332-4800 or abem@abem.org with questions related to your individual circumstances.

Heat-Related Illness

THERE'S MORE TO IT THAN HEATSTROKE

by ASHLEY A. JACOBSON, MD, AND NEHA P. RAUKAR, MD, MS

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TAKE-HOME POINTS

1. Heat illness is a spectrum of disease with clinical diagnosis. It requires supportive management. If after a period of observation there are no signs of end organ damage, most patients with mild heat illness can be discharged from the emergency department.
2. Always obtain a core body temperature for accuracy.
3. If you are concerned about heatstroke, initiate aggressive cooling measures as soon as possible and prior to transportation.

The United States' International Classification of Diseases (ICD-10) codes for 2020 contain updated definitions of heat illness that go beyond heatstroke.[1] Here, we will discuss definitions and treatment implications.

Hyperthermia is defined as an elevated core body temperature related to thermoregulation failure. The body combats hyperthermia with thermoregulation, causing sweating and cutaneous vasodilation, maximizing evaporative heat loss. When these compensatory measures do not suffice, gut ischemia can occur, sometimes releasing cytokines, which can trigger cytokine-mediated systemic inflammatory response leading to multiorgan system failure. Environmental risk factors for developing heat illnesses include high temperature and humidity, lack of air movement, and presence of a heat wave.[2] The spectrum to heat illness carries a stepwise approach to treatment.[1]

Definitions

Heat Edema: Heat edema is a mild illness caused by vasodilatation of the hands and feet. It typically occurs in unacclimatized elderly patients. Treatment is supportive with compressive stockings and relocation to a cooler environment.[2,3]

Heat Cramp: Heat cramp is characterized by generalized muscle pain and persistent involuntary contraction of the muscles. Treatment is supportive and involves oral hydration, stretching, and muscle massage.[2,3]

Heat Syncope: Also known as exercise-associated collapse, this clinical diagnosis typically occurs after completion of strenuous activity. The mechanism involves abrupt decrease in venous return once the activity has ceased, likely from peripheral venous pooling. It can occur in cold environments as well. Cardiac disease should be considered as part of the initial differential diagnosis, as this condition is correctly considered a diagnosis of exclusion. Treatment involves supine rest, elevation of the legs, and oral hydration.[3]

Heat Exhaustion: Heat exhaustion is an inability to continue adequate cardiac output resulting from strenuous exercise compounded by environmental heat stress. It typically presents as collapse during the exercise due to sodium derangements (versus heat syncope, which occurs *after* cessation of activity). Diagnosis is clinical and based on elevated core body temperature with signs of dehydration. Patients are typically anhidrotic. Treatment is the same as for heat syncope: supine positioning, elevation of the legs, and hydration. Cooling the patient to prevent possible progression to heatstroke is important.[2–4] ICD-10 classifies heat exhaustion into subcategories of anhidrotic, salt depletion, and unspecified. It is important to note that the salt depletion category also includes heat exhaustion due to salt (and water) depletion.[1]

Heat Fatigue, Transient: This is an ICD-10 code; however, it does not have a concurrent medical definition. Based on opinion, this code could be used for a patients not meeting criteria for nonexertional heatstroke (no end organ damage or CNS dysfunction) but still exhibiting transient symptoms of lethargy and weakness.

Other Effects of Heat and Light: Miliaria rubra, otherwise known as heat rash, is included in this category. It is a benign, pruritic condition secondary to obstruction of eccrine sweat glands. It is treated with supportive measures and topical corticosteroids.[2]

Heatstroke and Sunstroke: Heatstroke is defined as a core body temperature >104°F (40°C) with CNS dysfunction due to a substantial environmental heat load that cannot be adequately dissipated.[2,5] Exertional heatstroke typically affects younger, healthier individuals undergoing strenuous activity in a high-temperature and high-humidity environment. Individual risk factors include poor physical fitness, obesity, lack of acclimatization, underlying acute illness, initial dehydration, congenital disorders (eg, anhidrosis), alcohol use, and certain drugs and supplements, including amphetamines. Signs and symptoms include tachycardia, tachypnea, hypotension, nausea, vomiting, weakness, muscle flaccidity, ataxia, and encephalopathy. The differential diagnosis can include exertional hyponatremia and neuroleptic malignant syndrome.

