GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of April 10 - 14, 2023

SPOTLIGHT: Less is More - A Shortened vs Standard DAPT Duration Review

Less is More: A Shortened vs Standard DAPT Duration Review

Efficacy and Safety of Shortened Dual Antiplatelet Therapy in Patients Undergoing Percutaneous Coronary Intervention: A Meta-Analysis of Randomized Controlled Trials

Hui J, Bai T, Liang L, et al. Efficacy and Safety of Shortened Dual Antiplatelet Therapy in Patients Undergoing Percutaneous Coronary Intervention: A Meta-Analysis of Randomized Controlled Trials. *J Cardiovasc Pharmacol.* 2022;80(5):700-708. Published 2022 Nov 1. doi:10.1097/FJC.0000000000001348

KEY TAKEAWAY: When compared to the standard six to 12-month dual antiplatelet therapy (DAPT) following percutaneous coronary intervention (PCI), ≤3-month DAPT significantly reduced major adverse cardiovascular events, all-cause mortality, cardiovascular mortality, major bleeding, and any bleeding, without any significant differences in the risk of myocardial infarction, stent thrombosis, or stroke.

STUDY DESIGN: Systematic review and meta-analysis of randomized controlled trials (N=45,661)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: DAPT is used in the post-PCI period to prevent major cardiac events including re-infarction secondary to stent thrombosis, among other complications. However, there had been little formal analysis on the duration of therapy, especially among specific patient populations, to achieve maximum benefit with minimal adverse outcomes related to DAPT.

PATIENTS: Adult patients post-PCI with newer generation drug-eluting stent

INTERVENTION: ≤3-month DAPT

CONTROL: Six to 12-month DAPT

PRIMARY OUTCOME: Major adverse cardiovascular events (MACE)

Secondary Outcome: All-cause mortality, cardiovascular mortality, major bleeding, any bleeding, myocardial infarction, stent thrombosis, stroke

METHODS (BRIEF DESCRIPTION):

- MACE is defined as a composite of cardiac death, definite or probable stent thrombosis, myocardial infarction, or target-lesion revascularization.
- Database search for RCTs in December 2021 for article titles containing pertinent terminology: PCI, stent, various antiplatelet medications, aspirin, and duration.
- 3,876 records were identified in the initial database search, of which 2720 redundant records were removed. 2397 were excluded based on the relevancy of the title and abstract.
- The remaining 323 full-text articles were excluded based on having an older generation stent, no control group, >3-month duration short protocol, not an RCT, and general study protocol. Of these, nine RCTs were appropriate to include in the meta-analysis.

INTERVENTION (# IN THE GROUP): 24,420

COMPARISON (# IN THE GROUP): 21,241

FOLLOW-UP PERIOD: 12 to 24 months

RESULTS:

Primary Outcome –

- Compared with standard DAPT, ≤3-month DAPT significantly reduced MACE (HR 0.89; 95% CI, 0.82–0.97; I^2=0%).

Secondary Outcome –

- Compared with standard DAPT, ≤3-month DAPT significantly reduced:
  - All-cause mortality (HR 0.88; 95% CI, 0.78–0.99; I^2=0%)
  - Cardiovascular mortality (HR 0.79; 95% CI, 0.65–0.97; I^2=0%)
  - Major bleeding (HR 0.72; 95% CI, 0.56–0.93; I^2=64%)
  - Any bleeding (HR 0.57; 95% CI, 0.50–0.66; I^2=0%)
- There was no difference in stroke between the two groups.

LIMITATIONS:

- There was variation in the trials' definitions of MACE.
- Few trials were completed on DAPT duration in patients with HBR making this sub-group analysis less useful in this meta-analysis.

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The views expressed in this GEM are those of the author and do not reflect the official policy of the Department of the Army, the Department of Defense, or the U.S. Government.

SGLT2 Inhibitors: The Key to Saving Hearts?

