GEMs of the Week

Volume 3 - Issue 44

GEMs
GOOD EVIDENCE MATTERS

FPIN
Family Physicians Inquiries Network

What's in this week's issue?

Week of October 30 - November 3, 2023

SPOTLIGHT: Managing Low Back Pain Does Not Have to be a Pain in the Rear

Managing Low Back Pain Does Not Have to be a Pain in the Rear

Effectiveness of Treatments for Acute and Subacute Mechanical Non-Specific Low Back Pain: A Systematic Review with Network Meta-Analysis

Gianola S, Bargeri S, Del Castillo G, et al. Effectiveness of treatments for acute and subacute mechanical non-specific low back pain: a systematic review with network meta-analysis. *Br J Sports Med*. 2022;56(1):41-50. doi:10.1136/bjsports-2020-103596

KEY TAKEAWAY: Out of all the various nonpharmacologic and pharmacologic interventions for low back pain, exercise and manual therapy significantly improve both pain and disability with no added risk of adverse events.

STUDY DESIGN: Meta-analysis including 46 randomized control trials (N=8,765)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Low back pain is a common chief complaint in primary care. It can lead to significant disability and cause people to leave their jobs. Multiple estimates on the financial cost of low back pain comprising care, days of work missed, and hours of work lost amount to tens of billions of dollars in America. Current treatment options include nonpharmacologic interventions with exercises, heat wrap, acupuncture, manual therapy, and/or pharmacologic interventions. Most providers have varying approaches to treating back pain with no definitive superiority between treatment methods.

PATIENTS: Patients with mechanical nonspecific low back pain

INTERVENTION: Nonpharmacologic and pharmacologic treatments

CONTROL: Placebo or no treatment (inert treatment)

PRIMARY OUTCOME: Pain intensity and disability

Secondary Outcome: Adverse effects

METHODS (BRIEF DESCRIPTION):

- A systematic review protocol based on PRISMA-P was utilized to review studies on PubMed, CENTRAL, and Embase published between February 2019–October 2020.
- Patients included males and females with up to 12 weeks of acute or subacute nonspecific low back pain.
- The intervention was based on nonpharmacologic or pharmacologic treatments. This included exercise, heat wrap, acupuncture, manual therapy, NSAIDs, muscle relaxants, steroids, or opioids.
- The primary outcomes were pain and disability. They were assessed via various numerical scales.
- The secondary outcomes were adverse events identified as mild-moderate events including headache, diarrhea, or dyspepsia. However, these were not statistically analyzed due to heterogeneous reporting between studies.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: One week to 12 months

RESULTS:

Primary Outcome –

- Patients who received either nonpharmacologic or pharmacologic therapy had a statistically significant reduction in pain intensity and had an improvement in disability at one week compared to inert treatment.
  - Pain intensity:
    - Exercise (SMD –1.4; 95% CI, –2.4 to –0.40)
    - Heat wrap (SMD –1.4; 95% CI, –2.6 to –0.17)
    - Manual therapy (SMD –0.72; 95% CI, –1.6 to –0.10)
    - NSAIDs (SMD –0.53; 95% CI, –0.97 to –0.09)
    - Opioids (SMD –0.86; 95% CI, –1.4 to –0.04)
  - Interventions with significant improvement in disability at one week compared to inert treatment with:
    - Exercise (SMD –0.71; 95% CI, –1.2 to –0.26)
    - Heat wrap (SMD –0.59; 95% CI, –0.82 to –0.36)
    - Manual therapy (SMD –0.52; 95% CI, –0.89 to –0.16)
    - Education (SMD –0.28; 95% CI, –0.53 to –0.03)
    - NSAIDs (SMD –0.33; 95% CI, –0.55 to –0.11)
    - Muscle relaxants (SMD –0.24, 95% CI, –0.43 to –0.04)

Secondary Outcome –

- Adverse events were not statistically analyzed due to heterogeneous reporting between studies.

- Adverse events were observed with heat wrap, muscle relaxants, NSAIDs, opioids, paracetamol, steroids, and inert treatment.
- Exercise, manual therapy, education, and acupuncture did not have any adverse events.

