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PAIN

ABSTRACT & COMMENTARY

Osteopathic Manipulative Treatment for Low Back Pain

By Jared Dubey, DO

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

SYNOPSIS: Authors of a recent literature review found compelling evidence that osteopathic manipulative treatment is effective for treating low back pain, but not for other conditions.

SOURCE: Slattengren AH, Nissly T, Blustin J, et al. Best uses of osteopathic manipulation. *J Fam Pract* 2017;66:743-747.

Slattengren et al recently published a literature review of the current evidence base for osteopathic manipulative treatment (OMT).[1] They concluded that although evidence is compelling for treating low back pain, it was insufficient to change clinical practice for other conditions. OMT is a hands-on method of diagnosis and treatment taught to osteopathic physicians as part of a comprehensive medical education. The founder of osteopathic medicine, Andrew Taylor Still, MD (1828-1917), eschewed the dangerous medical practices of his day and instead favored structural manipulation as a method to correct aberrant physiology. Osteopathic practice is grounded in the following fundamental principles: Each person is a unit of body, mind, and spirit; structure and function are reciprocally interrelated; the body has a capacity for self-regulation and self-healing; and rational treatment is based on these principles.[2] These principles emphasize the inherently holistic and integrative nature of the osteopathic philosophy.

As a form of manual medicine, OMT has evolved over the ensuing years and now includes more than 50 specific techniques for addressing somatic dysfunction,

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[INSIDE]

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Summary Points

- Several randomized, controlled trials and meta-analyses support the efficacy of osteopathic manipulative treatment (OMT) for the treatment of acute, chronic, and pregnancy-related low back pain.
- OMT has been studied in a wide range of other conditions, but so far, compelling evidence to support consistent efficacy is lacking.
- Despite the lack of robust demonstrated efficacy, the low cost and low risk of harm associated with OMT makes it an attractive integrative treatment option for trial in a variety of clinical scenarios.

which is defined as "the impaired or altered function of the somatic system, including articulatory, myofascial, or skeletal structures, as well as related vascular, neurologic, and lymphatic elements."[2] OMT practitioners diagnose somatic dysfunction using the TART mnemonic — finding areas of Tissue texture change, Asymmetry, Restriction of motion, and/or Tenderness. Somatic dysfunction may exist secondarily to organic pathology or as a primary functional disturbance of otherwise normal anatomy. OMT may be used in either case, typically in an adjunctive fashion in the former or as primary treatment in the latter.[2]

EVIDENCE FOR LOW BACK PAIN

As Slattengren et al noted, small sample size and other methodological flaws historically have limited osteopathic clinical research, but recently, more robust randomized, controlled trials (RCTs) and meta-analyses have found favorable results for OMT, especially in the case of low back pain. Slattengren et al did not report their review methodology, but they discussed four meta-analyses and three RCTs, all of which demonstrated efficacy of OMT for low back pain.

The American College of Physicians now includes spinal manipulation (which overlaps with certain OMT techniques) as a first-line treatment option in its practice guidelines for low back pain.[3] Additionally, Slattengren et al presented a 2014 meta-analysis of 15 RCTs that found patients receiving OMT had significant pain relief and functional improvement compared to controls;[4] a 2005 meta-analysis of six RCTs that reported improved pain scores from OMT vs. controls;[5] and a 2013 randomized trial comparing OMT to therapeutic ultrasound that found that OMT decreased usage of pain medications.[6] Regarding low back pain in pregnancy, Slattengren et al presented two RCTs and a Cochrane review supporting the efficacy of OMT.[7,8,9]

EVIDENCE FOR OTHER CONDITIONS

Slattengren et al also discussed existing evidence for other conditions, including acute neck pain, headaches, postoperative status, pneumonia, and irritable bowel syndrome. They noted that "available data are not sufficiently significant to compel a change in clinical practice," citing limitations of existing studies such as small sample size, lack of reproducibility, poor methodology, and/or questionable clinical significance.

Acute Neck Pain. The authors summarized a 2005 RCT that compared OMT to intramuscular (IM) ketorolac. In this study, although the ketorolac dose may have been inadequate (30 mg IM), the response to OMT was significantly greater.[10] However, they noted that uncertainty regarding the clinical significance of the treatment effect limits the strength of these study results.

Headache. Slattengren et al briefly summarized two RCTs, one in which the addition of OMT to medications decreased migraine frequency compared to medication alone and sham OMT plus medication, and another in which OMT combined with progressive muscle relaxation decreased frequency of tension headaches as compared to progressive muscle relaxation alone.[11,12] However, both studies had limitations, including small sample sizes, questionable clinical significance of treatment effect, and lack of repeated results in other trials.

Postoperative Care. They summarized one retrospective study that analyzed the effect

of OMT on 17 of 55 patients after abdominal surgery. The treatment group had a significantly shorter time to flatus and a significantly shorter mean length of stay than the non-treatment group.[13] However, since this study was retrospective, there was risk of selection bias.

Pneumonia. The authors reviewed a 2010 RCT and a 2013 Cochrane Review, both of which looked at OMT as adjunctive treatment in adults hospitalized with pneumonia. In the RCT, there was no significant effect of OMT in the intention-to-treat analysis, but in the RCT protocol analysis and Cochrane review, OMT reduced length of stay and duration of intravenous antibiotics.[14,15]

Irritable Bowel Syndrome. Slattengren et al reviewed both a crossover study (n = 31) and an RCT (n = 30). In both studies, OMT significantly improved symptoms,[16,17] but the authors noted major limitations of both studies, including self-reported symptoms and small sample sizes.

■ COMMENTARY

Slattengren et al presented a succinct and practical summary of the state of osteopathic clinical research in the era of evidence-based medicine. However, the review had some concerning characteristics, which limit its usefulness in guiding clinical practice, including lack of transparency regarding review methodology, incompleteness in presentation of existing data, and absence of ECHO assessment (Efficacy, Cost, Harms, and patient Opinions) in consideration of application to practice.

