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Internal Medicine

Evidence-based summaries of the latest research in internal medicine [ALERT]

Vol. 43, Issue 14, July 30, 2021
ReliasMedia.com

ABSTRACT & COMMENTARY

Is a History of Palpitations Useful for Detecting Atrial Fibrillation?

By Michael H. Crawford, MD

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SYNOPSIS: An analysis of the utility of implanted loop recorders to detect subclinical atrial fibrillation in high-risk individuals showed that among common arrhythmia-compatible symptoms, only palpitation was predictive of discovering episodes of atrial fibrillation.

SOURCE: Reiffel JA, Verma A, Kowey PR, et al. Relation of antecedent symptoms to the likelihood of detecting subclinical atrial fibrillation with inserted cardiac monitors. *Am J Cardiol* 2021;145:64-68.

In the 2017 REVEAL AF study, the authors showed that in a population enriched by selecting subjects at risk for subclinical atrial fibrillation (SAF), 40% would experience one or more episodes of SAF lasting for at least six minutes. This, after 30 months of monitoring by a subcutaneously implanted loop ECG recorder.[1]

Entry into REVEAL AF required a CHA_2DS_2-VASc score ≥ 3 or a score of 2 with one or more of the following risk factors for SAF: coronary artery disease (CAD), impaired renal function, sleep apnea, or chronic obstructive lung disease (COPD). Excluded were patients with a history of AF, those on anticoagulant therapy, and those with a stroke or transient ischemic attack (TIA) within the last 12 months. REVEAL AF showed older age, body mass index, and a particular genetic profile were independently predictive of discovering SAF.

This report by Reiffel et al (who authored REVEAL AF) tested the hypothesis that symptoms would predict the occurrence of SAF in the REVEAL AF population. This substudy included 346 subjects (mean age, 71 years; 50% men) who were followed for a mean of 22 months. Comorbid conditions were common: two-thirds had diabetes or CAD, 40% reduced renal function, one-third remote stroke/TIA, one-quarter sleep apnea, and 20% heart failure or COPD. Arrhythmia-compatible symptoms were ascertained for the three months before enrollment in REVEAL AF, including palpitation, fatigue, chest discomfort, faster heart rate, syncope, dizziness, and dyspnea. Only 39 subjects showed no symptoms; most showed more than one.

Financial Disclosure: Dr. Brunton, physician editor, reports he is on the speakers bureau for AstraZeneca, Bayer, Lilly, and Novo Nordisk; and is a retained consultant for Abbott, Acadia, AstraZeneca, Bayer, Novo Nordisk, Sanofi, and Xeris. The relevant financial relationships listed have been mitigated. None of the remaining planners or authors for this educational activity have relevant financial relationships to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

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Internal Medicine Alert (ISSN 0195-315X) is published semimonthly by Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468. Periodicals postage paid at Morrisville, NC, and additional mailing offices. POSTMASTER: Send address changes to *Internal Medicine Alert*, Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468.

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SAF was detected in 6.5% of subjects at 30 days. By six months, more than 20% had SAF. Few showed SAF in the time frame of the usual external monitoring devices (less than 10 days). In a multivariate analysis, the only symptom associated with the detection of SAF was palpitation (HR, 1.6; 95% CI, 1.1-2.3; $P = 0.01$). Interestingly, palpitation was more common in those without SAF (61%) vs. those with SAF (39%), and symptoms in general were more common in those without SAF. The authors concluded that although symptoms are more common in subjects without SAF, palpitation is associated with an increased incidence of SAF, whereas other common arrhythmia-compatible symptoms are not.

■ COMMENTARY

AF often is discovered because of symptoms, adverse outcomes (e.g., stroke), or it is detected on routine ECG or implanted device monitoring for other reasons. The latter is so-called subclinical AF. Experience with such monitoring has shown most patients with SAF are symptomatic, but the symptoms often are not related to the episodes of AF. Other experience suggests symptoms are more common with paroxysmal AF than chronic AF. Patients with paroxysmal AF more often experience palpitation and chest discomfort, whereas those with chronic AF more often report dyspnea and fatigue. Brief episodes of AF usually are asymptomatic. This may be one reason why six minutes of AF was the criterion for SAF in REVEAL AF, since it more likely would be symptomatic and important to the patient.