Prehospital and hospital management centers on airway, breathing, and circulation. Rectal temperature and blood glucose should be monitored. Treatment prioritizes aggressive cooling measures within 30 minutes of presentation, which usually means initiation before transportation to a hospital.[2,3,5] There are limited studies surrounding first-line cooling measures, but based on the Wilderness Medical Society 2019 Update, ice water immersion carries a 1A recommendation (strong recommendation and high-quality evidence).[3] Ice water immersion consists of removing all clothing and placing the patient in a tub of cold water. Second-line treatment consists of tarp-assisted cooling, a cold shower, and cold water from a hose.

Third-line treatment is evaporative cooling (1C recommendation, indicating a strong recommendation but low-quality or very-low-quality evidence). Evaporative cooling combines evaporation and convection and involves spraying the exposed patient with lukewarm water with fans blowing over the skin. Cooling should continue until a rectal temperature of 100.4°F (38°C) is achieved. Shivering is a theoretical response found in normal patients but is not found in those who have heatstroke. If hypotension is present or there is concern for dehydration, patients can receive small isotonic crystalloid boluses while monitoring for signs of acute pulmonary edema.[3]

The fourth-line recommendation consists of ice packs to the entire body. If only chemical cold packs are available, application should to glabrous skin, palms, and soles only.[3,6] Cooling measures should be continued until core temperature has been lowered to 102.2°F (39°C).[3,4] Dantrolene has been considered as a pharmacological treatment option, but data are limited, and no consistent improvement in outcomes has been described. It is currently not recommended as a therapy.[3,7]

Nonexertional heatstroke is also a clinical diagnosis. This typically affects children who cannot escape hot environments and elderly people with impaired thermoregulation. Signs and symptoms are similar to exertional heatstroke: the characteristic sign is neurological dysfunction. Again, treatment is focused on aggressive cooling measures, along with rectal core body temperature and blood glucose measurements. Risk factors include lack of air conditioning, social isolation, underlying comorbid conditions, and certain drugs and supplements such as anticholinergics and beta-blockers. The differential diagnosis includes, but is not limited to, infection, endocrine dysfunction, or underlying CNS, toxic, and oncological processes.[2,5,7,8] Data are limited as to the best cooling technique, but experts recommend evaporative cooling, as most nonex-

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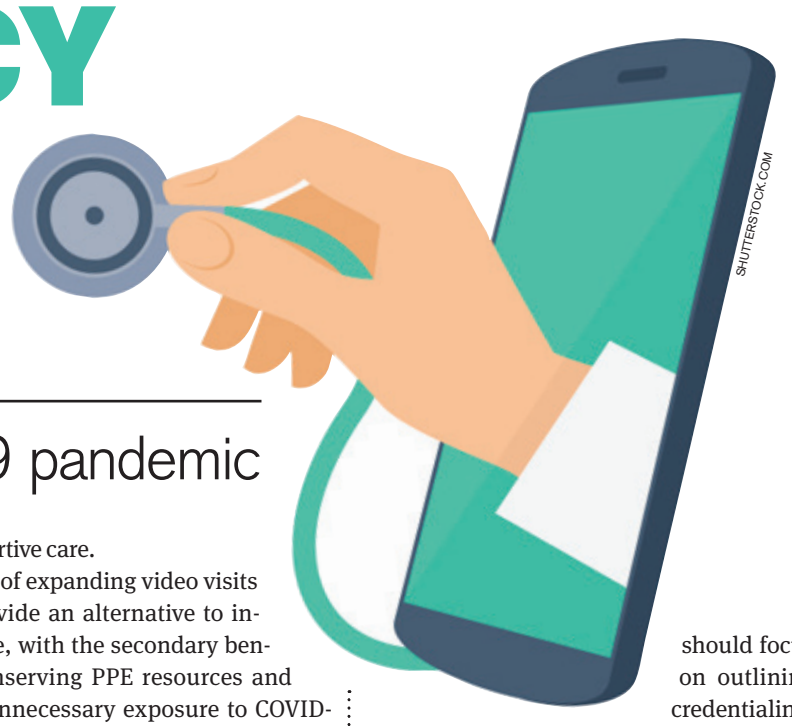
THE EMERGENCY PHYSICIAN HOUSE CALL



Telemedicine comes of age in the COVID-19 pandemic

by SHAYNA ADAMS, MD; MEETA SHAH, MD; AND BRADEN HEXOM, MD

Editors' Note: *This article was accepted on April 26, 2020, and was accurate at that time. Because information about SARS-CoV-2 and COVID-19 is evolving rapidly, please verify these recommendations and information.*

Telemedicine has long been suggested as a viable technological solution for improving access to care. But because of barriers around reimbursement, technological limitations, and scalability, health care institutions have been slow to adopt it. Physician and patient preference for in-person care has been another impediment to adoption.

