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ABSTRACT & COMMENTARY

Benefit of Bariatric Surgery for Obesity and Diabetes Maintained After Five Years

By David Fiore, MD

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Dr. Fiore reports no financial relationships relevant to this field of study.

SYNOPSIS: In this five-year follow-up of bariatric surgery (sleeve gastrectomy and gastric bypass) vs. medical management for overweight and obese patients with diabetes, those who underwent surgery experienced sustained weight loss and reductions in glycated hemoglobin, medication use, and improved quality of life.

SOURCE: Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes - 5-year outcomes. *N Engl J Med* 2017;376:641-651.

Previous studies by these investigators and others have demonstrated short- and mid-term (up to three years) benefits of bariatric surgery over medical management alone for type 2 diabetes and obesity.[1-5] In this report, Schauer et al examined five-year outcomes in the final analysis of the STAMPEDE trial, a non-blinded, randomized study of 150 obese diabetics at a single institution. All patients received intensive medical therapy and were assigned to either just medical therapy, Roux-en-Y gastric bypass, or sleeve gastrectomy. The mean body mass index (BMI) was 37 kg/m^2, but surprisingly, the inclusion criteria included patients with diabetes and a BMI of only 27-43 kg/m^2. The primary outcome was the ability to maintain a glycated hemoglobin (HbA1c) of ≤ 6% without medication. Prespecified secondary outcomes included measures of glycemic control, weight loss, blood pressure, lipid levels, renal function, ophthalmologic outcomes, medication use, adverse events, and quality of life using the 36-Item Short Form Survey (SF-36).

Of the 134 patients who completed the five years of follow-up, a HbA1c of < 6% was achieved in only two of 38 of patients in the medical therapy-only group, compared to 14 of 49 patients in the gastric bypass group and 11 of 47 in the sleeve-gastrectomy group. The surgical groups also contained more participants

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achieving an HbA1c of ≤ 6% without medication (remission), ≤ 6.5% without medication, and ≤ 7% with diabetes medication. Importantly, the reductions in HbA1c were similar in patients, regardless of whether their BMI was greater than or less than 35 kg/m^2.

Other secondary outcome measures also showed greater improvement with surgery compared to medical management. Mean HbA1c levels after five years were 8.5% in the medical group and 7.0% in the surgical group. Weight loss was greater in the surgery groups (medical management -5.3 kg, gastric bypass -23.2 kg, and sleeve gastrectomy -18.6 kg). Triglycerides also improved more in the surgical groups, but low-density lipoprotein was not different significantly between groups, nor was blood pressure. There were no major differences in renal or ophthalmologic outcomes. Lastly, quality of life was measured with the SF-36. Patients in both surgical groups demonstrated improvement in their physical functioning, general health, bodily pain, and energy-fatigue scores. Patients in the medical groups did not improve on any scales and worsened on bodily pain and emotional well-being (patients in the gastric bypass group also worsened in emotional well-being).

There were minimal adverse events reported in all groups. Four patients in the surgical intervention groups required repeat surgery in the first year, and one additional patient required late surgery to repair a gastric fistula. One patient in the medical therapy group died of a heart attack, and one patient in the sleeve-gastrectomy group died of a stroke. Mild anemia was more common in the surgical groups. Excessive weight gain occurred in 19% of the medical group and none in the surgical group.

■ COMMENTARY

This study was well-conducted and produced impressive results favoring bariatric surgery over medical management at five years. Patients in both surgical groups lost more weight, used fewer medications, achieved lower HbA1c measurements, and reported a better quality of life. There were few complications with either medical or surgical therapy, but anemia was more common in the surgical groups. One other important finding was that duration of diabetes for less than eight years was associated with maintaining a HbA1c of < 6%. Another important component of this study, which contrasts it to most studies on diabetes and bariatric surgery, is that the investigators enrolled diabetic patients with a BMI as low as 27 kg/m^2. Unfortunately, the authors did not report on outcomes based on BMI, so it is impossible to draw any conclusions on what the possible BMI break point is for when to consider surgery in a diabetic patient.