LIMITATIONS:

- Variable length in follow-ups.
- No standardized intensity, dosage, or technique for pharmacologic or nonpharmacologic interventions.

Daniel Idelkope, MD
Tripler Army Medical Center FMR
Honolulu, HI

The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Army Medical Department, the Army at large, or the Department of Defense.

A Landmark Study: Carvedilol Prevents Decompensation and Death in Cirrhosis

Carvedilol Reduces the Risk of Decompensation and Mortality in Patients with Compensated Cirrhosis in a Competing Risk Meta-Analysis

Villanueva C, Torres F, Sarin SK, et al. Carvedilol reduces the risk of decompensation and mortality in patients with compensated cirrhosis in a competing-risk meta-analysis. *J Hepatol*. 2022;77(4):1014-1025. doi:10.1016/j.jhep.2022.05.021

KEY TAKEAWAY: In patients with compensated cirrhosis, carvedilol significantly decreases the risk of decompensation of cirrhosis, mainly by reducing the risk of developing ascites. Carvedilol also significantly improves survival in this population.

STUDY DESIGN: Meta-analysis and systemic review of randomized controlled trials (N=352)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: The transition from compensated to decompensated cirrhosis is associated with markedly reduced life expectancy. Previous literature has been conflicting about the benefit of carvedilol in patients with compensated cirrhosis. This meta-analysis using individual participant data can be helpful to definitively answer this clinical question.

PATIENTS: Adults with compensated cirrhosis and portal hypertension

INTERVENTION: Carvedilol

CONTROL: Varied by individual RCT including placebo, no specific therapy, or monotherapy with endoscopic variceal ligation (EVL)

PRIMARY OUTCOME: Development of decompensated cirrhosis and death from any cause

Secondary Outcome: Development of ascites, gastrointestinal bleeding related to portal hypertension, encephalopathy, adverse events, and liver-related death (including death related to compensation but also hemoperitoneum and cholangiocarcinoma).

METHODS (BRIEF DESCRIPTION):

- Demographics of participants across the RCTs:
  - The median age was 53 years old in the carvedilol therapy group and 51 years old in the control group.
  - Both groups included a population of which consisted of 77% male and 23% female.
  - Causes of cirrhosis are categorized into: Alcohol, HCV, HBV, and others. The most common cause of cirrhosis was HCV (36% in the carvedilol group and 44% in the control group).
- Inclusion criteria: Adults with compensated cirrhosis without any previous decompensating event.
- Exclusion criteria: Previous variceal bleeding, prior episodes of decompensated cirrhosis, non-cirrhotic portal hypertension, hepatocellular carcinoma, end-stage liver disease, history of trans-jugular intrahepatic portosystemic shunt or sclerotherapy.
- Outcomes: Risk of decompensation (defined as the development of ascites, gastrointestinal bleeding related to portal hypertension, or encephalopathy) and death from any cause were evaluated.
- The development of minor and severe adverse events was evaluated as a secondary outcome. These were defined as side effects of treatment.
- Adverse events were considered severe if the health or safety of the patient was endangered.
  - Severe events included syncope, bradyarrhythmia, and hypotension.
  - Minor events included weakness, headache, and bradycardia.
- In the intervention group, some studies involved fixed dosing of carvedilol (12.5mg/day to 25mg/day) while others involved up-titration from a starting dose of 6.125mg/day. The median dose across studies was 12.5mg/day.
- Categorical variables were compared using the chi-square test and continuous variables using ANOVA.

INTERVENTION (# IN THE GROUP): 181

COMPARISON (# IN THE GROUP): Placebo: 92; EVL: 79

FOLLOW-UP PERIOD: Mean follow-up in each RCT varied between 13–36 months (no overall mean provided).

RESULTS:

Primary Outcome –

- The risk of decompensation was significantly lower in the carvedilol group than in controls (HR 0.51; 95% CI, 0.29–0.89).
- The risk of death from any cause was significantly lower in the carvedilol group than in controls (HR 0.42; 95% CI, 0.19–0.90).

- This survival benefit was consistent across subgroups reflecting liver function, etiology of cirrhosis, presence of varices, and age.