The COVID-19 pandemic shifted this paradigm; telemedicine use has become widespread. Its potential for decreasing emergency department volume, mitigating transmission of SARS-CoV-2, and saving precious resources such as personal protective equipment (PPE) is now apparent.

Case Use in Chicago

Rush University Medical Center in Chicago created its on-demand virtual care platform in 2019 primarily for patients with low-acuity complaints, much like a virtual urgent care. The online platform was expanded in March 2020 in anticipation of increased patient volumes due to the COVID-19 pandemic. The aim was to "flatten the curve" of COVID-19 by facilitating video visits in place of in-person hospital visits when possible. The pandemic created a large demand from patients with concerns about the coronavirus. Video visits were a channel through which health care workers could provide medical advice regarding testing, quarantine and isolation, supportive care, and whether patients should present for in-person care.

Patients with the chief complaint of "concern for novel coronavirus" were provided a free video visit by a physician or advanced practice provider. In anticipation of high volumes, Rush recruited quarantined emergency physicians, primary care physicians whose clinics had closed, residents, and advanced practice providers.

Prior to the pandemic, the platform saw about two patients daily. Within days of expanding operations of the COVID-19 module, use rapidly grew to 100 patients daily.

Resident Participation

This new demand for telemedicine visits spurred rapid institutional change that facilitated the opportunity for residents to deliver health care in novel ways. Emergency medicine residents in particular played an integral role in scaling telemedicine visits, specifically by creating training modules, recruiting practitioners, pilot testing, and conducting visits for patients.

On March 18, 2020, the Accreditation Council for Graduate Medical Education recognized the national demand for telemedicine visits and accelerated giving permission to residents and fellows to participate in telemedicine care.[1] Additionally, the federal government began relaxing regulations for telemedicine, notably with regard to restrictions for reimbursements.[2] In response to this need, Rush increased its training of health care workers for video visits. We also utilized residents on the telemedicine platform as demand continued to outstrip capacity.

To start conducting video visits, residents had to fulfill several requirements, including completing an online training module, registering their devices to be added to the practitioner pool, and attending an in-person or online tutorial conducted by an information technology specialist or health care worker. The entire training process took about an hour.

Rush achieved emergency medicine resident coverage by reassigning two full-time residents to the program after the cancelation of nonessential rotations. Additional emergency medicine resident coverage was provided by residents on nonclinical rotations on a part-time basis. By co-scheduling attendings and residents, Rush essentially doubled capacity for evaluating patients. Residents presented cases to attendings via the Epic electronic medical records system chat function, and faculty were immediately available by phone and video to troubleshoot difficult cases. Patients were dispositioned to outpatient testing centers, home isolation, or the emergency department. Patients directed to the emergency department for in-person care had their visits streamlined through the emergency physician's direct communication with the receiving charge nurse.

At Rush, emergency residents demonstrated the clinical acumen, adaptability, and technological savvy that allowed for the rapid expansion of the hospital's telemedicine platform. Although the residents only met with patients confirmed under investigation for having the novel coronavirus, the success of this venture suggests that residents can be assigned to a more diverse set of complaints and gain necessary skills that will become more valuable as telemedicine becomes commonplace.

Impact

The video visit platform proved so popular that the volume of patients seen online since its launch was comparable to or even exceeded the volume of patients seen in the emergency department. The large majority of patients using this platform were appropriate for outpatient supportive care.

The aim of expanding video visits was to provide an alternative to in-person care, with the secondary benefits of conserving PPE resources and reducing unnecessary exposure to COVID-positive individuals who did not require hospitalization. Theoretically, patients seen via virtual visit may have instead presented to the emergency department if the telemedicine service were not available. In fact, more than 40 percent of adult patients who completed post-visit surveys reported they would have sought in-person care had they not used this virtual service. Although this theory cannot be formally tested now because of decreased ED volumes resulting from Illinois shelter-in-place orders, it is reasonable to hypothesize that the telemedicine platform led to decreased ED visits.