As a primary care physician, I am both enheartened and disheartened by the results of this study. We can now be confident that there is therapy available to our overweight and obese diabetic patients that will help them lose weight and improve their HbA1c with fewer medications. However, it seems counterintuitive that surgery is the answer to a public health "epidemic" such as obesity. It seems that for an individual patient, we now can discuss the pros and cons of bariatric surgery compared with aggressive medical management with a fair bit of certainty about expected outcomes. Weighing our patients' preferences, we can make a joint decision about which treatment would be best. What this study doesn't tell us is whether surgery will lower the complications of diabetes, such as nephropathy, retinopathy, and heart disease, nor does it tell us how surgery compares with aggressive lifestyle modification, which may be the most important (but most difficult) intervention. ■

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ABSTRACT & COMMENTARY

Helping Disabled Patients Through Physical Activity

By Seema Gupta, MD, MSPH

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Dr. Gupta reports no financial relationships relevant to this field of study.

SYNOPSIS: A multicenter, single-blinded, randomized trial demonstrated that a structured physical activity intervention reduces reported severe mobility disability and difficulty on mobility tasks, but not all disability in older adults who experience functional limitations.

SOURCE: Manini TM, Beavers DP, Pahor M, et al. Effect of physical activity on self-reported disability in older adults: Results from the LIFE Study. *J Am Geriatr Soc* 2017 Feb 7. doi: 10.1111/jgs.14742.

Approximately one in five U.S. adults reports a disability, with state-level prevalence of any disability ranging from 16.4% in Minnesota to 31.5% in Alabama.[1] Although etiologies of state-level differences in disability across the nation are unclear, disability prevalence generally is higher in the South. Additionally, disability is associated with a higher prevalence of social determinants of poor health, which also are more common in the South. As per most recent estimates by the CDC, more than 30% of the population ≥ 18 years of age (approximately 75 million adults) report at least one basic action difficulty or complex activity limitation such as dressing and bathing.[2] Disability prevalence has been shown to increase with age. More than 60% (26 million Americans ≥ 65 years of age) report at least one basic action difficulty or complex activity limitation. Along with a tremendous effect on quality of life in patients and their caregivers, including the loss of independence, there is a significant financial burden associated with disability. In 2006, these disability-associated healthcare expenditures were estimated at nearly $400 billion, with more than half those costs attributable to non-independent living (e.g., institutional care or personal care services). Increasing the number of activities of daily living disabilities from zero to six can result in a seven-fold increase in healthcare costs. Older people who lose mobility are less likely to remain in the community; demonstrate higher rates of morbidity, mortality, and hospitalizations; and experience a poorer quality of life. Thus, as the number of older adults in the United States rises, maintaining health among people with disabilities is important. Preserving functional independence among older Americans has emerged as a major clinical and public health priority.[3] Several studies have shown that regular physical activity improves functional limitations and intermediate functional outcomes, but definitive evidence demonstrating that major mobility disability can be prevented is lacking.[4]

Manini et al conducted a multicenter, single-blinded, randomized trial that included 1,635 adults 70-89 years of age. All participants were at high risk for becoming physically disabled. Participants were randomized to a structured, moderate-intensity physical activity (PA) program (n = 818) that included aerobic, resistance, and flexibility exercises or to a health education (HE) program (n = 817). At the beginning of the study, participants could walk about five city blocks (one-quarter of a mile) without assistance. All participants received thorough tests for disability at the beginning of the study and then at six, 12, 24, and 36 months after the study started across three domains: basic activities of daily living, instrumental activities of daily living, and mobility. All outcomes were derived by self-report using periodic interviews that asked about the degree of difficulty and receipt of help during the last month.

Researchers found that study participants in both groups experienced about the same level of disability after the study. Over an average follow-up of 2.6 years, the cumulative incidence of BADL dependency was 15.%[1] among PA and 15.2% among HE participants (hazard ratio [HR], 1.0; 95% confidence interval [CI], 0.78-1.29). However, reporting of severe mobility disability (HR, 0.78; 95% CI, 0.64-0.96) and ratings of difficulty on mobility tasks were reduced in the PA group when compared with participants in the HE group.