Unfortunately, the authors did not report their methods regarding study selection or analysis. Results reporting was limited to synopsis of specific studies and did not include the total number of articles reviewed nor the number of studies omitted. For instance, in addition to the conditions reviewed by the authors, OMT has been studied in many other conditions, including but not limited to: asthma,[18] chronic obstructive pulmonary disease,[19] balance in the elderly,[20] chronic pelvic pain,[21] recurrent otitis media,[22] neonatal prematurity,[23] concussion,[24,25] and infantile colic.[26] It is not clear why the authors chose to omit a discussion of these data.

When engaging patients in shared decision-making, physicians should keep in mind the ECHO mnemonic as they consider potential treatment options.[27] As the authors noted, while robust data on the efficacy of OMT for many conditions may be lacking, the cost efficiency, low risk of harm, and, in many cases, favorable patient opinion may sufficiently compel the integrative provider to incorporate a trial of OMT into a treatment plan for a variety of diagnoses.

In terms of cost to the patient and the healthcare system, OMT appears to be well positioned. Medicare and many private insurers reimburse for OMT, leaving patients with manageable copays. This stands in contrast to many integrative therapies for which patients often must pay out of pocket. Furthermore, if a surgery or medication adverse event can be avoided, OMT may save the healthcare system money, as well. Although more research is needed on the effect of OMT on cost of care, existing studies support the intervention as cost-neutral or cost-saving.[28,29]

Regarding potential for harm, the incidence of serious adverse events after OMT is rare.[30] In a recent analysis of more than 1,800 OMT encounters, no serious adverse events were reported. However, it should be noted that the incidence of mild adverse events, such as increased pain or discomfort, was 2.5%.[31]

Patient opinion and preference also must be considered. Typically, patients favorably perceive treatment options that may allow them to avoid surgery and costly or potentially harmful medications. Furthermore, although many pharmaceutical or surgical procedures target downstream pathology, OMT is an inherently upstream intervention and may be better received by patients desiring to address the root cause of their symptomatology.

Overall, OMT is a safe, low-cost, noninvasive treatment option for a wide variety of conditions. There is now mainstream acceptance of its demonstrated efficacy for low back pain. For other conditions, robust evidence is lacking, but a trial of OMT still may be discussed with patients as a potential treatment option, especially if the service is readily available and patient preference is favorable. ■

REFERENCES

1. Slattengren AH, Nissly T, Blustin J, et al. Best uses of osteopathic manipulation. *J Fam Pract* 2017;66:743-747.
2. Chila A. *Foundations for Osteopathic Medicine*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2011: 3-21.
3. Qaseem A, Wilt TJ, McLean RM, et al. Noninvasive treatments for acute, subacute, and chronic low back pain: A clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2017;166:514-530.
4. Franke H, Franke JD, Fryer G. Osteopathic manipulative treatment for nonspecific low back pain: A systematic review and meta-analysis. *BMC Musculoskelet Disord* 2014;15:286.
5. Licciardone JC, Brimhall AK, King LN. Osteopathic manipulative treatment for low back pain: A systematic review and meta-analysis of randomized controlled trials. *BMC Musculoskelet Disord* 2005;6:43.
6. Licciardone JC, Minotti DE, Gatchel RJ, et al. Osteopathic manual treatment and ultrasound therapy for chronic low back pain: A randomized controlled trial. *Ann Fam Med* 2013;11:122-129.
7. Licciardone JC, Aryal S. Prevention of progressive back-specific dysfunction during pregnancy: An assessment of osteopathic manual treatment based on Cochrane Back Review Group criteria. *J Am Osteopath Assoc* 2013;113:728-736.
8. Hensel KL, Buchanan S, Brown SK, et al. Pregnancy Research on Osteopathic Manipulation Optimizing Treatment Effects: The PROMOTE study. *Am J Obstet Gynecol* 2015;212:108.e101-109.
9. Pennick V, Liddle SD. Interventions for preventing and treating pelvic and back pain in pregnancy. *Cochrane Database Syst Rev* 2013:CD001139.

