GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of December 2 - 6, 2024

SPOTLIGHT:

Beyond Morphine: Keterolac and Acetaminophen's Efficacy in Renal Colic Relief

- Colorectal Cancer Detection: An Appraisal of Multitarget Stool DNA Testing
- Stones Unturned: Lower Risk of Nephrolithiasis with SGLT2i Compared to GLP1 and DPP4i
- Non-Invasive Testing De-Livers in Identifying NASH and Advanced Fibrosis in Type 2 Diabetes
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Beyond Morphine: Keterolac and Acetaminophen's Efficacy in Renal Colic Relief

Comparison of Acetaminophen, Ketamine, or Ketorolac vs Morphine in the Treatment of Acute Renal Colic: A Network Meta-Analysis

Alghamdi YA, Morya RE, Bahathiq DM, et al. Comparison of acetaminophen, ketamine, or ketorolac versus morphine in the treatment of acute renal colic: A network meta-analysis. *Am J Emerg Med*. 2023;73:187-196. doi:10.1016/j.ajem.2023.08.029

KEY TAKEAWAY: Ketorolac alone and acetaminophen alone improve renal colic pain at 30 minutes compared to morphine.

STUDY DESIGN: Network meta-analysis of 12 randomized controlled trials (RCTs) (N=2,845)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Renal colic, characterized by intense pain, is typically managed with opioids. However, recent studies suggest the potential efficacy of alternative analgesics. This review aimed to compare the safety and efficacy of these alternatives for managing renal colic.

PATIENTS: Adults with a confirmed diagnosis of renal colic

INTERVENTION: Intravenous (IV) acetaminophen, IV ketorolac, and IV ketamine either alone or in combination with morphine

CONTROL: IV morphine alone

PRIMARY OUTCOME: Pain at 30 minutes

Secondary Outcome: Pain at 15 minutes, pain at 60 minutes, adverse events, utilization of rescue therapy

METHODS (BRIEF DESCRIPTION):

- PRISMA guidelines were employed to identify RCTs comparing various analgesic agents, either alone or in combination.
- Most studies used 0.1 mg/kg of parenteral morphine either as a bolus or infusion given over two-30-minute sessions.
- Some studies combined morphine with acetaminophen (1 g IV), ketorolac (15–30 mg) or another NSAID parenterally.
- The study focused on adults diagnosed with renal colic, with an initial pain intensity ≥6 out of 10 on the visual analog scale (VAS), an 11-point (0–10) numerical scale where a higher score represents increasing levels of pain.
- The assessment included evaluating pain scores on the VAS at 15, 30, and 60-minute intervals, along with monitoring adverse events and rescue therapy utilization.

INTERVENTION (# IN THE GROUP):

- IV acetaminophen: 901
- IV ketorolac: 208
- IV ketorolac and IV morphine: 144
- IV ketamine: 68
- IV ketamine and IV morphine: 153

COMPARISON (# IN THE GROUP): 1,371

FOLLOW-UP PERIOD: Up to 60 minutes

RESULTS:

Primary Outcome –

- Ketorolac improved pain at 30 minutes compared to morphine alone (8 trials; mean difference [MD] –1.6; 95% CI, –2.8 to –0.38).
- Acetaminophen improved pain at 30 minutes compared to morphine alone (8 trials; MD –1.0; 95% CI, –1.8 to –0.29).
- Ketamine + morphine did not improve pain at 30 minutes compared to morphine alone (8 trials; MD –1.1; 95% CI, –2.5 to 0.23).
- Ketamine did not improve pain at 30 minutes compared to morphine alone (8 trials; MD –0.40; 95% CI, –1.6 to 0.78).

Secondary Outcome –

- Neither acetaminophen nor ketorolac improved pain at 15 minutes compared to morphine.
- Ketorolac improved the pain at 60 minutes compared to morphine (6 trials; MD –2.9; 95% CI, –4.1 to –1.7).
- Ketamine with morphine, acetaminophen alone, and ketamine alone did not improve pain at 60 minutes compared to morphine.
- Ketorolac with morphine increased the risk of adverse events compared to morphine (10 trials; relative risk [RR] 4.0; 95% CI, 1.8–8.8).
- Ketorolac alone increased the need for rescue therapy compared to morphine (8 trials; RR 1.9; 95% CI, 1.2–3.1).