Effect of Empagliflozin on Worsening Heart Failure Events in Patients with Heart Failure and Preserved Ejection Fraction: EMPEROR-Preserved Trial

Packer M, Butler J, Zannad F, et al. Effect of Empagliflozin on Worsening Heart Failure Events in Patients With Heart Failure and Preserved Ejection Fraction: EMPEROR-Preserved Trial. Circulation. 2021;144(16):1284-1294. doi:10.1161/CIRCULATIONAHA.121.056824

KEY TAKEAWAY: The use of empagliflozin, a sodium-glucose transporter 2 (SGLT2) inhibitor reduces the risk and severity of worsening heart failure outcomes in both the outpatient and inpatient setting in patients with heart failure with preserved ejection fraction (HFpEF).

STUDY DESIGN: Randomized, double-blind, parallel-group, placebo-controlled, event-driven study

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Heart failure can progressively worsen over time without appropriate monitoring and intervention. A primary goal of outpatient pharmacological management of heart failure is reducing the risk of exacerbation events leading to possible hospitalization. While traditional regimens have often placed an emphasis on diuresis, agents such as empagliflozin, an SGLT2 inhibitor, may confer additional benefits in the treatment of HFpEF.

PATIENTS: Patients with class II through IV heart failure with an ejection fraction of >40%

INTERVENTION: Empagliflozin

CONTROL: Placebo

PRIMARY OUTCOME: Death, hospitalization from heart failure (HHF), emergency room or urgent care visits related to heart failure

METHODS (BRIEF DESCRIPTION):

- A total of 5,988 men and women with and without diabetes were enrolled through the (EMPagliflozin OutcomE tRial in Patients with chronic heaRt failure witht Preserved Ejection fraction (EMPEROR-Preserved), an international study recruiting patients from 22 countries.
- Inclusion criteria: preserved left ventricular ejection fraction (LVEF >40%) diagnosed no more than six months before study initiation; elevated levels of NT-proBNP (>300 pg/mL); preserved renal function.
- Patients were randomized in a double-blind 1:1 ratio to receive an intervention of empagliflozin 10 mg daily in addition to usual therapy or placebo.
- Patient data was collected every 2 to 6 months (depending on site-specific criteria) during the study for mortality, worsening heart failure, functional capacity, diuretic regimen changes, vital signs, and biomarkers.
- Data was collected prospectively on deaths, hospitalizations for any reason that also required IV vasopressor and/or positive inotropic agents, emergency room/urgent care events, and outpatient events related to a cardiac issue.
- Statistical analysis of outcomes was primarily completed using Cox regression models.

INTERVENTION (# IN THE GROUP): 2,997

COMPARISON (# IN THE GROUP): 2,991

FOLLOW-UP PERIOD: Median 26 months

RESULTS:

Primary Outcome –

- Empagliflozin reduced the risk of the following compared to placebo:
  - Death or HHF (HR 0.85; 95% CI, 0.76–0.95)
  - HHF (HR 0.73; 95% CI, 0.61–0.88)
  - Emergency room/urgent care visits for worsening heart failure (HR 0.55; 95% CI, 0.43–0.69)
  - Death/hospitalization for any cardiovascular reason (HR 0.89; 95% CI, 0.91–0.98)
  - Death/hospitalization for any reason (HR 0.92; 95% CI, 0.85–0.99)
  - First and recurrent hospitalizations for cardiovascular reasons (HR 0.84; 95% CI, 0.74–0.95)
  - Hospitalizations requiring intravenous diuresis (HR 0.67; 95% CI, 0.57–0.79)
  - Hospitalizations requiring intravenous vasopressor or positive inotropic agents (HR 0.73; 95% CI, 0.55–0.97)
  - Worsening heart failure events (HR 0.77; 95% CI, 0.67–0.87)
  - Interval outpatient intensification of diuretic regimen (HR. 0.73; 95% CI, 0.65–0.82).

- There was no significant difference between Empagliflozin and placebo in regard to the duration of heart failure.

LIMITATIONS:

- The study did not specifically address the effect a patient's other medications had on outcomes. Additionally, while the study was designed to allow patients to continue their previously prescribed medications, there is no mention of what those medications were for the patient population studied.
- Study did not standardize the process of non-invasive assessment of cardiac structure and function with an echocardiogram.
- Outpatient outcome data was limited to the emergency room/urgent care setting, thus unclear how frequently patients needed to be evaluated in the clinic setting for issues related to heart failure/ events.

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Is Tirzepatide Effective for the Treatment of Type 2 Diabetes?