10. McReynolds TM, Sheridan BJ. Intramuscular ketorolac versus osteopathic manipulative treatment in the management of acute neck pain in the emergency department: A randomized clinical trial. *J Am Osteopath Assoc* 2005;105:57-68.
11. Cerritelli F, Ginevri L, Messi G, et al. Clinical effectiveness of osteopathic treatment in chronic migraine: 3-armed randomized controlled trial. *Complement Ther Med* 2015;23:149-156.
12. Anderson RE, Seniscal C. A comparison of selected osteopathic treatment and relaxation for tension-type headaches. *Headache* 2006;46:1273-1280.
13. Baltazar GA, Betler MP, Akella K, et al. Effect of osteopathic manipulative treatment on incidence of postoperative ileus and hospital length of stay in general surgical patients. *J Am Osteopath Assoc* 2013;113:204-209.
14. Noll DR, Degenhardt BF, Morley TF, et al. Efficacy of osteopathic manipulation as an adjunctive treatment for hospitalized patients with pneumonia: A randomized controlled trial. *Osteopath Med Prim Care* 2010;4:2.
15. Yang M, Yan Y, Yin X, et al. Chest physiotherapy for pneumonia in adults. *Cochrane Database Syst Rev* 2013(2):CD006338.
16. Attali TV, Bouchoucha M, Benamouzig R. Treatment of refractory irritable bowel syndrome with visceral osteopathy: Short-term and long-term results of a randomized trial. *J Dig Dis* 2013;14:654-661.
17. Florance BM, Frin G, Dainese R, et al. Osteopathy improves the severity of irritable bowel syndrome: A pilot randomized sham-controlled study. *Eur J Gastroenterol Hepatol* 2012;24:944-949.
18. Guiney PA, Chou R, Vianna A, Lovenheim J. Effects of osteopathic manipulative treatment on pediatric patients with asthma: A randomized controlled trial. *J Am Osteopath Assoc* 2005;105:7-12.
19. Engel RM, Vemulpad SR. Immediate effects of osteopathic manipulative treatment in elderly patients with chronic obstructive pulmonary disease. *J Am Osteopath Assoc* 2008;108:541-542.
20. Lopez D, King HH, Knebl JA, et al. Effects of comprehensive osteopathic manipulative treatment on balance in elderly patients: A pilot study. *J Am Osteopath Assoc* 2011;111:382-388.
21. Marx S, Cimniak U, Beckert R, et al. [Chronic prostatitis/chronic pelvic pain syndrome. Influence of osteopathic treatment — a randomized controlled study]. *Urologe A* 2009;48:1339-1345.
22. Mills MV, Henley CE, Barnes LL, et al. The use of osteopathic manipulative treatment as adjuvant therapy in children with recurrent acute otitis media. *Arch Pediatr Adolesc Med* 2003;157:861-866.
23. Lanaro D, Ruffini N, Manzotti A, Lista G. Osteopathic manipulative treatment showed reduction of length of stay and costs in preterm infants: A systematic review and meta-analysis. *Medicine* (Baltimore) 2017;96:e6408.
24. Guernsey DT, Leder A, Yao S. Resolution of concussion symptoms after osteopathic manipulative treatment: A case report. *J Am Osteopath Assoc* 2016;116:e13-17.
25. Chappell C, Dodge E, Dogbey GY. Assessing the immediate effect of osteopathic manipulation on sports related concussion symptoms. *Osteopath Fam Phys* 2015;7:30-35.
26. Dobson D, Lucassen PL, Miller JJ, et al. Manipulative therapies for infantile colic. *Cochrane Database Syst Rev* 2012;12:CD004796.
27. Rakel D. *Integrative Medicine*. 4th ed. Philadelphia: Elsevier; 2018.
28. Gamber R, Holland S, Russo DP, et al. Cost-effective osteopathic manipulative medicine: A literature review of cost-effectiveness analyses for osteopathic manipulative treatment. *J Am Osteopath Assoc* 2005;105:357-367.
29. Schabert E, Crow WT. Impact of osteopathic manipulative treatment on cost of care for patients with migraine headache: A retrospective review of patient records. *J Am Osteopath Assoc* 2009;109:403-407.
30. Seffinger MA. The safety of osteopathic manipulative treatment (OMT). *J Am Osteopath Assoc* 2018;118:137-138.
31. Degenhardt BF, Johnson JC, Brooks WJ, Norman L. Characterizing adverse events reported immediately after osteopathic manipulative treatment. *J Am Osteopath Assoc* 2018;118:141-149.

EXERCISE

ABSTRACT & COMMENTARY

Running and Health

By Ellen Feldman, MD

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

SYNOPSIS: In a review and meta-analysis of the effects of running and longevity, researchers concluded that running provides specific and significant health benefits and proposed a threshold above which more running provides diminishing returns.

SOURCE: Lee DC, Brellenthin AG, Thompson PD, et al. Running as a key lifestyle medicine for longevity. *Prog Cardiovasc Dis* 2017; 60:45-55.

The roots of running as a sport are deep, dating back to ancient Greece and the original Olympic Games.[1] In 1896, the first organized marathon was run at the first modern Olympic Games. This race was created with a nod to the myth of Pheidippides, an ancient Greek long-distance running courier. According to legend, Pheidippides ran 25 miles from Marathon to Athens carrying news of victory in battle but died just after his proclamation, making him perhaps one of the most famous cases of sudden death associated with running.[2] Today, we know that physical activity is linked with a number of significant health benefits, including a reduction in all-cause mortality. Investigators are studying the intensity and type of exercise needed to maximize benefits as well as any adverse effects of intensive physical activity.[3]

In 2014, Lee et al published a study involving running, all-cause mortality, and cardiovascular mortality in more than 55,000 adults. The results pointed to a reduction in mortality with even minimal levels of running.[4] To address unanswered questions from the original 2014 study, Lee et al reviewed other related studies and conducted a meta-analysis. Among the stated goals of this comprehensive work were the following: review the effect of running on specific health conditions and longevity; explore the specificity of running vs. other physical

Summary Points

- Runners have a 25-40% reduced risk of premature death (even after controlling for multiple variables) and significantly lower risks of cardiovascular disease and some cancers.
- On average, runners live three years longer than non-runners.
- The effect of running on cardiorespiratory fitness may be key to understanding the health benefits of running.
- It remains unclear if there is a "running threshold" over which frequency adversely affects health, but the health benefits appear to flatten at over 4.5 hours or 30 miles weekly.

activities to health; explore mechanisms behind the health benefits; quantify any additional life expectancy associated with running; and investigate any evidence linking attenuation of health benefits with higher rates of running.

The Effect of Running on Longevity and Specific Health Conditions. The results in Table 1 were drawn from pooled results of five large studies published between 2008 and 2016. Adjustment for age and sex was followed by adjustment for multiple variables, including smoking, alcohol use, socioeconomic factors, and body mass index; adjustment for these multiple variables does not significantly affect results.

Running vs. Other Types of Physical Activity. The first results are drawn from results from the original group of more than 55,000 adults (most of whom were white, non-Hispanic) in the 2014 Lee et al study. To analyze specific health benefits from running compared to other forms of exercise, the data were re-analyzed and divided into four categories: inactive non-runners (reference group); active non-runners; solely runners inactive in other physical activities; and runners active in other physical activity. (*See Table* 2.)

Data collected from more than 44,000 men in the Health Professionals Follow-up study were consistent with these results with only running, brisk walking, and tennis, revealing an inverse association with cardiovascular disease risk. A British study of more than 80,000 men and women reported a reduction of mortality and cardiovascular disease only in association with swimming, racquet sports, and aerobics but not with running or cycling.

Proposed Mechanisms. Multiple studies have reported associations between robust exercise of any type and mitigation of chronic disease risk factors, such as hypertension, hypercholesterolemia, glucose regulation, and bone density. However, cardiorespiratory fitness (CRF) is emerging as the most strongly predictive factor associated with lowering of mortality. Lee et al noted that running enhanced CRF and found this association was key in understanding the health benefits of this exercise. A meta-analysis of 49 studies (all randomized, controlled trials) covering more than 2,000 adults found that after one year, runners showed improvements in CRF and lipid profile when matched with inactive peers. After adjusting for CRF, the mortality benefits of running were not significant. One of the studies showed a significant association between reduced adiposity and improved CRF in runners compared to energy expenditure equivalent to other forms of physical activity.