The Future of Emergency Medicine?

Telemedicine granted emergency medicine physicians the ability to perform house calls, albeit virtual ones. This was a unique opportunity to be present in a patient's home, understand their living situation, and speak to members of their family. Physicians gained a more holistic view of their patients, which allowed them to identify specific challenges that patients face and determine their ability to remain under self-quarantine. In the time of a pandemic, this was one of the few opportunities for patients to interact with their physicians without the barriers imposed by face masks. Perhaps this was a more personal and fulfilling experience for both patients and health care workers than what could be offered by the sterility of a gowned, gloved, and masked physician in an austere ED room.

Emergency physicians on the front lines will face tremendous adversity in the coming months. And although video visits have been suggested as a means of reducing burnout during a pandemic, perhaps this brief segue into telemedicine foreshadows a grander future for the technology even after the pandemic subsides.[3] The application of telemedicine in emergency medicine may allow us to identify nonemergent complaints prior to their presentation in the emergency department and increase overall efficiency while simultaneously increasing patient satisfaction.[4–7]

Reimbursement

In an effort to ensure continued access to health care during the pandemic, the Centers for Medicare & Medicaid Services has allowed for payment parity for telehealth visits. We believe that our specialty should advocate for continuing this parity post-pandemic. To be a truly effective intervention that complies with EMTALA regulations, telemedicine programs should focus on outlining credentialing, expectations, and privileges for its workers and specifying protocols for triaging patients and transferring patients for in-person care.[8] Ultimately, we believe that if executed with care and due diligence to hospital bylaws and governing regulations, telemedicine could serve as an impactful release valve for the exponential growth in ED volumes and waiting rooms that was seen prior to the COVID-19 pandemic.

Emergency physicians should be the driving force behind telemedicine efforts because we are arguably the most qualified specialty to determine when a patient requires emergency services and inpatient care. With this in mind, emergency medicine residency programs should incorporate telemedicine as a core component of training.

Sometimes it takes a crisis to sow seeds of innovation. Telemedicine has favorably disrupted medicine and paved the way to new approaches to health care delivery systems. Our response to the pandemic has accelerated the proof of concept that telemedicine can be successfully implemented to advance emergency medicine and, ultimately, better serve our patients.

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CODING WIZARD

NAVIGATE THE CPT MAZE,OPTIMIZING YOUR REIMBURSEMENT

Editor's Note: *Cutting through the red tape to make certain that you get paid for every dollar you earn has become more difficult than ever, particularly in our current climate of health care reform and ICD-10 transition. The ACEP Coding and Nomenclature Committee has partnered with ACEP Now to provide you with practical, impactful tips to help you navigate through this coding and reimbursement maze.*

COVID CODING TIPS

by CARAL EDELBERG, CPC, CPMA, CAC, CCS-P, CAC

Rapidly changing coding advisories keep coming as COVID-19 blazes its way across the United States. Here are some coding resources for various aspects of care related to COVID-19 patients.

Diagnosis of COVID-19: Providers should document whether the patient has **suspected or confirmed** COVID-19. In addition, document conditions related to COVID-19 such as acute respiratory distress syndrome, pneumonia, chronic obstructive pulmonary disease, asthma, or bronchitis. For more information, visit:

- www.acep.org/administration/reimbursement/covid-19
- www.cdc.gov/nchs/data/icd/COVID-19-guidelines-final.pdf

Telemedicine: The Centers for Medicare & Medicaid Services and the American Medical Association (AMA) provide guidance relating to who can manage a telemedicine encounter and where and how it may be managed during the COVID-19 emergency, with special information on the emergency department. Remember that you are still required to document your history and physical exam and medical decision making. For more information, visit:

- www.hhs.gov/sites/default/files/telehealth-faqs-508.pdf
- www.ama-assn.org/system/files/2020-04/covid-19-coding-advice.pdf (See Scenario 10 for ED telemedicine directions.)