Secondary Outcome –

- The risk of developing ascites was significantly lower in the carvedilol group than in controls (HR 0.49; 95% CI, 0.25–0.97).
- No significant difference in the risk of gastrointestinal bleeding or encephalopathy.
- The risk of liver-related death was significantly lower in the carvedilol group than in controls (HR 0.32; 95% CI, 0.13–0.76).
- Adverse events were more common in the carvedilol group than in controls (HR 3.08; 95% CI, 1.53–6.21) however, the risk of developing severe adverse events was similar in both groups (HR 1.96; 95% CI, 0.78–4.91).

LIMITATIONS:

- These results cannot be applied to patients with a history of decompensated cirrhosis. That is, no conclusions can be drawn for patients with currently compensated cirrhosis but with a history of ascites, gastrointestinal bleeding related to portal hypertension, or encephalopathy.
- Not all RCTs included were double-blinded.

Arta Gharib Parsa, MD
Kaiser Permanente Washington FMR
Seattle, WA

Lithium Does Not Reduce Repeat Suicide Events

Lithium Treatment in the Prevention of Repeat Suicide-Related Outcomes in Veterans with Major Depressive or Bipolar Disorder: A Randomized Clinical Trial

Katz IR, Rogers MP, Lew R, et al. Lithium Treatment in the Prevention of Repeat Suicide-Related Outcomes in Veterans With Major Depression or Bipolar Disorder: A Randomized Clinical Trial. *JAMA Psychiatry*. 2022;79(1):24-32. doi:10.1001/jamapsychiatry.2021.3170

KEY TAKEAWAY: Adding lithium to the treatment standard of care did not reduce the incidence of a suicide-related event in individuals with major depression or bipolar disorder, who experienced a preceding suicide event.

STUDY DESIGN: Multi-site, double-blind placebo control randomized clinical trial

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Suicide is a public health problem with devastating consequences. Mental illness plays a part in up to 90% of these events. Prior to the Veterans Affairs (VA) study, observational studies suggested that lithium may prevent suicide-related events in individuals with depression or bipolar disorder, however, randomized control trials were underpowered. Meta-analyses of this topic are conflicting. Despite this mixed data, the VA suggests the use of lithium alone or in combination with other psychotropic agents aims to decrease suicide-related events. Questions regarding lithium and the prevention of such events remain. This trial aims to determine if lithium affects suicide-related events.

PATIENTS: Veterans with depression or bipolar disorder with an episode of suicidal behavior

INTERVENTION: VA mental health care with lithium

CONTROL: VA mental health care with placebo

PRIMARY OUTCOME: Time to first reported suicide-related event

METHODS (BRIEF DESCRIPTION):

- Veterans from 29 VA medical centers who had a suicide-related event from 2015–2019 were screened.
- 519 veterans were enrolled with written consent and approval by their medical providers.
    - Eligibility criteria: Diagnosis of bipolar I or II disorder or major depression, consenting to provide an emergency contact, and deemed to have medical capacity.
    - Exclusion criteria: Schizophrenia; greater than six previous suicide attempts; use of lithium in the last six months; unstable substance use; pregnancy, lactation or not using birth control; and current use of clozapine, haloperidol, or diuretics.
- Participants were randomized to receive lithium or a placebo (cellulose).
- Study medications were added to usual VA mental health care including medications, psychosocial treatment, rehabilitation, and recovery services.
    - Lithium was started at 600 mg/day and titrated up until a steady state determined by blood draw (0.6–0.8 mEq/L).
    - Once a steady state was reached, lithium blood levels were measured monthly for six months, then quarterly.
    - Medications were provided in 1–2 week increments via blister packaging.
- Participant self-reports provided race, ethnicity, sex, and psychiatric and medical comorbidities.
- Mental health symptoms were measured by standardized instruments including the Columbia-Suicide Severity Rating Scale, the Patient Health Questionnaire 9, the Internal State Scale, the Barratt Impulsiveness Scale, and the Buss-Perry Aggression Questionnaire.