Prolonged monitoring with implanted loop recorders is a potential diagnostic tool for uncovering SAF in high-risk individuals. They can be prophylactically treated to prevent bad outcomes. The issue is when to perform such monitoring. Recommending a loop recorder to everyone older than age 70 years is not going to be feasible. Perhaps looking at an enriched population using the REVEAL AF entry criteria would be. In this regard, the Reiffel et al substudy adds another possible selection criterion: palpitation. This makes sense since one would predict more AF would be discovered in such patients compared to those without. However, REVEAL AF also showed palpitation was more common in those without SAF, even though it was the only symptom predictive of SAF in a multivariate analysis. Thus, even the presence of palpitation may not be selective enough to warrant prolonged invasive monitoring.

In addition to its post-hoc, retrospective design, there were other limitations to this substudy. Symptom collection happened before the monitoring period only. It is unclear whether the symptoms were associated with the actual SAF events. Palpitation could be the result of other events, such as re-entrant supraventricular tachycardia or even ventricular tachycardia. Many patients reported more than one symptom, yet the authors did not conduct a combination symptoms analysis. Also, they did not perform an analysis of the added value of palpitation to other clinical risk factors for AF. Consequently, at this point, it is certainly reasonable to conduct short-term external monitoring in patients with frequent arrhythmia-compatible symptoms and perhaps discuss an implantable loop recorder in those with less frequent symptoms. However, moving to implanting loop recorders in patients with only AF risk factors is an unproven way to reduce the morbidity and mortality of AF. This substudy of REVEAL AF does not establish that the additional presence of palpitation with risk factors for AF tips the balance toward implanting a loop recorder. ■

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ABSTRACT & COMMENTARY

Extensive Loss of Health at Six Months in Survivors of COVID-19

By Richard R. Watkins, MD, MS, FACP, FIDSA, FISAC

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SYNOPSIS: Researchers found many survivors of COVID-19 exhibited significant loss of health six months after their acute illness, with greater risk associated with severity of the acute infection.

SOURCE: Al-Aly Z, Xie Y, Bowe B. High-dimensional characterization of post-acute sequelae of COVID-19. *Nature* 2021;594:259-264.

Most individuals with COVID-19 experience a full recovery. However, a significant minority do not and instead experience long-lasting symptoms, for which the etiology remains poorly understood. Therefore, Al-Aly et al sought to comprehensively analyze the post-acute sequelae of COVID-19 using a high-dimensional approach.

The study included a cohort of 73,435 patients from the Veterans Health Administration (VHA) with COVID-19 who survived at least the first 30 days after a COVID-19 diagnosis and who were not hospitalized. These patients were compared to a control group of 4,990,835 VHA patients who did not have COVID-19 and were not hospitalized. More than 99.99% of standardized differences between the two groups were < 0.1 after adjustment, indicating their baseline characteristics were similar. The investigators also evaluated the risk of death associated with 379 diagnoses (based on ICD-10 codes), 380 medication classes, and 62 laboratory tests beyond the first 30 days from COVID-19 diagnosis.

After the first 30 days of illness, COVID-19 survivors were at a higher risk of dying (HR, 1.59; range, 1.46-1.73). The most commonly affected organ system for COVID-19 sequelae was the respiratory tract (28.51 per 1,000 COVID-19 patients at six months). There was an increased incidence of bronchodilator use (22.23 per 1,000 COVID-19 patients at six months), antitussive and expectorant use (12.83), anti-asthmatic use (8.87), and steroid use (7.65). An excess burden of nervous system disorders was found, including nervous system signs and symptoms (14.32 per 1,000 COVID-19 patients at six months) and headaches (4.10). Mental health problems were more frequent as well, including sleep-wake disorders (14.53 per 1,000 COVID-19 patients at six months), anxiety and fear-related disorders (5.42), and trauma and stress-related disorders (8.93). The led to an excess burden of incident use of antidepressants (7.83) and benzodiazepines, sedatives, and anxiolytics (22.23).