- Ketorolac with morphine increased the need for rescue therapy compared to morphine alone (8 trials; RR 2.5; 95% CI, 1.5–4.2).
- Acetaminophen alone increased the need for rescue therapy compared to morphine alone (8 trials; RR 2.7; 95% CI, 1.8–3.9).
- Ketamine with morphine did not decrease the need for rescue therapy compared to morphine.

LIMITATIONS:

- The majority of the patient population was men, which is not representative of the prevalence of renal colic.
- There were notable design inconsistencies observed across individual RCTs.
- Alternative analgesics, dosing regimens, and routes of administration were not considered.

Tarun Kakumanu, DO
Ocean University Medical Center
Brick, NJ

Colorectal Cancer Detection: An Appraisal of Multitarget Stool DNA Testing

Next-Generation Multitarget Stool DNA Test for Colorectal Cancer Screening

Imperiale TF, Porter K, Zella J, et al. Next-Generation Multitarget Stool DNA Test for Colorectal Cancer Screening. *N Engl J Med*. 2024;390(11):984-993. doi:10.1056/NEJMoa2310336

KEY TAKEAWAY: The next-generation multitarget stool DNA tests may be more sensitive but not more specific in detecting colorectal cancer (CRC) than fecal immunochemical test (FIT) when compared to colonoscopy.

STUDY DESIGN: Prospective, cross-sectional, multicenter study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: The current multitarget stool DNA test had a higher sensitivity for CRC and advanced precancerous lesions than FIT, but the specificity was lower. The study aimed to use a new generation of multitarget stool DNA tests that would improve specificity and sensitivity for detecting CRC and advanced precancerous lesions.

PATIENTS: Patients ≥40 years old

INTERVENTION: Next-generation multitarget stool DNA test and FIT test

CONTROL: Colonoscopy

PRIMARY OUTCOME: Sensitivity and specificity

METHODS (BRIEF DESCRIPTION):

- Symptomatic patients scheduled for screening colonoscopy in the US ≥40 years old were included in the study.
  - The racial and ethnic population resembled the US Census population.
- Exclusion criteria included incomplete screening, non-usable stool samples, and not receiving stool samples.
- Patients underwent next-generation multitarget stool DNA tests with stool specimens collected before colonoscopy preparation.
  - The new-generation test uses a novel molecular panel and algorithm.
- All patients enrolled received the next-generation multitarget stool DNA test and commercial FIT (OC-AUTO ®FIT, by Polymedco), followed by a colonoscopy to check for the effectiveness of the results.
- A colonoscopy is the gold standard for detecting CRC and was measured as the control.
- The primary outcome measured:
  - Sensitivity of CRC, advanced precancerous lesions, and high-grade dysplasia for the next generation multitarget stool DNA test and FIT.
  - Specificity of advanced neoplasia and non-neoplastic findings or negative colonoscopy for the next generation multitarget stool DNA test and FIT.
- The sensitivity comparisons for CRC and advanced precancerous lesions were done via exact McNemar tests.

INTERVENTION (# IN THE GROUP): 20,176

COMPARISON (# IN THE GROUP): The same 20,176 patients

FOLLOW-UP PERIOD: Not available

RESULTS:

Primary Outcome –

- Next-generation multitarget stool DNA test compared to colonoscopy:
  - Sensitivity for any CRC (94%; 95% CI, 87–98)
  - Sensitivity for advanced precancerous lesions (43%; 95% CI, 41–46)
  - Sensitivity for high-grade dysplasia (75%; 95% CI, 66–82)
  - Specificity for advanced neoplasia (91%; 95% CI, 90–91)
  - Specificity for non-neoplastic findings or negative colonoscopy (93%; 95% CI, 92–93)
- FIT compared to colonoscopy:
  - Sensitivity for CRC (67%; 95% CI, 57–77)
  - Sensitivity for advanced precancerous lesions (23%; 95% CI, 22–25)
  - Sensitivity for high-grade dysplasia (47%; 95% CI, 38–57)
  - Specificity for advanced neoplasia (95%; 95% CI, 94–95)
  - Specificity for non-neoplastic findings or negative colonoscopy (96%; 95% CI, 95–96)

LIMITATIONS:

- A high proportion of people who were enrolled had samples that could not be evaluated according to the protocol.
- No data compared the first-generation multitarget stool DNA test with the current next-generation version of the multitarget stool DNA test.