EMTALA: EMTALA waivers are in effect during the COVID-19 pandemic. Some waivers include medical screening that may be set up off campus under hospital management. Communities may set up screening clinics at sites not under the control of a hospital under an EMTALA waiver. For more information, visit:

- www.cms.gov/files/document/qso-20-15-emtala-requirements-and-coronavirus-0311-updated-003pdf.pdf-1

Lab Testing: Current Procedural Terminology (CPT) code revisions were approved by the AMA to cover pathology and laboratory codes for SARS-CoV-2. This information is required to allow identification and payment for COVID-19-related problems. For more information, visit:

- www.ama-assn.org/system/files/2020-04/coronavirus-long-descriptors.pdf

The ACEP reimbursement website will be updated throughout the pandemic:

- www.acep.org/administration/reimbursement/covid-19

The ACEP Coding and Nomenclature Committee will continue to monitor all COVID-19-related coding and documentation advisories. For COVID-19 and general coding guidance, go to:

- www.acep.org/administration/reimbursement/reimbursement-faqs-1

Brought to you by the ACEP Coding and Nomenclature Committee.

MS. EDELBERG is founder and chairman of Edelberg + Associates, faculty for ACEP Coding and Reimbursement Conference, an honorary member of ACEP, and chair of ACEP Coding and Nomenclature Advisory Committee (CNAC) Workgroup 4.

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Nucleic Acid-Based Tests

These tests have been the work horses in diagnosing acute cases of COVID-19. The two primary analytic methods are reverse transcriptase polymerase chain reaction (RT-PCR) and loop-mediated isothermal amplification (LAMP). Regardless of the technique, the basic principle is the same: RNA from viral particles are bound to complementary DNA sequences, which are then copied. Repeated cycles of copying produce exponential amplification that, in sufficient quantity, reaches a defined threshold for a positive test. Absent specific SARS-CoV-2 RNA, minimal amplification occurs, and the test never reaches the threshold for positivity.

These tests are designed for those actively infected and shedding virus. Their analytic sensitivity and specificity are considered excellent, with limitations related to mismatches between the DNA primers and small alterations in the SARS-CoV-2 RNA genome. The DNA primers used may match fragments of other RNA found in samples but typically not to the extent where cross-reactivity impairs amplification of the target.

The sensitivities for these tests are limited by two main factors. The first issue is the process through which the specimen is obtained. The most widely recognized version of this test is the nasopharyngeal swab. An inadequate sampling technique will diminish the quality

of the specimen, lowering sensitivity.

Second, viral load and shedding also decrease with time, contributing to diminishing sensitivity.[1] Overall clinical sensitivity in practice appears similar to our expectations for common influenza tests, in a range approximating 70 to 80 percent.[1] As many of us have already experienced in our clinical workflow, a single negative nasopharyngeal swab does not adequately exclude COVID-19 infection when the remaining clinical picture is supportive. A positive test is, however, virtually unimpeachable.

Antibody Tests

Serological tests are designed to detect the presence of antibodies to SARS-CoV-2. The antibodies of interest include the acute-phase immunoglobulin (IgM), the late-phase (IgG), and occasionally IgA.[1] These tests have been promoted widely as a critical part of plans to reopen America and are in frequent use in population prevalence studies.

Antibody tests are more complicated than DNA-based tests, however. Two main types, enzyme-linked immunosorbent assay (ELISA) and lateral-flow immunoassay (LFIA), are in use. These tests are more difficult to develop because the developers of these assays must synthesize their own novel viral fragments. This involves an analysis of the actual protein coat of the virus, typically focusing on the unique features of the spike protein and cell-entry apparatus. When serum or plasma containing antibodies to SARS-CoV-2 are mixed with the assay antigens, the test reporter systems provide a positive result.

> The most pressing issue with these antibody tests is accuracy.

The ELISA tests require significant time and reagent cost but offer the advantage of quantitative antibody titers. These tests are valuable for accurately identifying high levels of circulating antibody for those being considered as possible donors for convalescent plasma donation (although the efficacy of this strategy remains unknown). The prolonged turnaround time and biohazard safety requirements for ELISA reduce its practicality for widespread testing.

In far greater use are LFIA-based devices, which are the widely seen cartridge-based tests. These tests do not typically report a quantitative measurement but provide positive and control color-change lines using a technique similar to home pregnancy tests. The major advantages of these tests are speed and cost. However, they lack the quantitative precision of ELISA.