Many COVID-19 survivors had cardiovascular sequelae as a result of their infection, including cardiac dysrhythmias (8.41 per 1,000 COVID-19 patients at six months), circulatory signs and symptoms (6.65), chest pain (10.08), coronary atherosclerosis (4.38), and heart failure (3.94). Gastrointestinal issues included esophageal disorders (6.90), abdominal pain (5.73), and an increased use of laxatives (9.22) and antidiarrheal agents (2.87). An excess burden in incident acute pulmonary embolism (2.63 per 1,000 COVID-19 patients at six months) and use of anticoagulants (16.43) was found. Finally, there was an excess burden of poor general well-being in the COVID-19 survivors. They had increased malaise and fatigue (12.64 per 1,000 COVID-19 patients at six months), muscle disorders (5.73), and musculoskeletal pain (13.89). Abnormal laboratory values included decreased hemoglobin (31.03 per 1,000 COVID-19 patients at six months), decreased hematocrit levels (30.73), decreased serum albumin (6.44), and increased alanine aminotransferase (7.62).

Next, the investigators compared COVID-19 survivors who were hospitalized (n = 13,654) to subjects with influenza who survived at least 30 days after hospitalization (n = 13,997). Similar to the preceding findings, COVID-19 survivors had a higher burden of pulmonary and extrapulmonary sequelae, including neurologic disorders (19.78 per 1,000 hospitalized COVID-19 patients at six months), mental health disorders (7.75 [4.72, 10.10]), metabolic disorders (43.53), cardiovascular disorders (17.92), gastrointestinal disorders (19.28), coagulation disorders (14.31), pulmonary embolism (18.31), and malaise and fatigue (36.49).

Finally, investigators used the receipt of influenza vaccination in odd and even months as a negative control. They tested the association between receipt of influenza vaccination in even months (n = 762,039) vs. odd months (n = 599,981) with all 821 of the analyzed high-dimensional clinical outcomes in the study. None of the associations reached the threshold of statistical significance.

■ COMMENTARY

Post-acute COVID-19 syndrome, also known as long COVID, is now recognized as a multiorgan disease with

a multitude of symptoms. The study by Al-Aly et al is important because it quantifies the risk survivors of COVID-19 have for negative effects on their health six months after their acute illness. Although the idea is not proven, many experts believe that an overactive immune response to the acute COVID-19 infection, rather than ongoing viral replication, is the underlying biological mechanism. Sometimes, other viral illnesses can produce post-infectious sequelae, but COVID-19 appears to be unique in this regard in terms of the number of symptoms and their duration. The CDC is conducting multiyear studies to investigate post-COVID conditions further.[1]

There are a few limitations to the study. First, the investigators used a database from the VHA, so men were overrepresented in the patient population. Second, the effect of SARS-CoV-2 variant strains and widespread vaccination on long-term symptoms remains to be elucidated. Finally, with high-dimensional data sets, the number of features can exceed the number of observations, thus increasing the risk for confounding.

As more people survive COVID-19, many will need additional follow-up and care. Since this will burden an already-stretched healthcare system further, additional studies are needed urgently to help inform future health system planning. ■

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BRIEF REPORT

Party Affiliation and Social Distancing

By Carol A. Kemper, MD, FACP

Clinical Associate Professor of Medicine, Stanford University, Division of Infectious Diseases, Santa Clara Valley Medical Center

SOURCE: Leventhal AM, Dai H, Barrington-Trimis JL, et al. Association of political party affiliation with physical distancing among young adults during the COVID-19 pandemic. *JAMA Intern Med* 2021;181:399-403.

Disparate public health messaging from political officials, news media, and online outlets has occurred throughout the COVID-19 pandemic in the United States. Some have wanted to ascribe lower rates of compliance with public health guidance to political affiliation.