INTERVENTION (# IN THE GROUP): 255

COMPARISON (# IN THE GROUP): 264

FOLLOW-UP PERIOD: 52 weeks

RESULTS:

Primary Outcome –

- The trial was stopped for futility.
- No overall difference in repeated suicide-related events between treatments was found (HR 1.10; 95% CI, 0.77–1.55).
- No unanticipated safety concerns were appreciated.

LIMITATIONS:

- High rates of attrition.

- Low rates of adherence to study medications (48.1% of patients had therapeutic lithium levels).
- The VA findings are not generalizable to other healthcare settings or to other patient populations.
- The study was stopped for futility (unlikely to achieve statistical significance).
- The study did not reach its original recruitment goal.

Athena Konicki, MD
PeaceHealth Southwest FMR
Vancouver, WA

Accuracy of Point-of-Care Ultrasound in Patients with Acute Dyspnea

POCUS in Dyspnea, Nontraumatic Hypotension, and Shock; A Systematic Review of Existing Evidence

Kok B, Wolthuis D, Bosch F, van der Hoeven H, Blans M. POCUS in dyspnea, nontraumatic hypotension, and shock; a systematic review of existing evidence. *Eur J Intern Med*. 2022;106:9-38. doi:10.1016/j.ejim.2022.07.017

KEY TAKEAWAY: Implementing point-of-care ultrasound (POCUS) as a diagnostic tool for patients presenting with acute undifferentiated dyspnea significantly improves diagnostic accuracy, which results in faster diagnoses.

STUDY DESIGN: Systematic review of 89 cohort and observational studies

LEVEL OF EVIDENCE: STEP 2 (downgraded due to lack of meta-analysis inclusion)

BRIEF BACKGROUND INFORMATION: Primary care providers commonly encounter patients with acute undifferentiated dyspnea, which can be challenging to diagnose and manage. Prompt evaluation and appropriate treatments are crucial to ensure the best possible outcomes for patients. This systematic review analyzes current literature on the use of POCUS in patients experiencing respiratory or circulatory decline in different hospital settings.

PATIENTS: Adults with dyspnea

INTERVENTION: POCUS as the initial workup tool

CONTROL: No POCUS

PRIMARY OUTCOME: Diagnostic accuracy

Secondary Outcome: Time to diagnosis, narrowing the differential diagnosis

METHODS (BRIEF DESCRIPTION):

- PubMed and Embase databases were searched for the original studies published between March 2002–March 2022 on adult patients with dyspnea, nontraumatic hypotension, and shock, who were assessed using POCUS.
- Only English language prospective and retrospective clinical trials as well as observational studies were included.
- 22 studies investigated POCUS use in undifferentiated dyspnea in the emergency department, with diagnostic accuracy being the primary outcome in 18 studies.
- Nine studies used a multiorgan POCUS protocol, 12 used only lung ultrasound, and one used cardiac ultrasound.
- The reference standard was the final diagnosis based on medical record review by physicians blinded to the POCUS results.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Not available

RESULTS:

Primary Outcome –

- 21 studies showed increased diagnostic accuracy in patients with undifferentiated dyspnea when using POCUS compared to not using POCUS in the initial workup.
- Three studies found that POCUS narrows the differential diagnoses and decreases the time to diagnosis.
  - One study showed that chest X-ray reads, on average, took up to 95 minutes compared to immediately available POCUS results.
  - In a single study of patients with symptoms of pneumonia for less than 24 hours, POCUS was a more sensitive tool than chest X-ray (N=144, sensitivity using CT as reference standard 95% vs 60%, respectively; P<.01).
  - Three studies (N=102), showed LUS was concordant for the diagnosis of pneumonia, with a sensitivity ranging from 96.1% to 100% as compared to the reference standard of CT.

LIMITATIONS:

- Most studies did not blind the physician performing the POCUS study to clinical findings or involvement in patient care, potentially introducing bias.
- Accuracy levels may vary depending on the operator's level of experience and most included studies were performed by POCUS experts.
- A reduction in length of stay and duration of treatment remains uncertain as this was examined only in one study.

Daniela Lobo, MD
Indiana University School of Medicine
Indianapolis, IN

Mind the Exercise: Does Exercise Really Help the Brain?