The most salient issue with these antibody tests is accuracy. The sensitivity limitations of antibody tests are readily apparent because even acute-phase IgM responses are not immediate, usually taking a few days to develop. Therefore, a single antibody test should not be the sole mechanism for diagnosing acute infections. Consideration ought to be given to the time of symptom onset to determine the likelihood of a false negative, as well as either a DNA-based test or a plan to repeat the antibody test in a few days, if negative.

The other accuracy issues stem from antigen synthesis. The challenge for antigen synthesis involves creating a match for a piece of the virus that is both unique to SARS-CoV-2 while also stable enough not to result in mismatches as the virus naturally mutates. The most stable components of SARS-CoV-2 are also the ones conserved across multiple other coronaviruses, resulting in cross-reactivity and false positives. Several common-cold coronaviruses (eg, HKU1, NL63, OC43, 229E, etc.) are known to react with the antibodies in several developed serological tests. A false-positive test may endanger an individual by suggesting potential immunity from SARS-CoV-2 where none exists.

Antibody tests are also being deployed to evaluate the spread of COVID-19 in some communities. This renders false positives especially important. In communities in which little infection is thought to have occurred, the number of false positives can exceed the number of true positives, even in a test with high specificity. These false positives lead to overestimation of the number of potentially immune persons and may misinform public policy decisions.

Conclusion

Each of the several SARS-CoV-2 tests can play a role in detecting individual cases and evaluating the spread of COVID-19. Results must be carefully interpreted in the context of how common (and therefore likely) the disease is. Otherwise, both false-negative and false-positive results from these tests may ultimately place patients, their families, and health care professionals at elevated risk.

The opinions expressed herein are solely those of Dr. Radecki and do not necessarily reflect those of his employer or academic affiliates.

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Prehospital Bias

To combat potential implicit bias in EMS, diversify the workforce

by CEDRIC DARK, MD, MPH, FACEP

Unconscious bias, the subject Uché Blackstock, MD, wrote a November 2019 column on in *ACEP Now*, can be defined as "a person's tendency to associate a group or category attribute, such as being black, with a negative evaluation (unconscious prejudice) or another category attribute, such as being violent (unconscious stereotype)."[1] People in all walks of life throughout society, including physicians, possess these unconscious (or implicit) biases.

These subtle subconscious feelings that we and other health care workers might harbor toward our patients have likely been present since the beginnings of the profession. However, it is only relatively recently that we have recognized these implicit biases, sought to better understand them, and devised strategies to ameliorate them.[2] Racial and ethnic disparities in the emergency department delivery of analgesia for something as universally painful as a long-bone fracture have been known for several decades; a recent study extends the concern about a potential unconscious bias prevalent in prehospital care.[3]

Controlling for socioeconomic status and geography, researchers investigated if patients were transported to safety-net facilities based on their race. For black patients, transport to a safety-net facility by EMS occurred approximately 5 percent more often than for white patients; for Hispanic patients, transport to a safety-net facility occurred about 2.5 percent more often.[4]

These data reflect a snapshot in time, suggesting—but not proving—implicit biases may be at play in the prehospital setting. We should ask whether these are the results of individual decisions made by prehospital health care workers. Or are these results the effect of systemic issues involving medical direction protocols? Or perhaps they can be explained by less nefarious means, such as patient preference.

Regardless of the cause(s), the National Association of EMS Educators recommends the following as one possible solution: "A diverse EMS workforce, representative of the patients it serves, is crucial to promote understanding among EMTs and paramedics, patients and other providers in the health care system, and to eliminate disparities in care experienced by minority patients."

As in business and in medicine, the time for greater workforce diversity in prehospital care is at hand.

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Is There Systemic Racism in EMS?

by JOSHUA ELLIS, MD

Recent research has provided insight into what could prove to be another example of systemic racism in the delivery of health care.[1] According to a 2019 study, EMS are more likely to transport a black or Hispanic patient to a safety-net hospital than their white counterparts even when such patients come from the same ZIP code. The authors used data from a nationwide Medicare data bank and then identified ZIP codes with an adequate amount of diversity as well as transports by EMS services. They also controlled for a multitude of variables, including socioeconomic status and location. Ultimately, they assessed whether the patient was transported to a safety-net hospital versus a reference hospital based on the patient's race.