Leventhal et al examined the political affiliation of a group of young adults age 18 to 25 years, mostly residing in Los Angeles County, with their compliance with physical distancing guidelines and risk activities for COVID-19 infection between May 18 and Aug. 3, 2020. The cohort (n = 3,396) was recruited originally in high school in 2013 as part of an existing health behavior survey. Of those with currently valid contact information, 2,179 agreed to participate in this study. The mean age of the participants was 21.2 years, 61% were women, and 84.8% lived in Los Angeles County. Political party affiliation was collapsed into four categories: Democrat (43.1%), Republican (7.2%), Independent/other (15.8%), or don't know/declined to answer (34%). Questions regarding physical distancing (sometimes/rarely vs. always/usually/have not been in public places) were given a binary outcome (0 or 1). Engaging in four different kinds of social/recreational activities (visiting a public venue, such as a mall, attending or hosting a party with more than 10 people, or going to a restaurant) also were given binary scores (1 or 0), which were summed as continuous outcomes. Those who identified as Republican were twice as likely to engage in social/recreational activities as Democrats (mean standard deviation [SD] 3.6 vs. 1.9; $P < 0.001$), and somewhat more likely than either Independents/other (mean SD, 2.2) or those who don't know/declined to state (mean SD, 2.2; both $P < 0.001$). Participants identifying as Republicans also were significantly more likely to engage in infrequent physical distancing (24.3%) compared with any of the other three groups: Democrats (5.2%), Independent/other (6.6%), or don't know/decline to state (5.7%). For each comparison, $P < 0.001$). The proportion of participants who perceived a risk of contracting COVID-19 or a chance of dying of COVID-19 was no different between any of the groups. Further, substance use, impulsivity, and delinquency scores (as measured by inventory impulsivity scales or a sum of generally bad behavior in 9th grade) also had no apparent relationship with a willingness to disregard social distancing and to engage in social/recreational activities.

The psychology of behavior is difficult to pin down. We once participated in a study of safer sex behavior involving five medical centers on the West Coast. I was struck that none of our ongoing, repetitive, safe sex messaging, T-shirts, posters, and free condoms made much difference in either the frequency of safer sex or the number of partners. But one fundamental finding was that outcomes differed depending on where people

fell on the pessimism vs. optimism personality scales. Only those people classified as "pessimists" actually believed that bad things could happen to them and were willing to modify their behavior. People who scored higher on the "optimism" scale only saw the future as getting better, regardless. During the COVID-19 pandemic, perhaps mask-wearers are simply more pessimistic about the future? ■

ABSTRACT & COMMENTARY

Long-Term Effects of Cholinesterase Inhibitors on Cognitive Decline, Mortality

By Michael T. Lin, MD

Associate Professor of Neurology and Neuroscience, Weill Cornell Medical College

SYNOPSIS: Cholinesterase inhibitors are one of the few drug classes approved by the FDA to treat patients with Alzheimer's disease. This study shows a long-term benefit in slowing the decline of cognition, but it is unclear if there is any benefit in quality of life.

SOURCE: Xu H, Garcia-Ptacek S, Jonsson L, et al. Long-term effects of cholinesterase inhibitors on cognitive decline and mortality. *Neurology* 2021;96:e2220-e2230.

Cholinesterase inhibitors (CHEIs) are the main Alzheimer's disease (AD) drug therapies. However, the follow-up in most randomized clinical trials of CHEIs is less than one year, and there are few studies of their long-term effects.

Xu et al found CHEIs were associated with sustained benefit in cognition and decreased mortality over five years. One specific CHEI, galantamine, also was associated with a lower risk of severe dementia. The authors used the Swedish Dementia Registry, established in 2007 to register all patients with incident dementia in Sweden and follow them annually. From 2007 to 2017, 39,196 patients with AD or mixed AD dementia were registered. Subjects were considered CHEI nonusers if they were never given a CHEI and CHEI users if they were given a CHEI within three months of baseline Mini-Mental State Exam (MMSE). Subjects given their first CHEI more than three months after baseline were excluded because of faster decline. Without adjustment, CHEI nonusers were older, scored lower at baseline on the MMSE, presented with more comorbidities, and took more medications.

