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Perioperative Management in the Collegiate Athlete: An Integrated Approach

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ABSTRACT

Collegiate athletes face rigorous physical, academic, and emotional demands. While significant attention has been paid to injury prevention among young athletes in the past two decades, orthopedic injury rates remain high among collegiate athletes, and a significant number will undergo surgical management for injuries each year. In this narrative review, we describe techniques for perioperative management of pain and stress after surgery in collegiate athletes. In particular, we outline pharmacologic and non-pharmacologic management of surgical pain, with a goal of minimizing opiate consumption. We emphasize a multi-disciplinary approach to optimizing post-operative recovery in collegiate athletes help minimize reliance on opiate pain medication. Additionally, we recommend that institutional resources should be harnessed to support athletes in their well-being, from a nutritional, psychological and sleep standpoint. Critical to success in perioperative pain management is the communication among the athletic medicine team members and with the athlete and family to address pain and stress management and encourage timely, safe return to play.

Introduction

Nearly half a million college students participate in National Collegiate Athletic Association (NCAA) sports each year, with over 150,000 playing Division I athletics [1]. A significant number of athletes experience orthopedic injuries each year, and a proportion of those athletes go on to require orthopedic surgery [2]. In one study from a Division I institution, Wang et al. reported approximately that 16 % of collegiate athletes underwent orthopedic surgery during college, equating to 80,000 NCAA athletes annually. In particular, sports with the highest rates of orthopedic surgery include women's gymnastics, American football, and men's wrestling [3, 4].

Like professional, national team, and Olympic athletes, collegiate athletes face unique pressures and challenges when recovering from surgery. Athletes are frequently attempting to return to a high level of physical activity as quickly as is safe after surgery. This necessitates a focus on managing pain, sleep, and nutrition in such a way that optimizes bony and soft tissue healing while minimizing muscle mass loss (▶ **Fig. 1**). Furthermore, stress surrounding the athlete's role on the team, return to play, and future as an athlete can impact an otherwise uneventful recovery and should be addressed by the athletics staff.

No formal guidelines exist with regard to perioperative management in elite athletes. The purpose of this narrative review is to comprehensively present the methods to reduce pain and psychological distress and maximize outcomes among collegiate athletes undergoing orthopedic surgery.

Pain Management

Post-operative pain management should be discussed with the athlete before surgery. The athletic training, orthopaedic, and anesthesia team all play important roles in discussing expectations about pain management and addressing patient concerns. Some athletes may have the expectation that opiates will be the primary source of pain control, and re-education regarding multi-modal management including neural blockade and non-pharmacologic interventions is paramount. Additionally, personal history of exposure to opiates may affect a patient's expectations around surgical pain management. Standardization of the post-operative pain regimen can be helpful for setting boundaries and easing communication between team members.

Collegiate athletes share similarities to other elite athletes, such as Olympic athletes and professional athletes. The International Olympic Committee consensus statement regarding pain management in elite athletes delineates a multimodal approach that recognizes pain as a subjective experience with "neurobiological, cognitive, affective, contextual, and environmental factors" that all interact to result in the perception of discomfort [5]. Addressing each contributing factor is emphasized, utilizing pharmacologic management, physical and massage therapy, and psychosocial interventions. While not specific to perioperative management, these guidelines can be extrapolated to the post-surgical pain scenario.

Pharmacologic Management of Pain

The sensation of pain is a subjective interpretation of a noxious stimulus in the body. Numerous cytokines and substances have been implicated in pain signaling, and neurologic pathways also play a large role in pain perception. In the perioperative setting, nociceptive, inflammatory, and neuropathic pain may all be implicated. In this section, we address the pharmacologic methods for reduction of surgical pain as it relates to these pathways. In particular it should be noted that medications should be prescribed in the lowest effective dose for the least amount of time by a licensed healthcare provider familiar with the risks and benefits of the agent.

Peripheral Nerve Blocks

Intraoperative and early post-operative pain can be drastically reduced with a regional neural blockade. Peripheral nerve blocks have been popularized over the past two decades and generally are performed by anesthesia providers. While not available in every anatomic area, neural blockade has allowed for a reduction in sedation during surgery, as well as a reduction in post-operative opiate consumption.