Life Expectancy of Runners. The authors of several large studies concluded that after adjusting for multiple factors, the life expectancy of runners is increased by an average of three years when compared with non-runners. This is similar to the mortality benefits found for persons engaging in other forms of physical activity when meeting the minimum recommended threshold of 150 to 229 minutes per week of brisk walking.

Attenuation of Health Benefits. Excessive endurance exercise has been linked to potential adverse health events, such as increased inflammation and cardiac structural changes. Lee et al looked at three studies to compare results regarding "dosage" of running as well as address concerns of the potential adverse effect of running with increases in frequency and intensity.

In all three studies, longevity benefits of running were flattened at the highest levels of running. In two smaller

Table 1: Risk of All-cause Mortality in Runners vs. Non-runners (Five Pooled Studies)

Risk of all-cause mortality	25-40% reduction in runners compared with non-runners
Risk of cardiovascular-related mortality	45-70% reduction in runners compared with non-runners
Risk of cancer-related mortality	30-50% reduction in runners compared with non-runners

Table 2: Running vs. Other Physical Activity

	Risk of all-cause mortality
Inactive non-runners	Reference group
Active non-runners	12% lower risk
Solely runners (inactive in other physical activities)	30% lower risk
Active runners (participating in other physical activities)	43% lower risk

studies, there did seem to be a higher risk of mortality associated with the highest level of running. However, in the largest study,[4] no such association was found when comparing the highest frequency running group of > 4.5 hours/week with the lowest of < 51 minutes/week. To calculate an upper limit of running beyond which there are no noticeable health benefits, Lee et al extracted data from at least three large studies from the United States and Britain. The suggested upper limit of running is up to 4.5 hours or 30 miles weekly with at least one day off.

■ COMMENTARY

Public interest in these results was widespread, with articles appearing in *GQ* ("Science: Running Is Better Than Every Other Exercise"[5]) to *Runner's World* ("Experts: Surprisingly Little Running Extends Lifespan"[6]) to *The New York Times* ("An Hour of Running May Add 7 Hours To Your Life"[7]). Although these publications need headlines to attract attention, our job as physicians and clinicians requires a different slant — interpreting the research in a clinically relevant, factual manner to educate patients and enable informed decision-making.

[These authors found a significant decrease in all-cause mortality risk for "active" runners who engaged in other physical activity in addition to running; this is clear evidence in support of an active lifestyle for all ages.]

What can we tell patients regarding this comprehensive review and meta-analysis? Clearly, evidence for a link between physical activity and health is compelling. When discussing running, in particular, it is important to note that most of the studies were observational and the quantity of running was based on self-reporting. Thus, associations may be drawn, but we are not yet able to prove causation. Future randomized trials with objective measurable interventions are necessary.

The association with CRF and longevity is interesting. Lee et al noted that CRF improvement may be the most important factor in the link between running and longevity. If so, it would be useful to understand the extent to which other active pursuits increase CRF and if these are associated with a significant increase in longevity. Hopefully, future studies will delve into this relationship.

Understanding the benefits of specific forms of physical activity on health parameters certainly will advance this field and allow firm recommendations for patients. With relatively low cost, easy accessibility, and significant health benefits, running has the potential for clear public health effect. However, studies must be conducted under a variety of conditions and move from a relatively homogenous sample population to diverse gender, racial, socioeconomic, and ethnic groups.

Lee et al mentioned that increases in frequency of running often were accompanied by injury, which limits further running, even temporarily. Also noted was that running activity decreased with age. Studies of other physical activities that carry health benefits equivalent to running could address both of these problems.

Providers can tell patients that strong evidence exists linking physical activity to longevity, and, running in particular, to cardiovascular health and lower cancer mortality. These authors found a significant decrease in all-cause mortality risk for "active" runners who engaged in other physical activity in addition to running; this is clear evidence in support of active lifestyle for all ages. Equally important is the idea of balance and limits; even with exercise, more is not always better and may lead to diminishing or negative returns. The level of running associated with health benefits is unclear, but evidence suggests that even incremental changes in activity level may be significant — a welcome message to patients who find the prospect of running intimidating. In our role as healthcare providers, we are well situated to convey to patients the findings, nuances, subtleties, and limits to current research and assist with incorporating these results into personalized wellness plans. ■

REFERENCES

1. Olympic games. Available at: https://www.olympic.org/ancient-olympic-games/the-sports-events. Accessed April 5, 2018.
2. Brogan R. Run, Pheidippides, run! The story of the battle of Marathon. *Br J Sports Med* 1981;15:186-189.
3. Scholar Commons. Physical Activity and Public Health: Updated Recommendations for Adults from the American College of Sports Medicine and the American Heart Association. Available at: https://scholarcommons.sc.edu/sph_physical_activity_public_health_facpub/119/. Accessed April 5, 2018.
4. Lee DC, Pate RR, Lavie CJ, et al. Leisure time running reduces all-cause and cardiovascular mortality risk. *J Am College Cardiol* 2014;64:472-481.
5. Willis J. Science: Running Is Better Than Every Other Exercise at Making You Live Longer. Available at: https://www.gq.com/story/running-is-good. Accessed April 5, 2018.
6. Burfoot A. Experts: Surprisingly Little Running Extends Lifespan. Available at: https://www.runnersworld.com/health/experts-surprisingly-little-running-extends-lifespan. Accessed April 5, 2018.
7. Reynolds G. An Hour of Running May Add 7 hours to Your Life. Available at: https://www.nytimes.com/2017/04/12/well/move/an-hour-of-running-may-add-seven-hours-to-your-life.html. Accessed April 5, 2018.

ABSTRACT & COMMENTARY

Fish Consumption and Disease Activity in Rheumatoid Arthritis

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

SYNOPSIS: A cross-sectional analysis using baseline data from participants in the Evaluation of Subclinical Cardiovascular Disease and Predictors of Events in Rheumatoid Arthritis (ESCAPE-RA) cohort study demonstrated biweekly consumption of fish significantly decreased pain and progression of RA sufferers.