To balance these potential confounders, a propensity score-matching scheme was used. The final cohort consisted of 11,652 CHEI users and 5,826 nonusers, well-matched for demographics, comorbidities, and baseline characteristics. The investigators compared the groups with respect to cognitive trajectory, incidence of severe dementia, and mortality.

Over an average of five years of follow-up, MMSE scores in CHEI users were slightly higher than in CHEI nonusers at every point, and the benefit increased slightly over time (0.13 points/year). The benefit increased with dose up to a certain point (donepezil 7.5 mg, rivastigmine 9 mg, galantamine 16 mg) and then plateaued. The different CHEIs produced similar degrees of improvement. For all CHEI users as a group, the risk of developing severe dementia (MMSE < 10) was slightly lower compared to nonusers, but not statistically significant (HR, 0.84; 95% CI, 0.63-1.13). However, for galantamine users, the decrease in risk of severe dementia reached the edge of statistical significance (HR, 0.69; 95% CI, 0.47-1.00). The mortality rate was lower for CHEI users as a group compared to nonusers (HR, 0.73; 95% CI, 0.69-0.77), as well as for each CHEI individually.

■ COMMENTARY

The strengths of this study are a large sample size and long follow-up period. However, it is observational and can provide only class III evidence. Also, the main criticism of CHEIs is their modest benefit, and that remains the case here.

Although the cognitive benefit was sustained, and even increased slightly over time, after five years, the benefit of CHEIs was less than 0.5 MMSE points. Typically, this difference is not noticeable, and a graph of the MMSE scores illustrates that the CHEI user and nonuser trajectories are virtually superimposed.

A 27% lower risk of mortality over the follow-up period is of interest, but a more meaningful figure would be the duration of increased survival, presented as a Kaplan-Meier plot. It also is reasonable to ask whether prolongation of severe dementia even is desirable. Perhaps the most important question, still unanswered, is whether CHEIs produce long-term improvement in quality of life. It is important to make a distinction between a statistically significant improvement in a test and a quality-of-life improvement. ■

ABSTRACT & COMMENTARY

Blood Culture Contamination: Risks and Adverse Effects

By Stan Deresinski, MD, FACP, FIDSA

Clinical Professor of Medicine, Stanford University

SYNOPSIS: In addition to identifying several patient risk factors for contamination of blood culture specimens, the authors also highlighted various adverse clinical and financial adverse effects.

SOURCE: Klucher JM, Davis K, Lakkad M, et al. Risk factors and clinical outcomes associated with blood culture contamination. *Infect Control Hosp Epidemiol* 2021;1-7.

Klucher et al examined risk factors for blood culture contamination as well as clinical outcomes associated with such contamination at a single center in Little Rock, AR, between 2014 and 2018. Only 2% of specimens for culture were drawn through central venous access devices. During that time, 1,504 of 13,782 blood cultures were true positives. Of the remaining, 1,012 were considered contaminated and 11,266 were negative. These served as cases and controls, respectively.

A multivariate analysis revealed the following independent risk factors for contamination: increasing age, Black race, increasing BMI, COPD, paralysis, and sepsis with septic shock on presentation. The presence of metastatic cancer was protective. "Code sepsis" cases were associated with a numerically greater risk of contamination.

Blood culture contamination was associated on multivariate analysis with a one day longer length of hospital stay (7.9 days vs. 6.6 days), greater duration of antibiotic administration (6.2 days vs. 5.2 days), greater hospital charges ($35,008 vs. $28,875), higher rate of acute kidney injury (26.7% vs. 26.3%), higher frequency of ordered transthoracic echocardiograms (27.4% vs. 19.2%), and increased in-hospital mortality (8.0% vs. 4.6%). Individual antibiotics were not included in the multivariate model. However, on univariate analysis, blood culture contamination was associated with more frequent and prolonged vancomycin use.

