GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

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SPOTLIGHT:

Can the McKenzie Method Improve Back Pain?

- Silent Accelerator: Lipoprotein(a) and the Fast Track to Aortic Stenosis
- How Effective is Multicomponent Treatment for Women with Overactive Bladder?
- PPI Don’t Need This Medication: Pharmacological Considerations in Cirrhotic Patients
- Aspiring Aspirin in Metabolic Dysfunction-Associated Steatotic Liver Disease

Can the McKenzie Method Improve Back Pain?

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

The McKenzie Method for (Sub)Acute Non-Specific Low Back Pain

Almeida MO, Narciso Garcia A, Menezes Costa LC, van Tulder MW, Lin CC, Machado LA. The McKenzie method for (sub)acute non-specific low back pain. *Cochrane Database Syst Rev*. 2023;4(4):CD009711. Published 2023 Apr 5. doi:10.1002/14651858.CD009711.pub2

KEY TAKEAWAY: Using the McKenzie method rather than minimal intervention, manual therapy, or other interventions, does not improve subacute non-specific low back pain (NSLBP) in a clinically significant manner.

STUDY DESIGN: Meta-analysis of five randomized control trials (N=563)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Clinical practice guidelines do not include the McKenzie method as a non-pharmacological treatment plan for the management of people with subacute NSLBP. The use of the McKenzie method may improve short and intermediate-term pain relief as well as disability through individualized exercises for back pain alleviation. This study aimed to evaluate the use of McKenzie method exercises to improve subacute NSLBP.

PATIENTS: Patients with subacute low back pain

INTERVENTION: The McKenzie method

CONTROL: Minimal intervention, manual therapy, back massage, or standard back care device

PRIMARY OUTCOME: Pain relief

Secondary Outcome: Disability prevention

METHODS (BRIEF DESCRIPTION):

- The meta-analysis included adults 18–80 years old with non-specific low back pain.
- Common exclusion criteria involved previous spinal surgery, severe spinal pathology, or specific diagnostic reasons for back pain.
- The primary intervention examined across the studies was the McKenzie method, which emphasizes patient education, specific exercises, and postural advice tailored to individual patient needs.
- Control interventions varied among the studies, including chiropractic therapy, minimal intervention (educational booklets), standard back care devices, back massage, spinal thrust manipulation, and general advice to stay active and avoid bed rest.
- The outcomes assessed were pain and disability, measured with standardized tools such as the Numeric Rating Scale (NRS), Visual Analog Scale (VAS), Roland-Morris Disability Questionnaire (RMDQ), and Oswestry Disability Index (ODI).
    - The scales were assessed on a scale from 0–100 with lower scores indicating less pain and disability.
- Results were reported in terms of mean differences, with improvements categorized as small, moderate, or large based on standardized scales, providing a measure of treatment efficacy across different studies.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Varied (2 weeks to 3 months)

RESULTS:

Primary Outcome –

- The McKenzie method slightly improves pain compared to minimal intervention in the short-term (2 trials, n=328; mean difference [MD] –7.3; 95% CI, –12 to –2.6).
- The McKenzie method does not improve pain compared to minimal intervention in the intermediate term (1 trial, n=180; MD –5.0; 95% CI, –14 to 4.3).
- The McKenzie method does not improve pain compared to manual therapy in the short term (3 trials, n=298; MD –8.7; 95% CI, –27 to 10).
- The McKenzie method slightly increases pain compared to manual therapy in the intermediate term (1 trial, n=235; MD 7.0; 95% CI, 0.70–13).

Secondary Outcome –

- The McKenzie method does not improve disability compared to minimal intervention in the short term (2 trials, n=328; MD –2.7; 95% CI, –7.5 to 2.0).
- The McKenzie method does not improve disability compared to minimal intervention in the intermediate term (1 trial, n=180; MD –0.87; 95% CI, –7.3 to 5.6).