■ COMMENTARY

The findings demonstrate that compared with a health education program, a structured, moderate-intensity PA program incorporating walking, strength, flexibility, and balance can reduce the risk of severe mobility disability and ratings of difficulty on mobility tasks. This would be the equivalent of reporting improvements in "a lot of difficulty" or "unable" to perform three or more common mobility tasks. However, it is important to note that these positive effects on self-reported mobility did not translate to lower risk of self-reported dependency or disability in basic activities of daily living or disability in

instrumental activities of daily living in the study participants. This finding could be because of the way this study was designed, including not being able to examine the several psychosocial, environmental, and other factors that are related to disability occurrence. Although further research in this area is warranted, regular physical activity is a well-accepted approach for the management of severe disability, including that arising from chronic pain, and often is recommended as an adjunct to pharmacotherapy. Prevention of disability for the elderly can be as simple as a two-pronged approach: optimizing functional reserve with daily physical activity, such as a 30-minute walk, along with balance training and muscle strengthening exercises, and preventing common precipitants such as falls, cardiovascular events, and infection through timely and appropriate preventive care (screenings, immunizations, etc.). Finally, when seniors develop a precipitating event, it is critical to intervene early and offer a multidisciplinary, comprehensive approach designed to augment mobility resulting in rapidly enhanced functional outcomes. ■

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ABSTRACT & COMMENTARY

Antibiotic Treatment in Community-acquired Pneumonia

By Kathryn Radigan, MD

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Dr. Radigan reports no financial relationships relevant to this field of study.

SYNOPSIS: In patients with newly diagnosed community-acquired pneumonia, basing the duration of antibiotic treatment on clinical stability criteria led to a significant reduction in duration of antibiotic treatment without an increased risk of adverse outcomes.

SOURCE: Uranga A, España PP, Bilbao A, et al. Duration of antibiotic treatment in community-acquired pneumonia: A multicenter randomized clinical trial. *JAMA Intern Med* 2016;176:1257-1265.

Although the Infectious Diseases Society of America (IDSA)/American Thoracic Society (ATS) guidelines suggest a minimum of five days of treatment in patients with one or more community-acquired pneumonia (CAP)-associated instability criteria and who achieve an afebrile state for 48-72 hours, the optimal length of antibiotic treatment has not been formally investigated. To determine whether the duration of antibiotic treatment based on IDSA/ATS criteria was as effective as conventional treatment, Uranga et al conducted a multicenter, non-inferiority, randomized, clinical trial performed at four teaching hospitals in Spain. From Jan. 1, 2012, through Aug. 31, 2013, 312 hospitalized patients diagnosed with CAP were randomized to an intervention or control group on day five of their hospitalization. Pneumonia was defined as a new pulmonary infiltrate on chest X-ray in addition to at least one symptom compatible with pneumonia, including cough, fever, dyspnea, and/or chest pain. Patients were excluded if they were infected by HIV, exhibited chronic immunosuppression, resided in a nursing home or previously were in an acute care hospital/palliative care unit, ingested antibiotics within the previous 30 days, required a longer course of antibiotics based on identification of bacteria, required a chest tube, or presented with extrapulmonary infection. For patients randomized to the intervention group, treatment with antibiotics continued for a minimum of five days, with cessation of treatment at that time if their body temperature was ≤ 37.8°C for 48 hours and they had ≤ 1 CAP-associated sign of clinical instability. Signs of CAP-associated instability included systolic blood pressure < 90 mmHg, heart rate > 100 beats per minute, respiratory rate > 24 per minute, arterial oxygen saturation < 90%, or PaO_2 < 60 mmHg on room air. Physicians determined the duration of antibiotics in the control group. In both groups, physicians chose the type of antibiotic based on local guidelines. Main outcomes included clinical success rate at days 10 and 30 from hospital admission and CAP-related symptoms at days five and 10 (measured by the 18-item CAP symptoms questionnaire score, range 0-90).

Of the 312 patients who were enrolled, 150 patients were randomized to the control group and 162 to the