Efficacy and Safety of a Novel Dual GIP and GLP-1 Receptor Agonist Tirzepatide in Patients with Type 2 Diabetes (SURPASS-1): A Double-Blind, Randomised, Phase 3 Trial

Rosenstock J, Wysham C, Frías JP, et al. Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): a double-blind, randomised, phase 3 trial [published correction appears in *Lancet*. 2021 Jul 17;398(10296):212]. *Lancet*. 2021;398(10295):143-155. doi:10.1016/S0140-6736(21)01324-6

KEY TAKEAWAY: Tirzepatide reduces A1c and body weight compared to placebo while maintaining medication safety parameters similar to that of GLP-1 receptor agonists.

STUDY DESIGN: Randomized, double-blind, controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Tirzepatide, a novel dual GLP -1 and gastrointestinal peptide (GIP) receptor agonist could help achieve glycemic control and weight loss in patients with type 2 diabetes.

PATIENTS: Adults with type 2 diabetes

INTERVENTION: Tirzepatide

CONTROL: Placebo

PRIMARY OUTCOME: HbA1c

Secondary Outcome: Body weight, adverse events

METHODS (BRIEF DESCRIPTION):

- Participants were adults 18 years old and older with type 2 diabetes, with baseline HbA1c 7.0% to 9.5%, who were not controlled by lifestyle changes alone.
- The study was conducted at multiple medical research centers and hospitals located in India, Japan, Mexico, and USA.
- Participants were blinded and randomized 1:1:1:1 to either placebo or Tirzepatide 5 mg, 10 mg, or 15 mg once weekly groups for the 40-week study period.
- Changes in A1c and body weight were compared from baseline over the course of the study.
- Measurements were taken at four-week intervals at either the hospitals or research centers.
- Adverse outcomes were self-reported by participants, most notably gastrointestinal.

INTERVENTION (# IN THE GROUP):

- Tirzepatide 5 mg: 121
- Tirzepatide 10 mg: 121
- Tirzepatide 15 mg: 121

COMPARISON (# IN THE GROUP): 115

FOLLOW-UP PERIOD: Four weeks

RESULTS:

Primary Outcome –

- Tirzepatide 5 mg weekly significantly reduced baseline A1c mean treatment difference compared to placebo (–1.9% vs 0.04% respectively; mean between-group difference –1.9%; 95% CI, –2.2 to –1.6).
- Tirzepatide 10 mg did not significantly affect A1c mean difference compared to Tirzepatide 15 mg.

Secondary Outcome –

- Tirzepatide 5 mg weekly significantly reduced baseline body weight mean treatment difference compared to placebo (–7.0 kg vs –0.7 kg respectively; mean between-group difference –6.3 kg; 95% CI, –7.8 to –4.7).
- Adverse effects were primarily gastrointestinal, including nausea in 12%, 13%, and 18% of those receiving Tirzepatide 5mg, 10mg, and 15mg, respectively, versus 6% of those receiving placebo with no statistical significance.

LIMITATIONS:

- The study sample did not appropriately reflect the population due to the underrepresentation of African Americans (only 5%), thus limiting generalizability.
- The study was short with a duration of only 40 weeks, thus limiting the complete evaluation of the actual course of therapy for long-term effects.
- The study was industry-funded; thus, this study was not without conflict of interest.

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Is Social Anxiety Associated with Suicidality in Teens?

Social Anxiety and Suicidality in Youth: A Systematic Review and Meta-Analysis

Leigh E, Chiu K, Ballard ED. Social Anxiety and Suicidality in Youth: A Systematic Review and Meta-analysis [published online ahead of print, 2022 Dec 16]. *Res Child Adolesc Psychopathol.* 2022;10.1007/s10802-022-00996-0. doi:10.1007/s10802-022-00996-0

KEY TAKEAWAY: Social anxiety may be associated with suicidality in youth 10–25 years old.