- The McKenzie method does not improve disability compared to manual therapy in the short term (3 trials, n=298; MD –5.0; 95% CI, –15 to 5.0).
- The McKenzie method does not improve disability compared to manual therapy in the intermediate term (1 trial, n=235; MD 4.3; 95% CI, –0.72 to 9.3).
- The McKenzie method does not improve disability compared to other methods in the short term (1 trial, n=30; MD 4.0; 95% CI, –15 to 23).
- The McKenzie method does not improve disability compared to other methods in the intermediate term (1 trial, n=25; MD 10; 95% CI, –9.0 to 29).

LIMITATIONS:

- Very few studies were included with an overall small patient population.
- There is some concern about how some of the studies were conducted.
- Detailed numbers and demographics of the study group and comparison group were not included.

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Silent Accelerator: Lipoprotein(a) and the Fast Track to Aortic Stenosis

Lipoprotein(a) and Calcific Aortic Valve Stenosis Progression: A Systematic Review and Meta-Analysis

Arsenault BJ, Loganath K, Girard A, et al. Lipoprotein(a) and Calcific Aortic Valve Stenosis Progression: A Systematic Review and Meta-Analysis. *JAMA Cardiol*. 2024;9(9):835-842. doi:10.1001/jamacardio.2024.1882

KEY TAKEAWAY: Higher plasma lipoprotein(a) concentration is associated with faster hemodynamic progression of aortic stenosis (AS).

STUDY DESIGN: Systematic review and meta-analysis of five cohort studies (N=710)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: AS is a common and serious condition, particularly affecting older adults, with significant morbidity and mortality. There are currently no effective pharmacological treatments available to slow the hemodynamic progression of AS. Lipoprotein(a) concentrations have been shown to predict the onset of AS, but their role in the progression of AS is unclear. This study aimed to investigate the effect of lipoprotein(a) on disease progression in patients with AS.

PATIENTS: Patients with AS

INTERVENTION: Highest tertile of plasma lipoprotein(a)

CONTROL: Lowest tertile of plasma lipoprotein(a)

PRIMARY OUTCOME: Hemodynamic progression of AS

METHODS (BRIEF DESCRIPTION):

- The included studies were conducted in Canada and the UK between 2001–2023.
- Adults (mean age 65 years old ±13 years) with AS with lipoprotein(a) levels and underwent echocardiography monitoring of AS for hemodynamic progression were included in the study.
  - 70% of the participants were male.
- There were no specific exclusion criteria provided.
- Participants in each cohort were assigned to three groups (tertiles) of equal size based on the distribution of lipoproteins in their cohort.
- The study compared the hemodynamic progression in tertile three (highest concentration of lipoprotein) to tertile one (lowest concentration of lipoprotein) using annual echocardiography.
- The specific values for each tertile varied between cohorts since the measurement of lipoproteins was not consistent in each cohort.
- Hemodynamic progression was determined by the changes in echocardiographic measurements of peak aortic jet velocity, mean transvalvular gradient, and aortic valve area.

INTERVENTION (# IN THE GROUP): 253

COMPARISON (# IN THE GROUP): 256

FOLLOW-UP PERIOD: Not available

RESULTS:

Primary Outcome –

- Patients in the highest tertile lipoprotein(a) concentration group had a faster hemodynamic progression of peak AS compared to patients in the lowest tertile lipoprotein(a) concentration group (5 studies, n=757; ratio of means [ROM] 1.4; 95% CI, 1.1–1.8; I^2=0%).

LIMITATIONS:

- Lipoprotein(a) levels were not measured with the same method in each study.
- Aortic stenosis progression was only evaluated at selected lipoprotein(a) concentrations.
- The anatomic progression of aortic stenosis was not assessed.
- The results studied were disease-oriented outcomes so clinical significance is uncertain.

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How Effective is Multicomponent Treatment for Women with Overactive Bladder?

Multicomponent Intervention for Overactive Bladder in Women: A Randomized Clinical Trial

Funada S, Luo Y, Uozumi R, et al. Multicomponent Intervention for Overactive Bladder in Women: A Randomized Clinical Trial. *JAMA Netw Open*. 2024;7(3):e241784. Published 2024 Mar 4. doi:10.1001/jamanetworkopen.2024.1784

KEY TAKEAWAY: Multicomponent treatment consisting of behavioral therapy has a high efficacy for moderate to severe overactive bladder (OAB) in women.