Erick Aparicio, DO
Indiana University FMRP
Indianaopolis, IN

Stones Unturned: Lower Risk of Nephrolithiasis with SGLT2i Compared to GLP1 and DPP4i

Sodium-Glucose Cotransporter 2 Inhibitors and Nephrolithiasis Risk in Patients with Type 2 Diabetes

Paik JM, Tesfaye H, Curhan GC, Zakoul H, Wexler DJ, Patorno E. Sodium-Glucose Cotransporter 2 Inhibitors and Nephrolithiasis Risk in Patients With Type 2 Diabetes. *JAMA Intern Med*. 2024;184(3):265-274. doi:10.1001/jamainternmed.2023.7660

KEY TAKEAWAY: Sodium-glucose linked transporter 2 inhibitors (SGLT2i) reduce the risk of developing nephrolithiasis in patients with type 2 diabetes (T2DM) compared to those using dipeptidyl peptidase 4 inhibitors (DPP4i) and glucagon-like peptide 1 receptor agonists (GLP-1RA).

STUDY DESIGN: Population-based, active comparator, new-user retrospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Patients with T2DM have an increased risk of kidney stones. SGLT2is may have a lower risk of kidney stones based on their mechanism of action. Thus far, the association between SGLT2i use and nephrolithiasis risk has not been studied in a large US population. This study aimed to investigate the association between SGLT2i and the risk of nephrolithiasis in patients with T2DM.

PATIENTS: Adults with T2DM

INTERVENTION: SGLT2i

CONTROL: DPP4i or GLP-1RA

PRIMARY OUTCOME: Risk of nephrolithiasis

METHODS (BRIEF DESCRIPTION):

- Using three US data sources (Optum's deidentified Clinformatics Data Mart Database 2013–2020, IBM MarketScan 2013–2019, and Medicare Fee-for-Service Parts A, B, and D 2013–2018), patients were identified who were ≥18 years old and who initiated an SGLT2i or a comparator (GLP-1RA or DPP4i) between April 2013 and December 2020 using ICD-9/10 codes.
- Patients were excluded that had a prior history of kidney stones or urinary tract stones.
- New initiation was determined by a filled prescription for an SGLT2i or the specific comparator (DPP4I or GLP-1RA) without receiving a comparator drug within the past 365 days.
- The cohort entry date was defined as the date of the first prescription.
- Follow-up started the day after the cohort entry date and continued until the occurrence of the outcome event, discontinuation of treatment, switching to a comparator drug class, death, end of health plan enrollment, or end of the study period.
- A patient was considered at risk for an outcome event for up to 60 days after the expected completion of their last prescription.
- The primary outcome was nephrolithiasis diagnosed by ICD codes.
- Covariates included sex, race, ethnicity, combined comorbidity score, comorbid conditions such as chronic kidney disease (CKD), obesity, history of urinary tract infections (UTIs), and gout, history of diabetic complications, use of diabetic medications, use of other medication classes, and measures of health utilization were identified and controlled for in the results.

INTERVENTION (# IN THE GROUP):

- SGLT2i in the GLP-1RA cohort: 358,203
- SGLT2i in the DPP4i cohort: 331,028

COMPARISON (# IN THE GROUP):

- GLP-1RA: 358,203
- DPP4i: 331,028

FOLLOW-UP PERIOD:

Median follow up for SGLT2i vs GLP1RA cohort:

- SGLT2i: 194 days
- GLP1RA: 174 days

Median follow up for SGLT2i vs DPP4i cohort:

- SGLT2i: 201 days
- DPP4i: 194 days

RESULTS:

Primary Outcome –

- SGLT2i reduced the risk of nephrolithiasis compared to GLP-1RA (hazard ratio [HR] 0.69; 95% CI, 0.67–0.72).
- SGLT2i reduced the risk of nephrolithiasis compared to DPP4i (HR 0.74; 95% CI, 0.71–0.77).