intervention group. When comparing groups, there were no significant differences in age or sex distribution. The number of days receiving antibiotics was significantly longer for patients in the control group compared to the intervention group (median 10; interquartile range [IQR], 10-11 vs. median 5; IQR, 5-6.5 days, respectively; $P < 0.001$). An intention-to-treat analysis comparing patients at day 10 demonstrated clinical success of 48.6% (71 of 150) in the control group and 56.3% (90 of 162) in the intervention group ($P = 0.33$). There were no differences in clinical success between the control and intervention groups at day 30. At day five and day 10, the mean CAP symptom questionnaire scores were 24.7 (standard deviation [SD], 11.4) vs. 27.2 (SD, 12.5) and 18.6 (SD, 8.5) vs. 17.9 (SD, 7.4), respectively ($P = 0.69$). For the per-protocol analysis, clinical success was 50.4% (67 of 137) in the control group and 59.7% (86 of 146) in the intervention group at day 10 ($P = 0.12$). At day 30, clinical success was 92.7% (126 of 137) in the control group and 94.4% (136 of 146) in the intervention group ($P = 0.54$). At day five and day 10, the mean CAP symptoms questionnaire scores were 24.3 (SD, 11.4) vs. 26.6 (SD, 12.1) and 18.1 (SD, 8.5) vs. 17.6 (SD, 7.4), respectively ($P = 0.81$). The researchers agreed that basing the duration of antibiotic use on clinical stability criteria can be safely implemented in hospitalized patients presenting with CAP.

■ COMMENTARY

Even though CAP is one of the leading causes of morbidity and mortality,[1] the optimal duration of antibiotic treatment for CAP is unknown. For years, it was standard to treat patients until a clinical response occurred. Typically, this resulted in antibiotic length of therapy less than four days.[2] With the growing concern for antibiotic resistance after World War II, doctors increasingly were concerned about relapse of pneumonia and treated for an additional two to three days after resolution of symptoms. Unfortunately, this practice led to the philosophy that treating beyond resolution of symptoms could prevent antibiotic resistance. This mindset translated into common practice until 2007 with the release of the IDSA/ATS guidelines. These guidelines suggested five days of treatment in patients who were afebrile for 48-72 hours and exhibited no signs of clinical instability. Although many entertained these recommendations, they were not widely adopted.

To further investigate the optimal length of antibiotic treatment for CAP and support the IDSA/ATS guidelines, Uranga et al conducted a multicenter, non-inferiority, randomized, clinical trial that included 312 hospitalized patients diagnosed with CAP. At day five, patients were randomized either to an intervention group that limited antibiotics to five days if body temperature was ≤ 37.8°C for 48 hours with ≤ 1 CAP-associated sign of clinical instability or to antibiotics per determination of the caring physician. Through these inventions, researchers discovered there was no significant difference in either the clinical success rate or the CAP symptom questionnaire scores. Since this study was a non-inferiority study, its creators did not address specific benefits of shortened length of antibiotic therapy. For instance, the literature suggests that shortened length of antibiotics lead to lower rates of antibiotic resistance.[3] Reduced duration of antibiotics also may lead to improved adherence, decreased incidence and severity of side effects, and cost savings.[4,5]

Before widely adopting these guidelines, one should be aware of the exclusion criteria that may make this study inapplicable for many patients. These exclusion criteria were extensive and included patients with HIV or chronic immunosuppression (comprising solid organ transplant patients, patients post-splenectomy, taking ≥ 10 mg of prednisone daily or the equivalent for 30 days, on other immunosuppressive agents, demonstrating neutropenia); patients residing in nursing homes; patients discharged from acute care hospitals, onsite subacute care units, or palliative care units within the previous 14 days; and/or patients who had ingested oral antibiotics within 30 days of admission, required longer duration of antibiotics based on cause, required a chest tube, acquired an extrapulmonary infection, or transferred to the ICU prior to randomization. Depending on the site of practice, these exclusion criteria may include the majority of one's patient population. It also may be important to note that 80% of patients received a fluoroquinolone, and it is unclear if these same results would be achieved with alternative antibiotic regimens.

The IDSA/ATS recommendations for shorter duration of antibiotic treatment based on clinical stability criteria can be safely implemented in hospitalized patients with CAP. It should be noted that these recommendations must be applied safely, ensuring that the exclusion criteria of this study are respected. Future studies are needed to further delineate the benefits of shorter antibiotic courses. ■

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PHARMACOLOGY UPDATE

Deflazacort Tablets and Suspension (Emflaza)

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

Drs. Elliott and Chan report no financial relationships relevant to this field of study.

The FDA has approved an oral corticosteroid to treat Duchenne muscular dystrophy (DMD) in patients ≥ 5 years of age. This follows the approval of eteplirsen, which is indicated for the treatment of DMD in patients who have confirmed mutation of the DMD gene that is amenable to exon 51 skipping. Deflazacort received fast-track designation, priority review, and orphan drug designation. It is marketed as Emflaza.