Effects of Mindfulness Training and Exercise on Cognitive Function in Older Adults: A Randomized Clinical Trial

Lenze EJ, Voegtle M, Miller JP, et al. Effects of Mindfulness Training and Exercise on Cognitive Function in Older Adults: A Randomized Clinical Trial. *JAMA*. 2022;328(22):2218-2229. doi:10.1001/jama.2022.21680

KEY TAKEAWAY: Mindfulness training, exercise, and health education increase cognitive performance over time but do not significantly improve episodic memory, executive function, or structural brain changes.

STUDY DESIGN: Randomized, 2x2 factorial, and controlled clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Mindfulness improves working memory and reduces stress resulting in lower cortisol levels and improving sleep which are important changes in the older population. Previous studies have suggested that aerobic and strength training exercises change insulin sensitivity and body fat, improving patients' overall physical activity. Mindfulness meditation training in addition to exercise are promising interventions that can improve cognitive decline in older adults.

PATIENTS: Adults 65–84 years old

INTERVENTION: Mindfulness alone, exercise alone, or in combination

CONTROL: Education via book

PRIMARY OUTCOME: Episodic memory, executive function

Secondary Outcome: Structural MRI changes, functional cognitive capacity, cognitive concerns

METHODS (BRIEF DESCRIPTION):

- 585 older adults (65–84 years old) were included with a mean age of 71.5 years old and a mean education level of 16.2 years.
- 424 (72.5%) of those were women, two (0.3%) were American Indian, 27 (4.6%) were Asian, 69 (11.8%) were Black, 477 (81.5%) were White (the remaining individuals were unknown or >1 race), 39 (6.7%) were Hispanic/Latino.
- Intervention patients were placed into either:
  - Mindfulness-based stress reduction alone:
    - Acute phase: A brief introduction meeting, weekly 2.5-hour classes plus a half-day retreat.
    - The content included mindfulness meditation practices and exercises with a goal of 60 minutes daily for meditation.
  - Exercise alone:
    - Acute phase: The instructor supervised 1.5-hour aerobic, resistance training, or functional exercises twice a week; a total of 300 minutes per week of combined class and home exercises.
    - Maintenance phase: once per week facility exercise with the same goal of 300 minutes of combined exercise per week.
  - Combined MBSR and exercise intervention underwent both interventions listed above:
    - Health education was the control group.
    - It matched the MBSR intervention for a group setting, class time, frequency of sessions, attention with assignments weekly but no goals related to time spent.
    - Living a Healthy Life with Chronic Conditions book was used, avoiding mindfulness and exercise information.
- Episodic memory and executive function composite scores were calculated from a neuropsychological test battery conducted at zero, three, six, and 18 months.
- Memory tests were immediate and delayed recall using a 16-item word list and two paragraphs.
- The executive function tests included the Dimensional Change Card Sort test, Flanker Inhibitory Control and Attention Test, and List Sorting Working Memory Test from NIH Toolbox such as the Consonant-Vowel Odd-Even Switching Test, Sustained Attention to Response Test, and Stroop Test.
- Composite scores, using Z scores were compared to individual scores for reliability and to detect subtle changes in the scores.
- Secondary endpoint listed at 18 months:

- High-resolution T1 weighted MRI was used for cortical thickness, left and right hippocampal volume, and DLPFC surface area.
- Cognitive function measured with Revised Observed Tasks of Daily Living score and the Quality of Life in Neurological Disorders Cognitive Function.

INTERVENTION (# IN THE GROUP):

- MBSR: 150
- Exercise: 138
- MBSR+Exercise: 144

COMPARISON (# IN THE GROUP): 153

FOLLOW-UP PERIOD: 18 months

RESULTS:

Primary Outcome –

- At six months, there were no significant differences in memory and executive function between the MBSR, exercise, combined, or control group. (*P*=.12–.50).

Secondary Outcome –

- There were no significant differences at 18 months in memory or executive function in all four randomized groups.
- There were no major differences in hippocampal volume, DLPFC, or cortical thickness in all groups.
- Hippocampal volume showed a significantly greater reduction over 18 months with MBSR group compared to no MBSR group (mean difference –20 mm; 95% CI, –34 to –6.4).
- There was a significant decrease in hippocampal volume (*P*<.001) and DLPFC cortical thickness (*P*<.001) in all groups over the 18-month period.