STUDY DESIGN: Systematic review and meta-analysis of 16 studies (primarily cross-sectional and prospective) for quantitative synthesis (N=27,428)

LEVEL OF EVIDENCE: STEP 2 (downgraded due to poor quality of studies and high heterogeneity)

BRIEF BACKGROUND INFORMATION: Approximately 2% of the global population attempts suicide during their lifetime. Suicide is the fourth leading cause of death in young people globally. Risk factors include psychiatric disorders such as major depressive disorder and bipolar disorder. However, anxiety disorders in adult samples demonstrate and increased risk of lifetime suicidal thoughts and behaviors independent of mood or substance use disorders. Identifying risk factors for suicidal behaviors in youth may allow for intervention opportunities.

PATIENTS: Youth 10–25 years old

INTERVENTION: Social anxiety

CONTROL: Not applicable

PRIMARY OUTCOME: Suicide attempt, ideation, risk

METHODS (BRIEF DESCRIPTION):

- Three data meta-analyses were completed on suicide attempts, ideation, and risk.
- Inclusion criteria: Youth 10–25 years old with social anxiety
  - Individuals who met these criteria at the time of the first assessment received an assessment to measure/diagnose social anxiety and a dimension of suicidality.
  - Most studies were conducted in the United States.
  - Four studies controlled for depression; however, others did not which may be a confounding variable.
- Outcomes measured Pearson's correlation coefficient (r) to measure the relationship between the presence of social anxiety and suicidality.
  - A non-zero r value determines some association using Cohen's Guidelines:
    - Small Effect: r=0.10
    - Moderate Effect: r=0.30
    - Large Effect: r=0.50
  - Study designers created a coefficient for studies that did not have a correlation coefficient, or the study was eliminated.
- 12 different measurement tools were used to measure social anxiety and 12 were used to measure suicidality.

INTERVENTION (# IN THE GROUP): 27,428

COMPARISON (# IN THE GROUP): Not applicable

FOLLOW-UP PERIOD: Not available

RESULTS:

Primary Outcome –

- All suicide indices had small associations with social anxiety.
  - Social anxiety was associated with a suicide attempt (8 trials, n=15,890; r=0.10; 95% CI, 0.04–0.15; I^2=84.5%).
  - Social anxiety was associated with suicidal ideation (4 trials, n=4,088; r=0.22; 95% CI, 0.02–0.41; I^2=98.6%).
  - Social anxiety was associated with suicide risk (3 trials, n=4,888; r=0.24; 95% CI, 0.05–0.41; I^2=95.9%).

LIMITATIONS:

- High heterogeneity was observed.
- Outcomes were characterized as risk vs. behaviors vs. thoughts.
- Moderator effects such as depression and age could not be assessed.
- Quality of papers included were rated weak or moderate quality.

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the Army, the Department of Defense, or the U.S. Government.

Use of IV Fluids in P0s During the Induction of Labor

A Double-Blinded Randomized Controlled Trial on the Effects of Increased Intravenous Hydration in Nulliparas Undergoing Induction of Labor

Duffy JY, Wu E, Fong A, Garite TJ, Shrivastava VK. A double-blinded randomized controlled trial on the effects of increased intravenous hydration in nulliparas undergoing induction of labor. *Am J Obstet Gynecol*. 2022;227(2):269.e1-269.e7. doi:10.1016/j.ajog.2022.01.024

KEY TAKEAWAY: Increased intravenous (IV) fluids during induction of labor of nulliparous women likely do not decrease the length of labor.

STUDY DESIGN: Randomized, double-blind, controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Higher rates of IV fluids (250 cc/hr) are known to decrease the length of time to delivery in nulliparous women who present in spontaneous labor. With the increasing rates of induction of labor, little is known regarding the use of higher rates of IV fluids and its effect on the duration of labor, specifically in nulliparous women who are undergoing induction of labor.

PATIENTS: Nulliparous women undergoing induction of labor

INTERVENTION: Higher rate of IV fluids

CONTROL: Lower rate of IV fluids

PRIMARY OUTCOME: Length of labor

Secondary Outcome: Maternal and neonatal outcomes

METHODS (BRIEF DESCRIPTION):

- Nulliparous women undergoing induction of labor with a bishop score ≤6 were randomized into this study.
- Patients were blinded and randomized to one of the following treatments:
  - 125 cc/hr normal saline during induction
  - 250 cc/hr normal saline during induction
- Treatments were administered by nursing staff and IV pump settings were covered to blind both patient and clinician.
- Length of labor was defined as the time from the start of the study fluids to delivery.