Peripheral nerve blocks have numerous advantages. First, they minimize need for general anesthesia in the appropriate setting, allowing for rapid same-day recovery and reducing length of stay in the post-operative care unit or admission [6–8]. Second, they reduce post-operative pain scores and improve patient reported outcomes [9–11]. Third, patients who receive a peripheral nerve block consume less opiates compared to those who do not [9, 10]. For a collegiate athlete who may or may not have family available at the time of their surgery, these advantages can ease the burden on caregivers. Athletic trainers who frequently make day-to-day contact with the athletes should be well-versed in the typical timeline for surgical pain return after peripheral nerve blocks. When feasible, combined peripheral nerve blocks should be considered as an alternative to single-shot nerve blocks, as they can result in improved pain control, reduced opiate consumption, and increased patient satisfaction [5]. Furthermore, continuous analgesia with nerve catheters can be considered for longer-acting relief or larger surgical procedures, with options for patient-controlled analgesia [12, 13]. A central nervous system blockade (such as spinal/epidural) may be used in settings where a proximal blockade is desired but minimizes the risk of nerve injury or prolonged motor recovery.

Peripheral nerve blocks are not without risk. Perioperative neurologic symptoms, while infrequent, can be disconcerting to the patient and slow recovery. Permanent neurologic injuries of the femoral and sciatic nerves have been described and have resulted in litigation [14, 15]. Therefore, it is our practice to discuss the planned incisions and procedure with the anesthesia team and recommend the most distal block that would be effective. We avoid use of femoral and sciatic blocks in our athletes. Other rare complications include local anesthetic systemic toxicity, seizure, bleeding, and infection (most commonly with indwelling catheters) [16, 17].

Non-Opioid Pain Medications

In addition to a neural blockade, when indicated, the first-line management of surgical pain should include non-opioid pain medications, avoiding the deleterious side effect profile of opiates. In many cases, these medications can result in avoidance of opioids altogether.

Unless medically contraindicated, acetaminophen is a reliable first-line analgesic and can be safely combined with a number of other medications. While it has been in use since the 1800s, its mechanism of action remains an area of study [18]. Acetaminophen has been shown to affect the cyclooxygenase (COX) pathway by inhibiting COX enzymes, reducing inflammation; however, its main analgesic effects may be at other sites such as the receptors TRPV1 and cannabinoid 1 [19, 20]. Furthermore, acetaminophen has effects on the descending serotonergic pathways, which have been implicated in reducing pain through a prostaglandin E2 receptor. Serotonergic cell bodies in the nucleus raphe magnus send axons to the dorsal horn of the spinal cord, where pain regulation occurs. Although addiction has not been observed, acetaminophen is not without risks. At high concentrations, as it enters the liver, hepatocytes metabolize the drug by components

▶ **Fig. 1** Perioperative management considerations in the collegiate athlete. TENS: transcutaneous electrical nerve stimulation.

of the cytochrome P450 system to a reactive intermediate, *N*-acetyl-*p*-benzoquinone imine [21]. High NAPQI depletes cellular glutathione stores, and the resulting byproducts damage components of the electron transport chain, including ATP synthase. This process leads to formation of free radicals, damaging liver cells [22]. Consequently, acetaminophen dosage needs to be monitored and kept under 150 mg/kg or 4 g/day for adults. Furthermore, collegiate athletes should be screened for and counseled regarding hepatotoxicity as it relates to alcohol and illicit substance use concurrent with acetaminophen. It is not recommended to combine alcohol with acetaminophen, and patients with non-alcoholic fatty liver disease are also at risk of hepatotoxicity at standard doses [23, 24].

Nonsteroidal anti-inflammatory drugs (NSAIDS) are another useful adjunct for treatment of inflammatory pain in the perioperative setting. These drugs can help to reduce swelling and inflammation in addition to providing some analgesic effect. The analgesic effects of NSAIDs are due to the inhibition of the enzymes that synthesize prostaglandins. Additionally, they may influence prostaglandin function after translation. The primary effect involves inhibition of the cyclooxygenase COX-2 [25]. Cyclooxygenases convert arachidonic acid into prostaglandin, which is often a key molecule in pain pathways [26]. An overdose of NSAIDs can impact kidney health, but is mainly more common in older patients over 65 years of age [27]. Even in these cases, damage to the kidney is rare (1 %) following a 15-day treatment period. Since arachidonic acid metabolites and prostaglandins play a role in several systems, some complications, though rare, can occur in maintaining renal blood flow, electrolyte balance, and platelet function [28]. Interestingly, NSAIDs may slow healing in some cases. A combination of human and animal studies showed that soft tissue healing was disrupted specifically with respect to tenocyte proliferation, collagen glycosaminoglycan synthesis, and soft tissue healing in general [29]. However, in the clinical setting, the use of NSAIDS after orthopedic surgery remains controversial [30, 31]. It is our practice to provide NSAIDS post-operatively in all settings except those prone to nonunion, such as osteotomies about the knee or scaphoid fractures.