SOURCE: Tedeschi SK, Bathon JM, Giles JT, et al. Relationship between fish consumption and disease activity in rheumatoid arthritis. *Arthritis Care Res* (Hoboken) 2018;70:327-332.

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by synovial inflammation leading to pain, functional impairment, and joint erosions. Disease-modifying anti-rheumatic drugs (DMARDs) are the standard of care and significantly decrease inflammation, improve symptoms, and decrease erosions. Omega-3 fatty acids decrease pro-inflammatory cytokines and have been studied in the form of orally dosed fish oil in several randomized, controlled studies.[1,2] In double-blind, placebo-controlled studies, subjects ingesting fish oil had reduced pain in joints and higher rates of remission on DMARD therapy.[3,4] Since the benefits of eating fish had not been studied in relationship to reducing RA signs and symptoms, Tedeschi et al sought to investigate the benefits of eating fish for those with RA.

A total of 176 participants in the Evaluation of Subclinical Cardiovascular Disease and Predictors of Events in Rheumatoid Arthritis (ESCAPE-RA) study were included in this analysis. The majority were middle-aged, college-educated, white females taking DMARDs for seropositive, long-standing RA. These participants were enrolled in the ESCAPE-RA study from October 2004 to May 2006, were 45 to 84 years of age, and lived near Baltimore. Subjects with a previous cardiovascular event or weighing > 300 pounds were excluded.

In this study, baseline signs and symptoms were evaluated using the Disease Activity Score in 28 joints (DAS28) and C-reactive protein (CRP). The DAS28 includes examination of the joints for swelling and tenderness in 28 joints, global scores of pain and overall status, and questionnaires to assess function (HAQ). The median DAS28-CRP score at baseline was 3.5 (interquartile range, 2.9-4.3), reflecting moderate disease activity. A DAS28-CRP of > 5.1 implies active disease, < 3.2 low disease activity, and < 2.6 remission.

Summary Points

- Consuming more than two servings per week of fish has a greater benefit for rheumatoid arthritis than consuming low-dose or high-dose fish oil.
- The benefit of consuming fish was evident even in current smokers.
- The observed difference in DAS28-CRP in those who ate two servings of fish per week was approximately one-third the magnitude of DAS28-CRP in methotrexate users.

Dietary intake was measured using a baseline food frequency questionnaire assessing usual diet in the past year. Fish consumption was recorded in four categories: never to < 1 time/month, 1 time/month to < 1 time/week, 1 time per week, and ≥ 2 times per week. Fish included in the study were tuna, salmon, sardines, and "other broiled, steamed, baked, or raw fish (trout, sole, halibut, poke, grouper, etc.)." These fish were selected because of higher omega-3 content. Excluded were fried fish, non-fried shellfish, or fish mixed into dishes. The serving size was not recorded, as these data focused on frequency of consumption rather than quantity. Future studies could investigate serving size of fish and specific types of fish consumed and their individual effect on DAS-CRP.

Confounding variables in this study include age, gender, body mass index, depression, marital status, DMARD therapy, and fish oil use. A linear regression model adjusted to these variables was used to test the relationship between frequency of fish consumption and DAS-CRP.

Table 1: Linear Regression Model Estimates of Difference in DAS28-CRP Compared to Eating Fish Never to < 1/Month

Model adjusted for	never to < 1 time/month (n = 35)	1 time/month to < 1/week (n = 72)	1 time/week (n = 38)	> 2 times/ week (n = 31)	Difference in DAS28-CRP/1 additional serving of fish per week
Age and sex	0 (ref)	-0.32 (-0.73 to 0.10)	-0.32 (-0.79 to 0.15)	-0.65 (-1.15 to -0.15)	-0.22 (-0.40 to -0.04)
Age, sex, body mass index, depression, married	0 (ref)	-0.23 (-0.62 to 0.16)	-0.36 (-0.81 to 0.08)	-0.49 (-0.97 to -0.02)	-0.18 (-0.35 to -0.004)
Age, sex, body mass index, depression, married, DMARD, fish oil	0 (ref)	-0.24 (-0.64 to 0.15)	-0.39 (-0.85 to 0.06)	-0.51 (-0.99 to -0.02)	-0.18 (-0.35 to -0.003)

After adjusting for these confounders, subjects consuming fish more than two times per week had a significantly lower DAS28-CRP compared to subjects who ate fish never to less than one time per month (difference, -0.49; 95% confidence interval [CI], -0.97 to -0.02). To test for trends across categories of fish consumption, the authors calculated the difference in DAS28-CRP associated with increasing fish consumption (an increase of one serving per week). For each additional serving of fish per week, DAS28-CRP was reduced significantly by 0.18 (95% CI, -0.35 to -0.004). (*See Table 1.*)

■ COMMENTARY

Epidemiological data have shown the benefits of eating fish and decreased cardiovascular mortality, decreased rates of diabetes, lower rates of depression, and decreased risk of dementia.[5-8] To date, much research has been conducted on the benefits of supplementing with omega-3 rich fish oil. A recent randomized, controlled trial of fish oil supplementation among patients with RA included those with disease duration of 12 months and taking triple DMARD therapy. Subjects were divided into two categories: treatment with high-dose fish oil (eicosapentaenoic acid [EPA] + docosahexaenoic acid [DHA], 5.5 g/day) and treatment with low-dose fish oil (EPA and DHA, 0.4 g/day). There was no significant difference between the groups in the DAS28-ESR over 12 months. However, at 12 months, both groups had significant decrease in DAS28-ESR.

Now, with this current analysis, we can start to see a greater benefit with eating fish instead of simply supplementing with fish oil. Those in the highest fish consumption group (more than twice per week) consumed < 5.5 g EPA + DHA per day. A 1 ounce serving of fatty fish provides 2 to 4 g of EPA and DHA.[9] Whole fish provides a host of additional micronutrients and macronutrients that may account for the additional beneficial effect. Oily fish are good sources of vitamin B12, vitamin D, vitamin A, selenium, zinc, iodine, iron, potassium, and calcium. Seeing the added value of fish compared to fish oil, future studies could explore the benefit of these other nutrients in RA. However, one drawback to eating fish is the increased intake of mercury and PCBs present in fish. Fish oil often is purified to remove such contaminants. These contaminants may interfere with the anti-inflammatory effect of the omega-3s present in the fish. Future studies comparing therapeutic effectiveness of fish low in mercury and PCB contaminants with those that are higher also could yield useful information.