LIMITATIONS:

- Generalizability was reduced due to most of the population in the study being college-educated Whites, therefore limiting diversity.
- Brain health measurement was limited to only the hippocampus and DLPFC.
- The length of the study was only 18 months, possibly a longer period may show to be more beneficial.
- The study consisted of only healthy, older, cognitively intact adults.
- Subjective cognitive concerns can be vague and include those individuals with early dementia or individuals that may be under the influence of medications, or medical conditions.

Maria Munoz-Bramhall, MD
Northeast Georgia Medical Center Family Medicine
Gainesville, GA

Take Control of Your Anxiety with Yoga and CBT

Efficacy of Yoga vs Cognitive Behavioral Therapy vs Stress Education for the Treatment of Generalized Anxiety Disorders

Simon NM, Hofmann SG, Rosenfield D, et al. Efficacy of Yoga vs Cognitive Behavioral Therapy vs Stress Education for the Treatment of Generalized Anxiety Disorder: A Randomized Clinical Trial. *JAMA Psychiatry*. 2021;78(1):13-20. doi:10.1001/jamapsychiatry.2020.2496

KEY TAKEAWAY: Kundalini Yoga (KY) or cognitive behavioral therapy (CBT) is more effective than stress education (SE) in the treatment of generalized anxiety disorder (GAD). Kundalini Yoga was inferior and not as effective as CBT.

STUDY DESIGN: Three-arm, randomized control trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: GAD is prevalent and is often undertreated. Many patients with GAD pursue and are interested in complementary and alternative interventions, including yoga; however, data on its treatment efficacy is lacking.

PATIENTS: Adults with GAD

INTERVENTION: Yoga and CBT

CONTROL: Stress education

PRIMARY OUTCOME: Change in anxiety severity at 12 weeks

Secondary Outcome: Change in anxiety severity at six months

METHODS (BRIEF DESCRIPTION):

- Patients were adults with a diagnosis of GAD per structured clinical interviews using DSM-5 guidelines.
  - Mean age 33.4 years
  - 69.9% female
  - Exclusion criteria: PTSD, substance use disorder, eating disorder, significant suicidal ideation, mental disorder due to medical or neurocognitive condition, lifetime psychosis, bipolar disorder, developmental disorder, having completed more than five yoga or CBT sessions in the past five years
- Participants were placed into three groups: KY, CBT, or SE for twelve 120 minutes sessions which were followed with daily homework for 20 minutes.
- Outcomes were measured by treatment response via the Clinical Global Impression-Improvement (CGI-I) Scale.
  - CGI-I is a rating scale by an observer to track changes in participant symptoms.
  - This scale rates symptoms on a scale of 1 (improved) to 2 (very much improved).
  - This evaluation was conducted biweekly at 0 to 12 weeks and at the six-month follow-up.

INTERVENTION (# IN THE GROUP):

- KY: 93
- CBT: 90

COMPARISON (# IN THE GROUP): 43

FOLLOW-UP PERIOD: 12 weeks for primary outcome; six months for secondary outcome

RESULTS:

Primary Outcome –

- The KY group experienced greater symptom improvement after 12 weeks compared to the SE group (54% vs 33%, respectively; OR 2.5; 95% CI, 1.1–5.4).
- The CBT group experienced greater symptom improvement after 12 weeks compared to the SE group (71% vs 33%, respectively; OR 5.0; 95% CI, 2.1-12).

Secondary Outcome –

- The CBT group experienced greater symptom improvement after six months compared to the SE group (77% vs 48%, respectively; OR 3.6; 95% CI, 1.1–12).
- The KY group did not experience symptom improvement after six months compared to the SE group (63% vs 48%, respectively; OR 1.9; 95% CI, 0.52–6.7).
- Non-inferiority testing demonstrated that CBT is superior to KY during the post-treatment assessments.

LIMITATIONS:

- May not be generalizable as the way yoga and CBT vary in how they are delivered in the community.

- KY findings may not fully generalize to all types of yoga.