INDICATION

Deflazacort is indicated for the treatment of DMD in patients ≥ 5 years of age.[1]

DOSAGE

The recommended dose is 0.9 mg/kg/day.[1] Deflazacort is available as 6 mg, 18 mg, 30 mg, and 36 mg tablets and as an oral suspension (22.75 mg/mL).

POTENTIAL ADVANTAGES

Deflazacort may be associated with less weight gain than prednisone. Fewer subjects discontinue treatment because of adverse events.[2] The frequency of psychiatric adverse events may be lower with deflazacort.

POTENTIAL DISADVANTAGES

Common adverse events (> 10%) vs. placebo are cushingoid appearance (33% vs. 12%), weight increase (20% vs. 6%), increased appetite (14% vs. 2%), upper respiratory tract infection (12% vs. 10%), and pollakiuria (12% vs. 2%).[1] Deflazacort may cause reduced growth compared to prednisone and may be associated with a higher risk of cataracts.[2,3] The oral suspension contains benzyl alcohol, which is not recommended for use in pediatric patients < 5 years of age.

COMMENTS

Deflazacort is a prodrug to the active corticosteroid. The efficacy in DMD was evaluated in a randomized, double-blind, placebo-controlled, 52-week study.[1,2] The population consisted of 196 male subjects 5-15 years of age with documented mutation of the dystrophin gene and onset of weakness before age 5 years and serum creatinine kinase at least 10 times above normal. Subjects were randomized to deflazacort (0.9 mg/kg/day, 1.2 mg/kg/day), prednisone (0.75 mg/kg/day), or placebo at week 12. The primary endpoint was the change from baseline in average strength of 18 muscle groups. Individual muscle strength was graded using a modified Medical Research Council 11-point scale. Mean changes from baseline were 0.15 and 0.26 for deflazacort, 0.27 for prednisone, and -0.10 for placebo. Because of higher adverse events, only the lower doses of deflazacort were approved.

CLINICAL IMPLICATIONS

DMD is an X-linked recessive neuromuscular disorder resulting in the absence or near-absence of dystrophin protein in muscle cells. This leads to muscle damage, loss of physical function, and, ultimately, premature death due to respiratory and/or cardiac failure. A Cochrane Database systematic review suggested that there is moderate quality of evidence that corticosteroid therapy in DMD improves muscle strength and function in the short term and strength up to two years.[3] Limited data suggest prednisone and deflazacort possibly are equally efficacious in improving motor function.[3] Deflazacort is the first FDA-approved corticosteroid for the treatment of DMD. The cost for deflazacort is $294 per 6 mg tablet compared to 20 cents for prednisone 5 mg. ■

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Clinical Briefs

By Louis Kuritzky, MD

A Melodious Path to Addressing Dementia Issues

SOURCE: Long EM. The effect of a personalized music playlist on a patient with dementia and evening agitation. *Ann Longterm Care* 2016;24:31-33.

A substantial minority of the Medicare population suffering from dementia (31%) live in long-term facilities, and staff often must contend with such issues as agitation, aggression, wandering, and other mood changes.

Patients who present behavior problems often are treated with antipsychotic medications, since few other tools are known to be beneficial, despite the observation that antipsychotic medications feature a well-established adverse effect profile, including increased risk of death. Might music therapy be beneficial?

The author presented a case report of a dementia patient who had been treated with antipsychotics. A nursing student visited with the patient and shared headphones with her that played popular music from the time of the patient's youth and young adulthood. Ultimately, the patient began to demonstrate progressively more involvement with the music, including singing along and tapping her fingers. The previously reticent patient became progressively more communicative. Problem behaviors diminished to the point that caregivers discontinued antipsychotics (previous weaning efforts had failed).

I have had a similar experience with one 95-year-old dementia patient. She has been very religious through much of her life, and her personality blossoms forth if I bring in an old hymnal and sing songs with her (somehow, despite her inability to remember her own children or any specifics about her prior life, she remembers *dozens* of lengthy hymns).

Learning music that is meaningful to our patients is a time-intensive endeavor. On the other hand, problematic behavior issues also can be quite taxing. Clinicians might consider informing involved family members or caretakers of the potential positive effects of music therapy. ■

The Way to a Man's Heart Is Through His Stomach?