Ideally, clinicians want patients to adopt healthy, low-inflammatory lifestyles. In patients who live a more inflammatory lifestyle (i.e., smoking), there still is a benefit in eating oily fish regularly. Foods high in omega-3s have a direct anti-inflammatory effect and can offset the negative effects of a high inflammatory, standard American lifestyle. Interestingly, pack years were highest and depression scores were lowest among those who ate fish more than two times per week. It is impressive to note in smokers with a high inflammatory state that there is a significant benefit from eating fish. It also is important to note that consuming fish may have the additional beneficial effect on mood. Healthier mood encourages greater motivation for self-care and healthier lifestyle choices.

Encouraging consuming oily fish on a regular basis is wise clinical advice. The greatest anti-inflammatory benefit comes from eating oily fish at least twice per week. However, it is important to be especially careful with this recommendation for pregnant women and young children. In the most recent recommendation from the Environmental Protection Agency,[10] pregnant women and women who intend to become pregnant should consume only lower-mercury containing fish and a maximum of three servings per week. It is also recommended children eat fish once or twice per week, choosing lower-mercury fish. These include shrimp, pollock, salmon, canned light tuna, tilapia, catfish, and cod. The omega-3s in fish are very important for the development of a healthy nervous system, but the mercury in some fish is neurotoxic. The seven types of fish with higher levels of mercury that should be avoided include tilefish from the Gulf of Mexico, shark, swordfish, orange roughy, bigeye tuna, marlin, and king mackerel. One should consider the environmental effect of more people eating fish on

a regular basis. Some fish are severely over harvested and are at risk of becoming endangered. Seafood Watch (http://www.seafoodwatch.org) is a good resource for patients to learn which fish are safe to consume and which fish are sustainably harvested. ■

REFERENCES

1. Lee TH, Hoover RL, Williams JD, et al. Effect of dietary enrichment with eicosapentaenoic and docosahexaenoic acids on in vitro neutrophil and monocyte leukotriene generation and neutrophil function. *N Engl J Med* 1985;312:1217-1224.
2. Kremer JM, Bigauoette J, Michalek AV, et al. Effects of manipulation of dietary fatty acids on clinical manifestations of rheumatoid arthritis. *Lancet* 1985;1:184-187.
3. Proudman SM, James MJ, Spargo LD, et al. Fish oil in recent onset rheumatoid arthritis: A randomized, double-blind controlled trial within algorithm-based drug use. *Ann Rheum Dis* 2015;74:89-95.
4. Kremer JM, Lawrence DA, Petrillo GF, et al. Effects of high-dose fish oil on rheumatoid arthritis after stopping nonsteroidal anti-inflammatory drugs: Clinical and immune correlates. *Arthritis Rheum* 1995;38: 1107-1114.
5. Hodge AM, Bassett JK, Dugué PA, et al. Dietary inflammatory index or Mediterranean diet score as risk factors for total and cardiovascular mortality. *Nutr Metab Cardiovasc Dis* 2018; Feb 7. pii: S0939-4753(18)30027-9. doi: 10.1016/j.numecd.2018.01.010. [Epub ahead of print].
6. Schwingshackl L, Chaimani A, Hoffmann G, et al. A network meta-analysis on the comparative efficacy of different dietary approaches on glycemic control in patients with type 2 diabetes mellitus. *Eur J Epidemiol* 2018; Jan 4. doi: 10.1007/s10654-017-0352-x. [Epub ahead of print].
7. Parletta N, Zarnowiecki D, Cho J, et al. A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED). *Nutr Neurosci* 2017; Dec 7. doi: 10.1080/1028415X.2017.1411320. [Epub ahead of print].
8. Anastasiou CA, Yannakoulia M, Kosmidis MH, et al. Mediterranean diet and cognitive health: Initial results from the Hellenic Longitudinal Investigation of Aging and Diet. *PLoS One* 2017;12:e0182048. doi: 10.1371/journal.pone.0182048. eCollection 2017.
9. Health.gov dietary guidelines. EPA and DHA content of fish species. 2015. Available at: http://www.health.gov/dietaryguidelines/dga2005/report/HTML/table_g2_adda2.htm. Accessed March 28, 2018.
10 U.S. Food and Drug Administration. FDA and EPA issue final fish consumption advice [press release]. Published Jan. 18, 2017. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm537362.htm. Accessed March 28, 2018.

CARDIOVASCULAR DISEASE

ABSTRACT & COMMENTARY

Meditation for Reducing CVD Risk

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

SYNOPSIS: A recent American Heart Association topical scientific statement found meditation to be an accessible and inexpensive intervention that may be useful adjunctively for reducing the risk of cardiovascular disease.

SOURCE: Levine G, Lange R, Bairey-Merz C, et al. Meditation and cardiovascular risk reduction, a statement from the American Heart Association. *J Am Heart Assoc* 2017; 6:e002218. doi: 10.1161/JAHA.117.002218. [Epub ahead of print].

Despite the numerous advances made during the past decades, heart disease remains the number one cause of death in the United States, and the number of deaths has stabilized only recently in the years 2011-2015 (23.4% of deaths in 2015).[1,2] Heart disease statistics include the diagnoses of coronary heart disease, hypertension, and stroke.[2] With a life expectancy in the United States of 78.8 years,[1] continuing to look for means to reduce risk or ameliorate risk factors for cardiac diseases remains a high priority for the medical community.