LIMITATIONS:

- Cannot exclude potential residual confounders.

- The outcome of nephrolithiasis was determined based on diagnosis codes and, therefore, has the potential for outcome misclassification.
- Patients with known recurrent kidney stones were excluded and the focus was on incidental kidney stones, but the authors were unable to determine whether the kidney stones were truly incidental solely based on the diagnosis code alone.
- Unable to determine the composition of the kidney stones.
- An association between the individual types of SGLT2i agents and the risk of nephrolithiasis was not evaluated.
- Short follow-up and specific reasons for discontinuation were not provided. Therefore, the authors were unable to assess the duration of the effect of the drug class.
- The authors were unable to obtain information on over-the-counter medications that could potentially be associated with nephrolithiasis.

Madeline Carson, DO
Texas A&M FMRP
College Station, TX

Non-Invasive Testing De-Livers in Identifying NASH and Advanced Fibrosis in Type 2 Diabetes

High Prevalence of NASH and Advanced Fibrosis in Type 2 Diabetes: A Prospective Study of 330 Outpatients Undergoing Liver Biopsies for Elevated ALT, Using a Low Threshold

Castera L, Laouenan C, Vallet-Pichard A, et al. High Prevalence of NASH and Advanced Fibrosis in Type 2 Diabetes: A Prospective Study of 330 Outpatients Undergoing Liver Biopsies for Elevated ALT, Using a Low Threshold. *Diabetes Care*. 2023;46(7):1354-1362. doi:10.2337/dc22-2048

KEY TAKEAWAY: Non-invasive testing can accurately identify nonalcoholic steatohepatitis (NASH) and advanced fibrosis (AF) in patients with type 2 diabetes (T2DM).

STUDY DESIGN: Multicenter, prospective, cross-sectional study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Nonalcoholic fatty liver disease (NAFLD) is the most common cause of liver disease globally, affecting >25% of adults worldwide. Its prevalence has increased over time concurrent with the rise of obesity and diabetes. Unfortunately, NAFLD often remains undiagnosed, so the real prevalence of NASH and AF in T2DM is poorly known. Furthermore, the risk of progression to NASH and AF is higher in patients with T2DM, so identifying diabetic patients with NAFLD is an unmet need. Current methods to assess severity are invasive which can lead to missed opportunities for early intervention. Non-invasive ways to determine those at high risk who require additional testing would be beneficial.

PATIENTS: Adults with T2DM and elevated alanine transaminase (ALT)

INTERVENTION: Non-invasive testing

CONTROL: Liver biopsy

PRIMARY OUTCOME: Utility of non-invasive testing

METHODS (BRIEF DESCRIPTION):

- Adults ≥18 years old with T2DM seen for routine annual visits with a diabetologist were screened for NAFLD.
- Demographic characteristics:
  - Median age: 59 years old
  - 63% male, 37% female
  - Median BMI: 32 kg/m^2
  - Median HbA1c 7.5%
  - Diagnosed diabetic for nine years
  - 43% on insulin (alone or in combination)
- Patients with suspected NAFLD based on elevated ALT and/or steatosis on ultrasound were referred to a hepatologist for work-up including clinical assessment, fasting blood testing for Fibrosis-4 (FIB-4) and NAFLD fibrosis score, as well as controlled attenuation parameter (CAP) and liver stiffness measurement (LSM) measurements using vibration-controlled transient elastography (VCTE) with FibroScan.
- Non-invasive testing was compared with the gold standard of liver biopsy.
- Preset criteria for liver biopsy included persistently elevated ALT (above the low threshold of >20 IU/L for females and >30 IU/L for males) and no other liver disease.
- Multivariate models compared non-invasive methods with the histopathologic diagnosis from liver biopsy.
- Identification of non-invasive testing for the diagnosis and staging of NASH and AF in T2DM that is comparable to liver biopsy was measured as the primary outcome.
- Pathologists diagnosed NASH using the Fatty Liver Inhibition of Progression (FLIP) definition, meaning the presence of steatosis, hepatocyte ballooning, and lobular inflammation with at least one point per category.
  - Fibrosis was staged by the NASH Clinical Research Network scoring system on a scale from 0–4, where F0 is the absence of fibrosis, F3 is septal or bridging fibrosis, and F4 is cirrhosis. AF included F3 and F4.
- Statistical analysis was performed utilizing data from clinical assessments, blood testing, and VCTE to determine factors associated with NASH and AF.
- Since VCTE is not available in all clinics, multivariate logistic regression models for NASH and AF were made both with and without VCTE.