SOURCE: Afsar B, Vaziri ND, Aslan G, et al. Gut hormones and gut microbiota: Implications for kidney function and hypertension. *J Am Soc Hypertens* 2016;10:954-961.

Our primary concerns about hypertension relate to adverse cardiovascular effects. Who would have guessed that the gastrointestinal tract could play an important role?

As an example, glucagon-like peptide-1 (GLP1; agents such as exenatide, liraglutide, etc.) has been shown in animal studies to increase sodium excretion. In type 2 diabetes, GLP1 treatment reduces blood pressure. Indeed, a trial with liraglutide even found a reduction in cardiovascular events.

The microbial population of the gastrointestinal tract also may play a role. Two of the primary bacterial teams of the gastrointestinal microbiome, *Bacteroidetes* and *Firmicutes*, have been demonstrated to be elevated in spontaneously hypertensive rats; rebalancing of the flora by antibiotic treatment improved blood pressure.

Alimentary bacteria generate a variety of short-chain fatty acids, some of which can stimulate the sympathetic nervous system and induce renin release from the afferent arteriole. Pharmacologic treatments that address potential toxicities produced by the gastrointestinal microbiome are under study and show some promise.

Although the aphorism "the way to a man's heart is through his stomach" may have been intended to reflect another agenda, it may turn out to be far more true than most of us expected. ■

Cardiovascular Risk Induced by NSAIDs

SOURCE: Nissen SE, Yeomans ND, Solomon DH, et al. Cardiovascular safety of celecoxib, naproxen, or ibuprofen for arthritis. *N Engl J Med* 2016;375:2519-2529.

Ever since the publication of the VIGOR trial, in which it was noted that cardiovascular (CV) events were four times more frequent in patients receiving rofecoxib (subsequently withdrawn from the market) than naproxen, warnings about the risk of CV events attributable to nonsteroidal anti-inflammatory drugs (NSAIDs) have become progressively more strident. For instance, the most recent American College of Cardiology/American Heart Association guidelines on acute coronary syndromes place NSAIDs at the bottom of the list of choices to treat musculoskeletal pain, preferring instead even opioid agents such as tramadol.

How does the CV safety profile of various NSAIDs stack up? To address that question, the administrators of the PRECISION trial randomized a large group of arthritis patients (n = 24,081) who were high risk for CV events to naproxen, ibuprofen, or celecoxib. The population was followed for approximately three years.

Although celecoxib produced fewer adverse gastrointestinal and renal events, there was no statistically significant difference among the three agents for CV events. No safe harbor among the NSAIDs has yet been confirmed in a large randomized trial, and the previous supposition that naproxen was a safer NSAID (from the CV perspective) appears to be incorrect. ■

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CME INSTRUCTIONS

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CME QUESTIONS

1. **Compared to medical management alone, at five years, patients who underwent bariatric surgery (gastric bypass or sleeve gastrectomy) plus medical management experienced:**

   a. more weight loss and higher HbA1c.

   b. more weight loss and lower HbA1c.

   c. less weight loss and higher HbA1c.

   d. less weight loss and lower HbA1c.

2. **Based on the study by Manini et al, a structured physical activity intervention compared with health education reduces:**

   a. severe mobility disability and difficulty on mobility tasks.

   b. disability in basic activities of daily living.

   c. disability in instrumental activities of daily living.

   d. disability in vision and hearing.

3. **In the study by Uranga et al, length of antibiotic therapy in uncomplicated community-acquired pneumonia should be:**

   a. based on clinical stability criteria.

   b. seven days.

   c. 14 days.

   d. All of the above

4. **In the study by Uranga et al, basing the length of antibiotic therapy on clinical stability criteria may be safely implemented in community-acquired pneumonia patients, but notable populations excluded from this trial were patients:**

   a. presenting with HIV or taking chronic immunosuppression.

   b. residing in nursing homes.

   c. discharged from acute care hospitals, onsite subacute care units, or a palliative care units within the previous 14 days.

   d. who used oral antibiotics within 30 days of admission.

   e. All of the above

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.

[IN FUTURE ISSUES]

Pioglitazone Improves Fibrosis Scores in Non-alcoholic Steatohepatitis in Patients With and Without Diabetes.

Polyneuropathy in the Metabolic Syndrome

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