The American Heart Association (AHA) publishes scientific statements on various topics related to heart disease and stroke, using a rigorous review process of scientific studies from recognized journals. In September 2017, it released a statement suggesting that meditation practice has the potential to be a cost-effective adjunctive strategy to aid in reducing cardiovascular disease (CVD) risk. The authors stated that current research data are modest in quantity and quality and that further research, powered adequately with reduced bias in outcome and for longer term than is what is currently available, is warranted. The

Summary Points

- Meditation is an inexpensive and accessible practice that has been studied for long-term health benefits for cardiovascular risk factors.
- For patients interested in a lifestyle change approach to cardiovascular disease risk reduction, meditation may be considered as an adjunctive therapy to standard strategies, with the understanding that the overall quality and quantity of data need to be better established.

Table 1: Cardiovascular Disease Risk Factor Topics Reviewed by AHA

Meditation Study	Number of Studies	Findings	Significant Benefit?
Primary prevention of cardiovascular disease	3	No conclusions can be drawn because of small study groups and limited follow up time. Larger studies, with multicenter trials are needed.	NC
Secondary prevention of cardiovascular disease	11	Data suggest benefit, but small study groups and limited follow-up time makes analysis difficult.	Y?
Inducible myocardial ischemia	3	Studies >15 years since published and were limited in group size. Data suggest benefit; there are no recent studies using advanced imaging techniques.	Y?
Subclinical atherosclerosis	5	Studies with mixed study variables approach; parsing out meditation benefit is difficult. Small study sizes.	NC
Endothelial function	3	No change in brachial reactivity noted and no conclusions can be drawn about endothelial function.	N
Insulin resistance/ metabolic syndrome	6	Studies with limited group size, short duration.	NC
Neurophysiology and neuroanatomy	30	Meditation has long-term effects on brain anatomy and physiology, but different forms of meditation have differing anatomic and physiologic effects. Findings from one form of meditation cannot be generalized to others.	Y
Psychological, psychosocial, and physiologic response to stress	37	Meditation benefits psychological and psychosocial indices in many studies. Study limitations were small sample sizes and lack of randomization.	Y
Blood pressure	11	Blood pressure changes, study sizes, methods of blood pressure determination, and group makeup vary widely, making conclusions difficult.	Y?
Smoking/tobacco use	8	Meditation instruction improved smoking cessation rates in randomized studies. Limited by small study sizes.	Y

Key to significance: Y – yes, Y? – benefit suggested, NC – no conclusions drawn, N – no.

AHA commissioned this study, recognizing that previous studies and surveys revealed that a significant number of patients with CVD already participated in mind-body therapies or meditation or were interested in trials using alternative therapies.[4-7]

The authors used search terms covering topics associated with CVD risk reduction to search PubMed for studies on meditation and CVD risk reduction. These topics became the subsets of their study of mediation effects. They limited their research studies to sitting mental practices (meditation) alone to reduce the confounding influence of studying the combined effects of medical and physical therapies, as regular physical activity already is associated with cardiovascular risk reduction. Thus, mind-body practices such as yoga, Qigong, and tai chi were excluded from this study. The authors provided a table describing the common forms of siting meditation, adapted from Rakel's *Integrative Medicine*,[8] to illustrate the various meditative practices assessed in the study.

A primary author with no ties to industry and a secondary author drafted the text and conclusions for the individual CVD topics reviewed. The group members reviewed and revised the combined sections, tables, and conclusions; then these were reviewed by four external reviewers prior to the final revision of the statement. The authors did not assess the studies using a standard methodology. They provided a table that summarized their primary findings on the individual studies included in the review and provided additional comments regarding the sample size, biases found, and control groups used. (*See Table 1.*)

The reviewers noted that there are long-term effects of meditative practice on the brain that affect the anatomical structure of the brain. The areas affected through the process of neuroplasticity include the prefrontal cortex (personality and behavioral cognition), anterior cingulate cortex (decision-making and emotional regulation), ventral striatum, and amygdala (emotional processing). There may be long-standing beneficial effects on CVD

risk through changes in the basal state of the brain and its physiological responses, but the research is limited by non-randomized studies of only modest numbers of participants, who often were experienced meditators.

Studies of meditation and the response to stress have shown an overall positive response. However, few studies have focused on patients with CVD and inferences were drawn to reach this conclusion, using those studies available across the general population and studies that included laboratory findings. Those findings revealed that markers of increased stress (salivary cortisol and amylase, telomere activity, and pro-inflammatory cytokines) were altered by the practice of meditation. Likewise, research of the effects of meditation on smokers has shown that there is an overall improvement in smoking cessation compared to controls, although the studies are limited by small study group size.

Unfortunately, the assessment of studies in which meditation was used for primary CVD prevention revealed that the studies were short-term, included small study groups that were not randomized or well-controlled, and were carried out mostly on healthy individuals. Some studies had hopeful and suggestive findings of decreased cardiovascular death, but ultimately, no conclusions could be drawn by the review group.

Assessing secondary CVD prevention was muddied by the great variability of study sample size, multifactorial interventions, and study quality. Overall, the effect on secondary prevention of CVD was characterized as suggestive, but not establishing benefit.

A previous 2013 AHA scientific statement concluded that transcendental meditation had a modest effect on reducing blood pressure, but also noted that studies of other meditative practices were lacking, making comment about them difficult.[9] The studies of meditation relating to hypertension control varied widely in study size and term length, with few high-quality published randomized studies. Conclusions were difficult to make because of this variability. Some studies revealed modest benefits, but others revealed no change in blood pressure.

Studies assessing the effect of meditation on inducible myocardial ischemia are older; the newer, more sophisticated techniques of assessing and quantifying myocardial ischemia are lacking. However, two small studies from the 1980s and 1990s showed that meditation and a combined stress management program including meditation would delay ST-segment depression significantly, while increasing maximal work and exercise duration. More research is needed to substantiate these older findings.

No conclusions were drawn by the assessment of meditation effects on CVD risk factors of subclinical atherosclerosis or insulin resistance/metabolic syndrome. Studies were assessed as small and short-term in duration and contained mixed study variables, making conclusion too hard to draw out. There was no benefit seen in the studies of endothelial functioning.