INTERVENTION (# IN THE GROUP): 330

COMPARISON (# IN THE GROUP): The same 330 patients

FOLLOW-UP PERIOD: Not applicable

RESULTS:

Primary Outcome –

- The prevalence of NASH and AF in T2DM was high despite the use of a low ALT threshold:
  - NASH (58%; 95% CI, 53–64)
  - AF (38%; 95% CI, 32–43)
- Compared to the gold standard, the model with VCTE was effective in diagnosing NASH.
  - Sensitivity: 0.90
  - Specificity: 0.58
  - Positive Likelihood Ratio (+LR) (2.1; 95% CI, 1.8–2.6)
  - Negative Likelihood Ratio (-LR) (0.17; 95% CI, 0.09–0.32)
- Compared to the gold standard, the model without VCTE was effective in diagnosing NASH.
  - Sensitivity: 0.90
  - Specificity: 0.47
  - +LR (1.7; 95% CI, 1.5–2.0)
  - -LR (0.21; 95% CI, 0.11–0.42)
- There was no difference in the performance of the two models for NASH.
  - Models with VCTE (adjusted odds ratio [aOR] 0.82; 95% CI, 0.77–0.87)
  - Models without VCTE (aOR 0.81; 95% CI, 0.76–0.86)
- Compared to the gold standard, the model with VCTE was effective in diagnosing AF.
  - Sensitivity: 0.90
  - Specificity: 0.62
  - +LR (2.4; 95% CI, 2.0–2.9)
  - -LR (0.16; 95% CI, 0.10–0.27)
- Compared to the gold standard, the model without VCTE was effective in diagnosing AF.
  - Sensitivity: 0.90
  - Specificity: 0.50
  - +LR (1.8; 95% CI, 1.6–2.1)
  - -LR (0.2; 95% CI, 0.11–0.35)
- The model that included VCTE outperformed the model without VCTE for AF.
  - Models with VCTE (aOR 0.82; 95% CI, 0.81–0.89)
  - Models without VCTE (aOR 0.78; 95% CI, 0.73–0.83)

LIMITATIONS:

- The high prevalence of NASH and AF may be related to tertiary referral centers vs typical community settings.
- The population may differ from primary care as 45% of these patients were on insulin.
- The transjugular route was used in certain patients not normally eligible for percutaneous liver biopsy.
- Metabolic syndrome components are independently associated with NASH so not a causal relationship.
- This study focused on T2DM patients with positive screening for NAFLD so not generalizable to all diabetic populations.
- Used a low ALT threshold for liver biopsy that is within the normal reference range of many lab tests.

Shauna LaFleur, MD, FAAFP
University of Iowa Hospitals and Clinics FMRP
Sioux City, IA

Head-to-Head: Symptom Reports vs Standardized Assessments for Sports-Related Concussion Diagnosis

Diagnosis of Sports-Related Concussion Using Symptom Report or Standardized Assessment of Concussion

Harmon KG, Whelan BM, Aukerman DF, et al. Diagnosis of Sports-Related Concussion Using Symptom Report or Standardized Assessment of Concussion. *JAMA Netw Open*. 2024;7(6):e2416223. Published 2024 Jun 3. doi:10.1001/jamanetworkopen.2024.16223

KEY TAKEAWAY: The Standardized Assessment of Concussion (SAC) demonstrates excellent diagnostic accuracy for symptom score and symptom severity score, but fair accuracy for total score. In contrast, the subcomponents of the Sports Concussion Assessment Tool, 5th edition (SCAT5) show poor to fair diagnostic accuracy. The SAC exhibits poor test-retest reliability across all measures.