Amy Olivares, DO
Inspira Health-Mullica Hill Family Medicine
Mullica Hill, NJ

Is Early Postpartum Placement of Intrauterine Devices Comparable to Interval Placement?

Early vs Interval Postpartum Intrauterine Device Placement: A Randomized Clinical Trial

Averbach S, Kully G, Hinz E, et al. Early vs Interval Postpartum Intrauterine Device Placement: A Randomized Clinical Trial. *JAMA*. 2023;329(11):910-917. doi:10.1001/jama.2023.1936

KEY TAKEAWAY: Intrauterine device (IUD) placement at 2–4 weeks postpartum is non-inferior when compared to placement at 6–8 weeks for rates of complete expulsion but may have higher rates of partial expulsion.

STUDY DESIGN: Randomized, non-inferiority, unblinded controlled trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to being an unblinded study)

BRIEF BACKGROUND INFORMATION: IUDs are an effective method of contraception and have been recommended for placement in the immediate postpartum period, or at 6–8 weeks postpartum. Immediate postpartum placement of IUDs has an increased risk of expulsion compared to placement at 6–8 weeks; however, placement at 2–4 weeks, when postpartum follow-ups are increasingly scheduled, has been studied less. IUD placement at 2–4 weeks may be beneficial for protection against unintended pregnancy and prevention of patients lost to follow-up.

PATIENTS: Postpartum adults

INTERVENTION: IUD placement at 14–28 days postpartum

CONTROL: Placement at 43–56 days postpartum

PRIMARY OUTCOME: IUD expulsion

Secondary Outcome: Partial IUD expulsion, removal of IUD, malposition, pelvic infections, uterine perforation, and patient satisfaction

METHODS (BRIEF DESCRIPTION):

- Participants included adults within 10 days postpartum who spoke English or Spanish and desired IUD placement.
- Exclusion criteria included the presence of leiomyomata, intrauterine infection treated with antibiotics, fourth-degree perineal laceration, or medical contraindication to IUD per the CDC medical eligibility criteria.
- Both groups were similar with 56% identifying as White, 10–13% Black, 20–24% Multiracial, and 40–46% Hispanic/Latino, and most had vaginal deliveries (75%).
- Patients were randomly assigned to one of the following groups:
  - IUD placement at 14–28 days postpartum
  - IUD placement at 42–56 days postpartum
- Treatments were administered by the patients' postpartum provider.
- Complete IUD expulsion, partial IUD expulsion, uterine perforation, and IUD malpositioning were determined by a combination of a pelvic examination, transvaginal ultrasound, and radiography as needed at six months postpartum.
- Rates of expulsion and malposition were compared between the two groups using a multivariate logistical regression and controlled for cofounders, a cutoff of 6% was utilized to determine non-inferiority.
- Patient satisfaction was measured via a 5-point Likert scale.

INTERVENTION (# IN THE GROUP): 203

COMPARISON (# IN THE GROUP): 201

FOLLOW-UP PERIOD: Six months

RESULTS:

Primary Outcome –

- Early IUD placement was non-inferior to interval IUD placement when comparing rates of complete expulsion (Between-group difference 2.0%; 95% CI, –0.5% to 5.7%).

Secondary Outcome –

- Early IUD placement was inferior to interval IUD placement with regards to partial expulsion (Between-group difference 1.8%; 95% CI, –4.8% to 8.6%).
- Rates of IUD malposition in the early IUD placement group were inferior to the interval IUD placement group (Between-group difference 5.4%; 95% CI, 2.1%–10%).
- Rates of IUD removal, uterine perforation, and infection following IUD placement were not significantly different between the two groups.

- Satisfaction after IUD placement was not significantly different between the two groups.

LIMITATIONS:

- The patient population was recruited from an academic medical center and may not be representative of a community setting.
- More patients than originally intended did not have an IUD placed; this may have underpowered the study.
- The COVID-19 pandemic may have contributed to nonadherence to IUD placement timing.
- Ultrasound was more commonly utilized for early placement (19%) vs interval placement (2%), which may have impacted outcomes.

Lexi Kremer-Callahan, MD
St. Louis University FMRP
St. Louis, MO