STUDY DESIGN: Open-label, randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Multicomponent intervention for OAB treatment is used less frequently than pharmacotherapy. However, 43–83% of OAB patients discontinue pharmacotherapy within one month due to inefficacy/adverse events. Multicomponent intervention could be a high-yield alternative treatment in primary care.

PATIENTS: Women with moderate-severe OAB.

INTERVENTION: Cognitive behavioral therapy, bladder training, and OAB education

CONTROL: No multicomponent intervention

PRIMARY OUTCOME: Health-related quality of life (HRQOL)

Secondary Outcome: Subjective OAB symptom improvement

METHODS (BRIEF DESCRIPTION):

- Women 20–80 years old with a prior OAB diagnosis were included in the study.
- Individuals with bladder abnormalities, UTIs, prior bladder surgery, and pregnancy were excluded from the study.
- Patients were randomized 1:1 using a central randomization algorithm into intervention and control (waitlist) groups.
- The intervention group participated in weekly 30-minute sessions and learned six techniques over four weeks:
  - Urinary habits self-monitoring
  - Voiding pathophysiology education
  - Lifestyle modifications
  - Pelvic muscle training
  - Exposure-based bladder training
  - Relapse prevention
- The control group was placed on the waiting list for treatment and received no intervention during the duration of the study.
- Pharmacotherapy continuation was allowed in both groups. Both groups each had 15 participants (38%) on current treatment.
- Changes in the patient's health-related quality of life were assessed by the Overactive Bladder Questionnaire (OAB-q).
  - OAB-q consists of 33 questions and six subscales measuring symptom bother, coping behaviors, concerns or worries, sleep patterns, social interaction, and total HRQOL score.
  - The subscale score is measured from 0–100 points, with higher scores indicating improvement.
  - A minimal important change of the OAB-q was 10 points.

INTERVENTION (# IN THE GROUP): 34

COMPARISON (# IN THE GROUP): 36

FOLLOW-UP PERIOD: 13 weeks

RESULTS:

Primary Outcome –

- The multicomponent intervention largely improved quality of life more than no intervention (standardized mean difference [SMD] 0.82; 95% CI, 0.33–1.3).

Secondary Outcome –

- The multicomponent intervention improved OAB symptoms on the patient global impression-improvement scale compared to no intervention (difference 49%; 95% CI, 28–65).
- The multicomponent intervention improved OAB symptoms on the patient global impression-severity scale more compared to no intervention (difference 30%; 95% CI, 9–47).
- The multicomponent intervention resulted in more patients reporting they were very satisfied compared to no intervention (difference 35%; 95% CI, 14–52).

LIMITATIONS:

- The identity of the intervention group was shared by both participants and therapists. Susceptible to detection bias favoring intervention group during patient-reported outcomes.
- Lower sample size, the initial target was 150 participants with a 15% dropout rate. Recruitment reached 79 participants with 70 completing the trial throughout follow-up.

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PPI Don't Need This Medication: Pharmacological Considerations in Cirrhotic Patients

High-Dose Proton Pump Inhibitor Treatment is Associated with a Higher Mortality in Cirrhotic Patients: A Multicentre Study

Yoon JS, Hong JH, Park SY, et al. High-dose proton pump inhibitor treatment is associated with a higher mortality in cirrhotic patients: A multicentre study. *Aliment Pharmacol Ther.* 2024;59(8):973-983. doi:10.1111/apt.17909

KEY TAKEAWAY: In hospitalized patients with decompensated cirrhosis and hepatic encephalopathy, high-dose proton pump inhibitor (PPI) use is associated with an increased risk of mortality compared to no or low-dose PPI use.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: PPIs are one of the most commonly used medications in the world and are extensively used in patients experiencing complications of liver cirrhosis. Evidence has shown conflicting reports regarding the safety of these medications in the general population and patients experiencing cirrhotic complications. Many of these studies, however, have categorized patients as having a current or history of PPI use and have not examined how dosage affects their safety. This study aimed to investigate the impact of high-dose PPI use on the development of cirrhotic complications compared to low-dose or no PPI use.