STUDY DESIGN: Prospective, case-controlled study

LEVEL OF EVIDENCE: STEP 4

BRIEF BACKGROUND INFORMATION: Concussions in athletes are commonly diagnosed through self-reported symptoms and standardized assessments. One widely used tool is the SCAT5, which evaluates symptoms, cognitive function, balance, and neurological status to diagnose concussions and guide return-to-play decisions. The SAC, a key part of the SCAT5, specifically tests cognitive abilities like memory, concentration, and orientation. This study compared the effectiveness of symptom reporting alone with the combined use of the SAC to determine how well it diagnoses concussions.

PATIENTS: National Collegiate Athletic Association (NCAA) Division I athletes

INTERVENTION: SAC

CONTROL: Symptom report

PRIMARY OUTCOME: Diagnostic accuracy and test-retest reliability

METHODS (BRIEF DESCRIPTION):

- NCAA Division I athletes from any sport, including contact and non-contact sports from four different universities were followed from Summer 2020 to Winter 2022.
- Athletes or controls were excluded from the study if they had been diagnosed with a concussion in the previous year.
- Athletes completed baseline Sports Concussion Assessment Tool (SCAT5) testing, which was repeated when an athlete presented with a suspected concussion.
- If concussion was diagnosed, testing was also performed on an athlete within the control group, identified and matched based on comorbidities, gender, sport, season, and baseline scoring.
- Concussion diagnosis was made primarily based on symptom reports, scores, and severity for participants.
- The primary outcome measured the diagnostic accuracy utilizing area under the curve (AUC) and test-retest reliability utilizing intraclass correlation coefficient (ICC) for the following:
  - Symptom score
  - Symptom severity score
  - Total SAC score assessing cognitive function including orientation, immediate memory, concentration, and delayed recall.
  - Subcomponent scores on the SCAT5 included orientation, immediate memory, concentration, and delayed recall.
- Diagnostic utility was defined as:
  - Excellent diagnostic utility was defined as an AUC of 0.9–1.0.
  - Good diagnostic utility was defined as an AUC of 0.8 to <0.09.
  - Fair diagnostic utility was defined as an AUC of 0.07 to <0.08.
  - Poor diagnostic utility was defined as an AUC of <0.6.

INTERVENTION (# IN THE GROUP): 92

COMPARISON (# IN THE GROUP): 92

FOLLOW-UP PERIOD: Post-concussion injury

RESULTS:

Primary Outcome –

- SAC had excellent diagnostic utility for symptom scores (AUC 0.93; 95% CI, 0.89–0.96).
- SAC had excellent diagnostic utility for symptom severity score (AUC 0.94; 95% CI, 0.90–0.97).
- SAC had fair diagnostic utility for the total SAC score (AUC 0.70; 95% CI, 0.63–0.77).

- SAC had the following utility for the subcomponent scores of the SCAT5:
  - Poor diagnostic utility for orientation (AUC 0.49; 95% CI, 0.43–0.56)
  - Fair diagnostic utility for immediate memory (AUC 0.68; 95% CI, 0.61–0.75)
  - Poor diagnostic utility for concentration (AUC 0.52; 95% CI 0.44–0.61)
  - Fair diagnostic utility for delayed recall (AUC 0.69; 95% CI 0.62–0.77)
- SAC had poor test-retest reliability for all measures:
  - Symptom score (ICC 0.57; 95% CI, 0.42–0.70)
  - Symptom severity score (ICC 0.60; 95% CI, 0.45–0.72)
  - Total SAC score (ICC 0.29; 95% CI, 0.09–0.47)
  - Subcomponent scores on the SCAT5:
    - Orientation (ICC 0.17; 95% CI, 0.04–0.37)
    - Immediate memory (ICC 0.19; 95% CI, 0.01–0.37)
    - Concentration (ICC 0.43; 95% CI, 0.25–0.59)
    - Delayed recall (ICC 0.24; 95% CI, 0.04–0.43)

LIMITATIONS:

- All tests had poor test-retest reliability resulting in significant variation in testing even in athletes without a concussion.
- The possibility of inaccurate reporting of symptoms by athletes, as determined by self-report.
- Variations may exist within individual timelines for the development of concussion symptoms.
- Incidence and prevalence of concussion may be higher on average in participants and athletes from contact sports than in non-contact sports.
- The study was limited to NCAA Division I athletes and may not represent other populations including professional, or high school athletes.
- Concussion history was not controlled for, although, athletes who sustained a concussion in the previous year were excluded from the study.