The point is quite clear: There are disparities in the way prehospital medicine is administered to minority patients. It is not understood whether this disparity has resulted in a difference in outcomes. However, it points to a need for more focused studies on prehospital medicine and the potential for racial disparities.

There is more to be done, and it can be done now. Of the limitations with this paper, I find the most astonishing to be a product of American society: Out of 38,423 ZIP codes, only 5,606 of them had enough diversity to be included in the study. The requirements for diversity in this study meant having at least 10 percent white, black, and Hispanic patients in the same ZIP code. Only 15 percent of ZIP codes in America contain at least 10 percent of the three largest races and ethnicities in this country. These are the real-life ramifications of generations of segregation and redlining. Our generation must still actively and aggressively challenge segregation, a problem possibly now worse than ever due to gentrification.

Nationwide, EMS personnel are 83 percent white, and in the last 10 years, there has not been much increase in the 8 percent of black paramedics. This aspect of health care workforce diversity has not garnished as much attention as the racial disparities among physicians.

We don't need a study to tell us this is unacceptable. We should diversify our EMS personnel, especially given that blacks are nearly 50 percent more likely to use the emergency department for health care than whites.

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DR. FUNK is a practicing emergency medicine physician in Springfield, Missouri, and owner of Med Mal Reviewer, LLC. He writes about medical malpractice at www.medmalreviewer.com.

Bounceback Blowback

An elderly patient falls while leaving the emergency department

by ERIC FUNK, MD

Patients who have been discharged from the emergency department and rapidly return for another complaint present a challenge to the emergency physician. It is frustrating to see a patient return so quickly after spending hours on a thoughtful and thorough workup. However, it is important to consider the circumstances of their return and focus on any change in their condition that might necessitate a new approach. This case illustrates the medicolegal risk involved in rapid patient bouncebacks, handoffs, and safe discharge planning.

The Case

A 70-year-old male presented to an emergency department by private vehicle with a chief complaint of left leg pain. He had a history of atrial fibrillation for which he was prescribed warfarin. Approximately one week before the ED visit, he had been walking on a deck and fell about two feet to the ground. He had ongoing left leg pain from his knee to his ankle. On arrival to the emergency department, he was using crutches and was helped into a wheelchair by ED staff.

The patient was seen by a physician. His initial vital signs were unremarkable, and his pain was rated as 9/10 in the left leg. He was noted to have left leg bruising and severe unilateral edema. A neurovascular exam was normal. The remainder of the physical exam was normal. Multiple tests were ordered, including a complete blood count (CBC), comprehensive metabolic panel (CMP), coagulation panel (the patient was anticoagulated on warfarin for atrial fibrillation), ultrasound for deep venous thrombosis (DVT), chest X-ray, and left tibia/fibula X-ray.

Figure 1 shows the X-ray results. The results were significant for an international normalized ratio (INR) of 1.5. The CBC and CMP were unremarkable. The lower extremity imaging did not show any fractures.

Unfortunately, obtaining the DVT exam was complicated. The facility at which the patient was seen did not have an ultrasound technician, so to get an ultrasound performed and read by a radiologist, the patient was transferred to another hospital to undergo the ultrasound study, then returned to the original emergency department to wait for results.

Prior to the patient leaving to get the DVT ultrasound, the physician ordered 5 mg of oral warfarin and 100 mg of subcutaneous enoxaparin (Lovenox) to treat the patient's subtherapeutic INR (see Figure 2). Additionally, 80 mg of furosemide (Lasix) was ordered to treat his edema. While the patient was away at the other facility getting the DVT ultrasound, there was a shift change and the original physician signed out the patient's care to the oncoming doctor.

```
Impression:
   1. Diffuse lower extremity edema without evidence of acute
  osseous injury.

  2. Unchanged appearance of proximal tibial osteochondroma and
  sequela of previous distal tibial fracture.
```

Figure 1: The patient's X-ray results.

```
1300 lasix 80mg given po

/es/ [redacted]
R.N.
Signed: 08/02/[redacted] 13:04

08/02/2014 ADDENDUM                              STATUS: COMPLETED
1530 urine output 700ml
1535 warfarin 5mg po given. enoxaparin 100mg Sub Q to L side of abd given.

/es/ [redacted]
R.N.
Signed: 08/02/[redacted] 15:51
```

Figure 2: The physician's warfarin and Lovenox order.