INTERVENTION (# IN THE GROUP): 89

COMPARISON (# IN THE GROUP): 84

FOLLOW-UP PERIOD: From admission through delivery

RESULTS:

Primary Outcome –

- Increased IV fluids did not decrease the length of time to delivery compared to lower IV fluids (28 hours vs 27 hours, respectively; *P*=.91).

Secondary Outcome –

- No difference was seen in the secondary outcomes for maternal or neonatal outcomes including:
  - Rate of Cesarean Section: 125 cc/hr 38.2% vs 250 cc/hr 36.9% (*P*=.86)
  - Clinical Iatrogenic intraamniotic infection: 125 cc/hr 22.7% vs 250 cc/hr 27.4% (*P*=.48)
  - 1 min Apgars: 125 cc/hr 7.9 vs 250 cc/hr 7.2% (*P*=.88)
  - Need for phototherapy: 125 cc/hr 10.2% vs 250 cc/hr 7.1% (*P*=.47)
  - NICU admission: 125 cc/hr 21.3% vs 250 cc/hr 17.9% (*P*=.56)

LIMITATIONS:

- The study was unable to differentiate between active vs latent labor and therefore the evaluation was for the entire duration of labor. The author acknowledges that fluids may be beneficial during the active stage of labor given the understood physiology, however, this could not be adequately evaluated.
- This study was not powered to evaluate potential side effects from increased fluids such as pulmonary edema, renal dysfunction, and postpartum diuresis. This information would be critically important in making clinical decisions regarding the use of increased fluids.

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Jumpstart Your Cardiovascular Health as Early as Childhood

Childhood Cardiovascular Risk Factors and Adult Cardiovascular Events

Jacobs DR Jr, Woo JG, Sinaiko AR, et al. Childhood Cardiovascular Risk Factors and Adult Cardiovascular Events. *N Engl J Med.* 2022;386(20):1877–1888. Doi:10.1056/NEJMoa2109191

KEY TAKEAWAY: Childhood cardiovascular risk factors increase the risk for fatal and nonfatal cardiovascular events in adulthood.

STUDY DESIGN: Prospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Cardiovascular disease is the leading cause of death among adults in the United States. However, research demonstrating a link between childhood risk factors and adult cardiovascular events is lacking.

PATIENTS: Children and adolescents

INTERVENTION: Cardiovascular risk factors

CONTROL: Not applicable

PRIMARY OUTCOME: Cardiovascular events

METHODS (BRIEF DESCRIPTION):

- 38,589 participants were gathered from the International Childhood Cardiovascular Cohort (i3c) Consortium.
  - Participants were from Australia, the United States, and Finland.
  - 50.3% were female.
  - 15% were Black.
- Childhood cardiovascular risk factors were evaluated to include the following: body mass index, systolic blood pressure, total cholesterol, triglyceride level, and youth smoking.
- Childhood cardiovascular risk factors were evaluated from 3 to 19 years old.
- Identification of cardiovascular disease and death was investigated between 2015 and 2019 using:
  - Death records with ICD-10 codes associated with cardiovascular disease
  - Finnish national medical registry
  - Interviews of U.S. and Australian participants with supportive medical records request
- Unadjusted childhood combined-risk z-scores were utilized to calculate hazard ratios to determine correlations between adult fatal vs non-fatal cardiovascular events and childhood risk factors.

INTERVENTION (# IN THE GROUP): 38,589

COMPARISON (# IN THE GROUP): Not applicable

FOLLOW-UP PERIOD: Mean 35 years

RESULTS:

Primary Outcome –

- Smoking in childhood significantly increased the likelihood of a cardiovascular event in adulthood (HR 1.6; 95% CI, 1.2–2.1).
- Elevated BMI in childhood significantly increased the likelihood of a cardiovascular event in adulthood (HR 1.4; 95% CI, 1.3–1.6).
- Elevated triglycerides in childhood significantly increased the likelihood of a cardiovascular event in adulthood (HR 1.5; 95% CI, 1.3–1.7).
- Elevated cholesterol in childhood significantly increased the likelihood of a cardiovascular event in adulthood (HR 1.3; 95% CI, 1.1–1.5).
- Combined risk factors in childhood significantly increased the likelihood of a cardiovascular event in adulthood (HR 2.7; 95% CI, 2.2–3.3).
- Each risk factor was independently associated with adverse cardiovascular events and when multiple risk factors were present, the effect was compounded.