■ COMMENTARY

It is no surprise that blood culture contamination leads to unnecessary antibiotic administration, but, as reported here, it leads to an array of negative effects. These include the ordering of additional laboratory tests, such as more blood cultures and transthoracic echocardiograms, the occurrence of acute kidney injury, prolongation of hospital stay, and higher costs. Another effect in some cases is unnecessary hospitalizations in patients discharged from the ED and then recalled when the laboratory reports the blood culture result.

The authors noted identification of patient characteristics associated with an increased risk of blood culture contamination may allow focusing on them in attempts to reduce the rate. Among the methods employed to avoid contamination is the use of phlebotomy teams. However, in this study, and as is true at many hospitals, blood cultures were obtained by nurses in the ED. Another method is avoidance of central line draws. In this study, only 2% were obtained from this site. Enforcement of the use of sterile collection techniques is critical, and feedback of contamination rates to individual phlebotomists may be useful. Another approach for which there is evidence of benefit is using diversion devices, which are a response to evidence that it is the initial 1 mL to 2 mL that often is the source of culture contamination. Such a device actively diverts and sequesters a small amount of the initial recovered blood, with blood for culture collected via a separate flow path. ■

PHARMACOLOGY UPDATE

Semaglutide Injection (Wegovy)

By William Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Assistant Clinical Professor of Medicine, University of California, San Francisco.
Dr. Chan is Associate Clinical Professor, School of Pharmacy, University of California, San Francisco.

The FDA has approved a new treatment for chronic weight management. Semaglutide is a glucagon-like peptide (GLP-1) receptor agonist initially approved in 2017 to treat type 2 diabetes mellitus at a lower dose (1.2 mg) as Ozempic and in 2019 as oral tablets (Rybelsus). Semaglutide for weight management is marketed as Wegovy.

INDICATIONS

Semaglutide can be prescribed as an adjunct to a low calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of ≥ 30 kg/m^2 (obese) or ≥ 27 kg/m^2 (overweight) in the presence of at least one weight-related comorbidity condition.[1] These include hypertension, type 2 diabetes mellitus, and dyslipidemia.

DOSAGE

The recommended maintenance dose is 2.4 mg given subcutaneously once weekly on the same day each week without regard to meals.[1] To alleviate gastrointestinal side effects, the recommended escalation schedule is 0.25 mg (weeks 1-4), 0.5 mg (weeks 5-8), 1 mg (weeks 9-12), 1.7 mg (weeks 13-16), and 2.4 mg (week 17 and beyond). Semaglutide is available as prefilled, single-dose pens of 0.25 mg, 0.5 mg, 1 mg, 1.7 mg, and 2.4 mg.

POTENTIAL ADVANTAGES

Semaglutide injection may be more effective in reducing weight than other FDA-approved drugs, such as naltrexone/bupropion, phentermine/topiramate, and liraglutide.

POTENTIAL DISADVANTAGES

As with other GLP-1 receptor agonists, semaglutide carries a warning for the risk of thyroid C cell tumors and is contraindicated in patients with a personal or family history of medullary thyroid carcinoma of multiple endocrine neoplasia syndrome type 2.[1] Acute pancreatitis and acute gallbladder disease have been reported in clinical trials. Antidrug antibodies were observed in 2.9% semaglutide-treated subjects. The most frequently reported (≥ 20%) adverse reactions (vs. placebo) were nausea (44% vs. 16%), diarrhea (30% vs. 16%), vomiting (24% vs. 6%), constipation (24% vs. 11%), and abdominal pain (20% vs. 10%).[1] In clinical trials, 6.8% of semaglutide-treated subjects discontinued the study drug because of adverse reactions vs. 3.2% for placebo-treated subjects.[1] Based on animal data, semaglutide may carry risk for the fetus.[1]