PATIENTS: Adults with decompensated cirrhosis experiencing hepatic encephalopathy

INTERVENTION: High-dose PPI use

CONTROL: No or low-dose PPI use

PRIMARY OUTCOME: Overall survival

Secondary Outcome: Recurrence of hepatic encephalopathy (HE) and the development of spontaneous bacterial peritonitis (SBP), hepatorenal syndrome (HRS), gastrointestinal bleeding (GIB)

METHODS (BRIEF DESCRIPTION):

- Adults 18–75 years old who experienced their first episode of cirrhosis-associated HE from seven different referral centers in Korea were included in the study.
  - The presence of HE was defined as a West Haven grade of ≥1.
- Patients outside the age range, with dementia, who underwent transjugular intrahepatic portosystemic shunts or liver transplantation, and with a current or previous history of hepatocellular carcinoma were excluded from the study.
- Patient demographics included a median age of 61 years old, 61% male, 39% female, average MELD score of 15.
- Baseline differences between study groups, such as the severity of cirrhosis, were addressed using a 2:1 propensity score (PS) matching analysis.
- All patients were treated with lactulose with or without rifaximin.
- PPI dosage was analyzed using the mean defined daily dose (mDDD) and participants were categorized into:
  - High-dose: mDDD ≥0.5
    - Patients in the high-dose group were stratified by cirrhosis severity using the Child-Turcotte-Pugh (CTP) classes.
  - Low-dose: mDDD ≤0.5
  - No dose: mDDD=0
- Overall survival was measured using the date of resolution from initial encephalopathic symptoms and the date of all-cause mortality, which was found using data from the Korean Ministry of the Interior and Safety.
- The incidence and risk of cirrhotic complications were measured using the amount of time from the resolution of symptoms from the first episode of hepatic encephalopathy (index date) to the experience of initial symptoms from a subsequent cirrhotic complication.
- Research subjects were monitored every 1–2 months.

INTERVENTION (# IN THE GROUP): 232

COMPARISON (# IN THE GROUP):

- Low-dose: 592
- No dose: 661

FOLLOW-UP PERIOD: Median 20 months

RESULTS:

Primary Outcome –

- High-dose PPI use was associated with an increased risk of death compared to low-dose or no PPI use (adjusted hazard ratio [aHR] 1.7; 95% CI, 1.4–2.1).
- High-dose PPI use was associated with increased mortality compared to low-dose PPI (aHR 2.2; 95% CI, 1.8–2.6).
- No PPI use was associated with increased mortality compared to low-dose PPI (aHR 2.3; 95% CI, 1.8–2.9).

Secondary Outcome –

- High-dose PPI was associated with more cirrhotic complications compared to low-dose or no PPI.
  - Recurrent HE (aHR 2.0; 95% CI, 1.7–2.5)
  - SBP (aHR 1.8; 95% CI, 1.4–2.4)
  - HRS (aHR 1.5; 95% CI, 1.0–2.2)
  - GIB (aHR 1.5; 95% CI, 1.1–1.9)
- Any PPI use was associated with a higher risk of the following compared to no PPI use.
  - Recurrent HE (aHR 2.1; 95% CI, 1.6–2.7)
  - GIB (aHR 1.8; 95% CI, 1.2–2.6)
- Any PPI use was not associated with SBP or HRS compared to no PPI use.

LIMITATIONS:

- It is possible that some patients experienced cirrhotic complications before their initial episode of HE, which could affect the ultimate prognosis for the patient.
- Study patients with a history of HE were not excluded and generally had more advanced cirrhosis according to the CTP class. These patients could have impaired PPI metabolism compared to patients with less advanced cirrhosis.
- Study participants were initially hospitalized, so outpatient initiation of PPIs could not be studied.