Dennis Garcia-Rhodes, MD, MPH
Texas A&M FMRP
Bryan, TX

Crushing the Weekend Workout: Any Cardiovascular Benefits?

Accelerometer-Derived "Weekend Warrior" Physical Activity and Incident Cardiovascular Disease

Khurshid S, Al-Alusi MA, Churchill TW, Guseh JS, Ellinor PT. Accelerometer-Derived "Weekend Warrior" Physical Activity and Incident Cardiovascular Disease. *JAMA*. 2023;330(3):247-252. doi:10.1001/jama.2023.10875

KEY TAKEAWAY: Moderate to vigorous physical activity condensed to one to two days or evenly distributed over four to five days effectively decreases cardiovascular risk compared to inactivity.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 4 (downgraded due to poor follow-up)

BRIEF BACKGROUND INFORMATION: Engaging in ≥150 minutes of moderate to vigorous physical activity (MVPA) per week reduces cardiovascular events. It may be easier to achieve this in one or two days (weekend warriors), but is unclear if this reduces cardiovascular risk as effectively as regular, evenly distributed activity.

PATIENTS: Adults

INTERVENTION: Active weekend warriors; regularly active throughout the week

CONTROL: Inactivity

PRIMARY OUTCOME: Incidence of cardiovascular outcomes

METHODS (BRIEF DESCRIPTION):

- UK Biobank prospective cohort data reviewed associations between physical activity and cardiovascular events on a sub-study of participants who wore a wrist-based accelerometer for one week.
- The participants included were adults 40–69 years old. 97% were White, with other ethnicities represented at <1% each, and most were from a higher socioeconomic status.
- Excluded were those with insufficient wear time to support utilization, inadequate signals for calibration or MVPA estimation, and non-physiologic mean acceleration values.
- Thresholds for physical activity measurement were guideline-based (≥150 minutes per week) and the sample median (≥230 minutes) duration of physical activity.
- Participants were categorized into the following three groups:
  - Active weekend warrior (active WW): At or above MVPA threshold, dispersed across one to two days
  - Active regular: At or above MVPA threshold, activity dispersed across four to five days
  - Inactive: Below MVPA threshold
- The primary cardiovascular outcomes consisted of atrial fibrillation, myocardial infarction, heart failure, and stroke.

INTERVENTION (# IN THE GROUP):

- Weekend warrior: 37,872
- Active regular 21,473

COMPARISON (# IN THE GROUP): 30,228

FOLLOW-UP PERIOD: Median 6.3 years

RESULTS:

Primary Outcome –

- Active weekend warriors reduced the risk of cardiovascular outcomes compared to inactivity.
  - Atrial fibrillation (hazard ratio [HR] 0.78; 95% CI, 0.74–0.83)
  - Myocardial infarction (HR 0.73; 95% CI, 0.67–0.80)
  - Heart failure (HR 0.62; 95% CI, 0.56–0.68)
  - Stroke (HR 0.79; 95% CI, 0.71–0.88)
- Regular activity reduced the risk of cardiovascular outcomes compared to inactivity.
  - Atrial fibrillation (HR 0.81; 95% CI, 0.74–0.88)
  - Myocardial infarction (HR 0.65; 95% CI, 0.57–0.74)
  - Heart Failure (HR 0.64; 95% CI, 0.56–0.73)
  - Stroke (HR 0.83; 95% CI, 0.72–0.97)

LIMITATIONS:

- The short duration of accelerometer use and modified behavior may affect study outcomes.
- Lack of racial diversity and predominantly healthy participants, limiting applicability to clinics with diverse populations and varying socioeconomic statuses and health.
- Most covariates were collected several years before accelerometer use, potentially leading to misclassification.

Catherine Porras, MD

Northside Hospital-Gwinnett FMRP
Lawrenceville, GA