LIMITATIONS:

- Only 15% of the participants were Black. The study did not include many Hispanics, and participants were all from high-income countries creating poor generalizability.
- There was a component of response bias, due to 46.5% of participants being lost to follow-up.
- The average age for a cardiovascular event was 47 years old and results may not correlate to lifelong cardiovascular risk.
- Due to the relatively young age of the first cardiovascular event, future studies may benefit from following participants for another 10–15 years for further events.

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Novel Concussion Head/Neck Cooling Therapy Appears Safe in Children

Preliminary Safety and Efficacy of Head and Neck Cooling Therapy after Concussion in Adolescent Athletes: A Randomized Pilot Trial

Congeni J, Murray T, Kline P, et al. Preliminary Safety and Efficacy of Head and Neck Cooling Therapy After Concussion in Adolescent Athletes: A Randomized Pilot Trial. *Clin J Sport Med*. 2022;32(4):341-347. doi:10.1097/JSM.0000000000000916

KEY TAKEAWAY: Head and neck cooling therapies may be safe in pediatric populations and effective at reducing symptom severity and recovery times.

STUDY DESIGN: Prospective, randomized, nonblinded, dual-arm comparative pilot study

LEVEL OF EVIDENCE: STEP 3 (downgraded due to low power and a non-blinded study design)

BRIEF BACKGROUND INFORMATION: Concussions are a prevalent and significant public health concern with approximately 1.6 to 3.8 million concussions reported annually in the USA alone. Currently, there is no medical treatment for concussions other than short-term brain rest. Researchers are investigating head and neck cooling as a novel therapy to reduce the severity of concussion symptoms and hasten recovery time.

PATIENTS: Adolescent athletes with concussion

INTERVENTION: Head and neck cooling therapy + short term brain rest

CONTROL: Short term brain rest alone

PRIMARY OUTCOME: Concussive symptoms

Secondary Outcome: Adverse events

METHODS (BRIEF DESCRIPTION):

- Male and female athletes 12–17 years old with sports-related concussions were included.
- Patients were randomized and assigned to two treatment arms.
    - Intervention: Short-term brain rest plus two 30 min long Pro-2cool head and neck cooling treatment sessions. The first treatment session was at the post-injury assessment and the second treatment session was at a 72 hr follow-up visit.
    - Control: Short-term brain rest alone.
        - Short-term brain rest instructions were for 72 hr of rest from almost all physical and cognitive activity.
- Treatments were administered by a trained professional who ensured proper fitting of the Pro-2cool device.
- Symptom severity was monitored twice during the treatment session using the SCAT-5 self-reported concussion symptom questionnaire.
- Adverse events were reported at each study visit including unintended disease, injury, and clinical exam/laboratory abnormalities.

INTERVENTION (# IN THE GROUP): 28

COMPARISON (# IN THE GROUP): 27

FOLLOW-UP PERIOD: 28 days

RESULTS:

Primary Outcome –

- Head and neck cooling with short term brain rest reduced concussion symptoms compared to short term brain rest alone.
    - At 72 hours: mean reduction 16 (95% CI, 8.2–23)
    - At 10 days: mean reduction 5.8 (95% CI, 1.9–14)
    - This was no significant at 28 days (mean reduction 0.7; 95% CI, –9.5 to 11).

Secondary Outcome –

- There was no difference in adverse events between the groups.

LIMITATIONS:

- Pro2Cool head and neck cooling device is currently designated as a breakthrough device by the FDA and is being studied in a multi-center clinical trial. It is not yet available commercially.
- This pilot study had a low power (N=55) and requires a larger scale investigation to ensure the validity and replicability of results.
- This study was non-blinded.
- The patient population was randomized with comparable demographics and comorbidities between study arms; however, there was a large underrepresentation of Hispanic patients in both treatment groups. Hispanic patients comprised only 3% of the total study population.
- There were injuries from a wide variety of sports included in both study arms; however, football was

over-represented in the control group and lacrosse was over-represented in the treatment group.

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