■ COMMENTARY

In explaining its statement, the AHA group acknowledged the difficulties of the current state of meditation research. The lack of randomized, controlled trials with large study groups, well-designed methodology, and incomplete follow-up made conclusions difficult. The authors noted that many of these studies may have an unintended bias, since many investigators likely believed in the benefits of the activities studied and many studies were performed by the same groups of researchers, making verification of findings difficult.

There is no mention as to the safety or side effects noted throughout this review. As the breadth of practices and wide range of therapists who offer these services exists, risk is hard to assess and further research will need to be undertaken.

The availability of training for meditation and the incorporation of a mind-body practice into a healthy lifestyle is gaining popularity in the United States. Costs of meditation training are nominal and training is accessible for many. Meditation is used to promote stress reduction, awareness, mindfulness, and relaxation, while settling the mind in the moment.

As a mind-body practice, meditation can be practiced in many ways, but all forms are rooted in silence and stillness of compassionate and nonjudgmental awareness of the present moment. Although historically associated with Eastern philosophies and religion, references to meditative practices can be found in other major religions, such as Islam, Judaism, and Christianity, and it has become increasingly secular, with successful outcomes using mindfulness-based stress reduction.[10]

As medical providers, we are faced daily with caring for individuals with multiple system dysfunction, financial and social stress, and burnout from an increasingly frantic cultural lifestyle. Meditation offers the opportunity for alterations in brain anatomy and physiology while eliciting physical ease and relaxation as well as emotional balance and stability. One learns to be present with emotions, but not to apply judgment to those emotions. A meditative practice can form the basis from which to meet the daily challenges of our lives, and thereby help release the personal judgmental constraints of fear, anxiety, isolation, depression, and helplessness that can lead to further dysfunction of the emotional and physical body. In doing so, meditation has the potential to reduce the risk of damage and dysfunction to the cardiovascular

system. In acknowledgement of this potential, this statement noted that the most benefit seen in meditative research involves neuroanatomical changes and improvement in biomarkers of stress. There is more work to be done in assessing the benefits of CVD risk and the potential of side effects, but it seems to be an easy prescription to discuss and write for ourselves and our patients, considering the availability and low cost of training. ■

REFERENCES

1. Murphy SL, Jiaquan X, Kochanek, KD, et al. Deaths: Final Data for 2015. National Vital Statistics Reports. Available at: https://www.cdc.gov/nchs/data/nvsr/nvsr66/nvsr66_06.pdf. Accessed March 15, 2018.
2. National Center for Health Statistics. Health, United States, 2016: With Chartbook on Long-term Trends in Health. Available at: https://www.cdc.gov/nchs/data/hus/hus16.pdf#019. Accessed March 15, 2018.
3. Blackwell DL, Villarroel MA. Tables of Summary Health Statistics for U.S. Adults: 2015 National Health Interview Survey. National Center for Health Statistics. 2016. Available at: http://www.cdc.gov/nchs/nhis/SHS/tables.htm. Accessed March 15, 2018.
4. Prasad K, Sharma V, Lackore K, et al. Use of complementary therapies in cardiovascular disease. *Am J Cardiol* 2013;111:339-345.
5. Saydah SH, Eberhardt MS. Use of complementary and alternative medicine among adults with chronic diseases: United States 2002. *J Altern Complement Med* 2006;12:805-812.
6. Leung YW, Tamim H, Stewart DE, et al. The prevalence and correlates of mind-body therapy practices in patients with acute coronary syndrome. *Complement Ther Med* 2008;16:254-261.
7. Yeh GY, Davis RB, Phillips RS. Use of complementary therapies in patients with cardiovascular disease. *Am J Cardiol* 2006;98:673-680.
8. Rakel D. *Integrative Medicine*. 3rd ed. Philadelphia: Saunders; 2012.
9. Brook RD, Appel LJ, Ruben re M, et al. Beyond medications and diet: Alternative approaches to lowering blood pressure: A scientific statement from the American Heart Association. *Hypertension* 2013;61.
10. Parswani MJ, Sharma MP, Iyengar S. Mindfulness-based stress reduction program in coronary heart disease: A randomized control trial. *Int J Yoga* 2013;6:111-1117.

CME QUESTIONS

1. Which statement regarding osteopathic manipulative treatment (OMT) is *false*?
a. OMT may be considered as part of an evidence-based, first-line treatment plan for chronic low back pain and low back pain related to pregnancy.
b. OMT has been shown to cause more harm than good when applied to hospitalized patients recovering from surgery or treated for pneumonia.
c. OMT comprises many distinct treatment modalities that have developed since osteopathic medicine's inception more than 100 years ago.
d. Despite lack of definitive evidence supporting its efficacy, OMT may be recommended to patients suffering from chronic migraine or tension headaches.

2. Which of the following statements is most true regarding running and longevity research?
a. The research is clear that running leads to specific health benefits, longer life spans (approximately three years longer), and improved cardiovascular health.
b. The research reveals an association between running, cardiovascular health, and longevity; future prospective studies with multiethnic, multigender, and diverse socioeconomic subjects are needed before attributing causation.
c. The research is inconclusive regarding running and health benefits; most likely the studies showing an association between running and longevity reflect the benefits of physical activity in general.
d. The few studies that exist are poor quality, making any conclusions regarding running and health benefits premature.

3. Which of the following statements in true about fish consumption and rheumatoid arthritis (RA)?
a. Subjects with RA had an equal reduction in symptoms and signs of RA with supplemental fish oil when compared to eating whole fish.
b. Subjects with RA had no change in DAS28 C-reactive protein when eating whole fish.
c. Subjects with RA who ate oily fish twice per week saw a significant reduction in joint pain, joint swelling, and C-reactive protein.
d. Smokers with RA did not see any improvement in DAS28 C-reactive protein from consuming whole fish.

4. Current research supports that meditation has a beneficial effect on which of the following?
a. Reducing overall blood pressure
b. Smoking cessation rates
c. Secondary cardiovascular disease risk
d. Insulin resistance

[IN FUTURE ISSUES]

Saffron as Adjunctive Therapy for Opioid Withdrawal

Acupuncture and Urinary Incontinence

Low-fat Dairy and Parkinson's Disease Risk

Mindfulness-based Intervention and Anxiety