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Aspiring Aspirin in Metabolic Dysfunction-Associated Steatotic Liver Disease

Aspirin for Metabolic Dysfunction-Associated Steatotic Liver Disease Without Cirrhosis: A Randomized Clinical Trial

Simon TG, Wilechansky RM, Stoyanova S, et al. Aspirin for Metabolic Dysfunction-Associated Steatotic Liver Disease Without Cirrhosis: A Randomized Clinical Trial. *JAMA*. 2024;331(11):920-929. doi:10.1001/jama.2024.1215

KEY TAKEAWAY: Six months of daily aspirin 81 mg significantly reduced the hepatic fat content in patients with metabolic dysfunction-associated steatotic liver disease (MASLD) without cirrhosis.

STUDY DESIGN: Single-site double-blinded randomized clinical trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to disease-oriented results)

BRIEF BACKGROUND INFORMATION: Studies on MASLD demonstrate a high prevalence of disease burden (30% of the United States population). Aspirin is thought to reduce liver fat content after six months, as shown by a preliminary nonrandomized study of 22 adults. However, the study was small and could not distinguish between P2Y12 inhibition and statins, which were initiated in all but four aspirin-treated patients. As a result, this study investigated the therapeutic effects of aspirin for treating MASLD.

PATIENTS: Adults with MASLD

INTERVENTION: Aspirin

CONTROL: Placebo

PRIMARY OUTCOME: Change in hepatic fat fraction
Secondary Outcome: Relative change in hepatic fat fraction, reduction of at least 30% hepatic fat, adverse events

METHODS (BRIEF DESCRIPTION):

- Patients 18–70 years old were recruited from a single Boston hospital who met the criteria for MASLD without cirrhosis.
  - Participants had steatotic liver disease confirmed with liver histology or an appropriate imaging modality (>5% hepatic fat content).
- Patients were excluded if they had significant alcohol use, alternative causes of liver disease such as hepatitis B or C infection, and who used aspirin-containing medications within the prior three months.
  - The mean age was 48 years old and 55% were female with an overall mean body mass index of 34 and mean hepatic fat fraction by magnetic resonance spectroscopy (MRS) of 35% (39% in the aspirin group and 21% in the placebo group).
- For six months, the treatment group received aspirin 81 mg once daily by mouth while the control group received an identical placebo pill by mouth once daily.
- In the baseline visit, patients received a magnetic resonance imaging (MRI) assessment of hepatic fat fraction and markers of intrahepatic inflammation and fibrosis, anthropometrics, laboratory testing, standardized bio-nutrition, physical activity assessments, and liver stiffness measurements of fibrosis by vibration-controlled transient elastography were conducted.
- A repeat hematocrit was collected at three months and six months repeat assessment of testing conducted at the baseline visit was obtained.
- The primary outcome (hepatic fat fraction) was measured via single voxel breath-hold 1H-MRS as the area under the spectroscopic lipid peak divided by the total area under the water and lipid peak, which was measured at baseline and six months.
  - Higher lipid peaks on MRS indicate a greater hepatic fat fraction.
- Secondary outcomes were measured via MRS as well, including a six-month relative change in hepatic fat fraction (range of 0–100%) and attainment of at least a 30 percentage point relative reduction in hepatic fat at six months.

INTERVENTION (# IN THE GROUP): 40

COMPARISON (# IN THE GROUP): 40

FOLLOW-UP PERIOD: Six months

RESULTS:

Primary Outcome –

- Aspirin significantly reduced absolute hepatic fat fraction compared to placebo (mean difference [MD] –10%; 95% CI, –28 to –2.6).

Secondary Outcome –

- Aspirin significantly reduced relative hepatic fat fraction compared to placebo (MD –39%; 95% CI, –67 to –11).
- Aspirin resulted in higher rates of achieving a 30% or greater reduction in hepatic fat compared to placebo (MD 30%; 95% CI, 12–49).
- Patients in both groups had similar rates of anemia, reports of bleeding, and adverse events leading to discontinuation of therapy.

LIMITATIONS:

- This study had a small sample size.
- Follow-up was limited to a six-month duration.
- Important clinical or patient-oriented endpoints including progression to cirrhosis or death were not included or evaluated.

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