COMMENTS

The safety and efficacy of semaglutide for reducing body weight were evaluated mainly in three 68-week, randomized, placebo-controlled trials.[1-4] Trials 1 and 3 included subjects with BMI of ≥ 30 kg/m^2 or overweight (27 kg/m^2 to 29.9 kg/m^2) with ≥ 1 weight-related coexisting conditions (but not diabetes). Trial 2 included subjects with BMI of ≥ 27 kg/m^2 and type 2 diabetes (mean HbA1c = 8.1%). Subjects in trials 1 and 3 were randomized (2:1) to semaglutide 2.4 mg or placebo (n = 1,306/655; n = 407/204, respectively). Subjects in trial 2 were randomized 1:1:1 to semaglutide 2.4 mg, 1 mg, or placebo (404/403/403). Trials 1 and 2 participants received instructions for a reduced caloric meal diet and increased physical activity. Trial 3 participants received intensive behavioral therapy. The coprimary endpoints were the percent change in mean body weight from baseline and weight reduction of at least 5%. Secondary endpoints included achieving a 10% reduction in weight and various anthropometric and cardiometabolic parameters (e.g., waist circumference, SF-36 functioning score, BP, HbA1c, lipid profile).

At week 68, the percent weight changes from baseline (semaglutide/placebo) were -14.9/-2.4, -9.6/-3.4, and -16/-5.7 for the three trials. The percentage of patients losing ≥ 5% of body weight was 83.5/31.1, 67.4/30.1, and 84.8/47.8, respectively. The percentage achieving ≥ 10% weight reduction was 66.1/12.0, 44.5/10.2, and 73.0/27.1. Semaglutide generally improved anthropometric and cardiometabolic parameters.

CLINICAL IMPLICATIONS

Obesity is a common multifactorial condition that negatively affects mortality and morbidity. Approximately 70% of American adults are obese or overweight.[5] Since 2012, the FDA has approved four medications to enhance weight loss along with diet and physical activity (lorcaserin, phentermine-topiramate, naltrexone-bupropion, and liraglutide). Lorcaserin has since been withdrawn because of cancer risk (2020).[6] The drug combinations feature their own adverse reaction profiles and limitations (e.g., suicide ideation with bupropion, phentermine/topiramate is a schedule CIV drug). GLP-1 receptors are located in the central nervous system and are involved in appetite regulation,[1] which is the likely mechanism of action of both GLP-1 receptor agonists, semaglutide and liraglutide. In terms of relative effectiveness, there are no published direct comparisons of

the older drugs to semaglutide. Also, study duration was 68 weeks for semaglutide and one year for the others. In terms of percent difference between drug effect and placebo, indirect comparisons suggest semaglutide may be more effective. For example, in obese and overweight subjects, the percentage who experienced ≥ 5% body weight reduction on the study drug was 54.1% for semaglutide, 25% for naltrexone/bupropion, 39.8% for phentermine/topiramate, and 27.9% for liraglutide.[1,7,8,9]

Semaglutide offers a new and highly effective treatment option for treating obese and overweight adults with or without diabetes. It should be used as part of a structured multimodality weight management program. The cost for semaglutide as Wegovy is $1,349 for a four-week supply. ■

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CME QUESTIONS

1. Which symptom during long-term implantable loop ECG recorders was associated with episodes of atrial fibrillation?
a. Dizziness
b. Syncope
c. Dyspnea
d. Palpitation

2. Which is correct regarding the adverse sequelae of COVID-19 survivors in the Veterans Health Administration study at six months?
a. The respiratory tract was the most frequently affected organ system.
b. Cardiovascular symptoms were absent.
c. Mortality was not greater than that seen in non-COVID-19 patients.
d. The frequency of adverse sequelae did not differ from that seen in patients who had influenza rather than COVID-19.

3. For patients with Alzheimer's disease, cholinesterase inhibitors:
a. improved memory.
b. improved sleep maintenance.
c. decreased mortality.
d. improved the quality of life for dementia patients.

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages, and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.