IV. CAUSE OF DEATH: ACUTE SUBDURAL HEMATOMA SECONDARY TO FALL AND ANTICOAGULATION.
V. MECHANISM OF DEATH: DECREASING RESPIRATORY EFFORT SECONDARY TO INCREASING INTRACRANIAL PRESSURE.
VI. MANNER OF DEATH: ACCIDENTAL.

Figure 3: The patient's autopsy report.

After the patient's return, the ultrasound results were finalized and were negative for DVT. The patient was placed in a knee immobilizer and discharged to follow up with orthopedics. He was offered a wheelchair but declined in favor of using his crutches. While he was making his way out of the front of the hospital, the patient lost his balance, fell, and hit his head on the ground. A nurse witnessed this, and he was brought back into the emergency department and evaluated by the same physician who had discharged him only minutes earlier.

The patient denied loss of consciousness, and his vitals were again unremarkable. An abrasion to the head was noted, but otherwise he had a normal exam and no complaints. He was discharged home without any further workup.

The patient made it back to his apartment. The next morning, a friend was unable to contact him and went to check on his well-being. Unfortunately, he was found dead. An autopsy was performed, and a large subdural hematoma was discovered (see Figure 3).

Legal Blowback

The patient's family filed lawsuits against the nurses involved as well as the physician who discharged him. The lawsuit was filed in federal court because the emergency department was a Veterans Affairs facility. Ultimately, the federal case was dismissed without trial. The case against the physician was then refiled in state court, and an undisclosed settlement was reached prior to trial.

This case illustrates several key points. Although some emergency physicians comfortably perform DVT exams at the bedside, many are not in the practice of doing so or were trained before point-of-care ultrasound was in wide use. Performing a DVT study at the bedside could have been completed in just a few minutes, negating the need to transfer this patient. The argument can be made that he would not have required empiric anticoagulation while waiting for transfer and there would also not have been a handoff of his care.

The patient presented back to the emergency department only several minutes after having been discharged. Every ED physician knows the frustration of a rapid bounceback. After a patient has a long ED stay with a complicated workup, it can be difficult to start over again with an entirely new workup for a new chief complaint. However, it is important to avoid early mental closure in these situations and not brush off a subtle but life-threatening presentation. Working quickly toward a rapid disposition is an important skill in emergency medicine, but it must be balanced against the risks of causing harm.

In hindsight, it is obvious the patient needed a CT scan of his head. He was an elderly patient on warfarin, and due to his subtherapeutic INR, he had been given additional anticoagulation hours before his head injury. There are no clinical decision rules that would suggest this patient could safely be discharged without obtaining a head CT.

Another possible contributing factor to his fall was the fact he was placed in a knee immobilizer. An elderly man on anticoagulation with limited mobility is an obvious fall risk. There is no indication for using a knee immobilizer in this case given that he did not have any fractures or injury to the extensor mechanism of his knee. Simple compression with an ACE bandage would have been appropriate and allowed for safer mobility.

SEE THE RECORDS

To read more details on the lawsuit, visit www.medmalreviewer.com/case-5-knee-pain.

ertional heatstroke occurs in elderly patients with baseline comorbidities that require advanced monitoring. In addition, elderly patients may not be able to tolerate cold water immersion. This method, however, does cool at a slower rate in actual heatstroke victims (versus in study subjects) and is slower than cold water immersion.[3,4] Antipyretics will not treat the cause of heatstroke and should be withheld.

In the hospital setting, patients experiencing exertional or nonexertional heatstroke should have a complete blood counts, basic metabolic panels, liver function tests, coagulation studies, and urinalyses. An ECG and chest X-ray are recommended for elderly patients. Administering a dose of antibiotics may be warranted if the differential diagnosis favors infection as a cause or contributing cause. Other laboratory tests to consider include creatine kinase, urine myoglobin, ECG, troponins, blood gas, lactate, toxicology screen, chest X-ray, and CT of the head as needed.

Complications of these illnesses include permanent neurological sequelae, seizures, noncardiogenic pulmonary edema, acute respiratory distress syndromes, arrhythmias, hypotension, gastrointestinal ischemia, hepatic injury, acute kidney injury, rhabdomyolysis, and disseminated intravascular coagulation. In most cases, admitting patients to the hospital for further observation is recommended.[3,5,7,8]

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BFR0000-8741-01