NSAIDs may be critical for post-operative pain protocols that allow minimal use of opioids. A combination of acetaminophen with an NSAID has been shown to be superior to most other non-opioid treatments [32]. In some cases they can be used as an alternative to opioids or can allow opioid use to be minimized after injury or surgery. A combination of treatments including neuraxial and peripheral nerve block with NSAIDs can be used for surgical patients to further decrease opioid use [33]. A meta-analysis study showed that when the NSAID ketorolac was administered after knee arthroscopy resulted in lower pain scores at one and two hours postoperatively and increased the time before additional analgesics were required [33]. These multimodal approaches could prove useful for decreasing the need for treatment with opioids.

The use of gabapentin has become popular in multimodal pain regimens in the last decade. This drug is structurally related to GABA, but functionally works through unrelated pathways. The mechanism of action is linked to the calcium channel subunit α2δ-1. Overexpression of this voltage-gated channel results in presynaptic and postsynaptic NMDAR activity at spinal dorsal horn neurons. The resulting pain perception can be blocked when this channel is knocked down. It appears that gabapentin inhibits trafficking of α2δ-1-NMDAR complexes, which then decreases the associated pain signaling [34]. Prevalence of gabapentin misuse in the general population has been reported to be 1 %. Of that group, 40–65 % were among individuals with prescriptions. Nearly 22 % of abusers also abused opiates [35]. As seen in other multimodal approaches, use of gabapentin can help to minimize opioid use. For example, in one study of a mixed surgical cohort, perioperative use of gabapentin resulted in decreased opiate consumption and early opiate cessation following surgery [36]. In cases of ACL reconstruction, oral gabapentin taken preoperatively also resulted in a decreased need for opioid use postoperatively [37]. As with NSAIDs discussed earlier, gabapentin can be a used to limit the need for opioids and avoid the potential consequences of long-term opioid use.

Opioid Pain Medications

Opioids work by binding to the mu, kappa, and delta opioid receptors. Euphoric feelings and decrease in pain are mainly related to the mu receptor. Symptoms related to dysphoria are related to kappa receptors. Delta receptors have a role in decreasing pain perception, often through influencing mu opioid receptors [38]. Opioids binding in the periaqueductal gray region can inhibit descending pain processing pathways. In dorsal ganglion cells, opioids can inhibit pain signaling on the ascending pathway to the brain. Over time, the pleasant effects can decrease, with an increase in physiologic dependency.

Although they provide relief from pain, opioids bring significant risk of addiction and overdose in some patients [39]. In the US, opioid-related hospitalizations increased 64 % between 2005 and 2014 [40]. In 2016, there was a 27 % increase in death rates from opioid overdoses from the previous year [41]. Patients with prior opiate use and those with underlying mental health diagnoses have increased the likelihood of prolonged opiate use after surgery [41–

43]. Risk factors for opiate related morbidity and mortality have also been shown to include substance use disorder (in particular, prior opiate use or cocaine use), psychiatric illness, and male sex [44, 45]. In the collegiate population, prior use of opioids as a high school athlete correlated with long term misuse of opioids with an AOR of 1.36 to 1.43 depending on the number of sports played [46]. Additionally, these students were more likely to be involved in giving opioids to other college students for potential recreational use. Given the risk associated with these behaviors, multimodal treatment that minimizes postoperative opioids should be strongly considered in younger patients.

Non-Pharmacologic Pain Management

Non-pharmacological modalities to manage post-surgical pain have also been studied. TENS (transcutaneous electrical nerve stimulator) has been studied to treat both acute and chronic pain [42–44]. TENS application may result in neural sensory gating or may affect the perception of pain through another mechanism [31]. In randomized studies examining the use of TENS for post-operative pain management, there are mixed results [45–48]. However, TENS is commonly employed in our training room for post-operative pain management in the collegiate athlete population.

Other non-pharmacological options include icing, compression, and elevation. Cryotherapy can reduce tissue temperature to levels that are optimal for therapy. Evidence supporting this and the exact mechanisms that make icing useful are debatable. In a controlled study, however, some benefits have been noted. Cold, thought to cause vasoconstriction, was able to decrease swelling, as shown following ankle injuries [49]. This decrease in swelling appeared to be due to intermittent application of icing. Continuous application has been associated with increased swelling due to localized tissue damage from the low temperatures and intermittent application seems to prevent such damage. Following intermittent application of ice, patients also reported a decrease in pain, specifically during activity, but there is little evidence of any additional benefit [49]. Similarly, there is little support for compression and elevation, although the effects may depend on the site of injury. Most work has been done in ankle injuries as well as other joints. In these cases, data on pain, swelling, mobility, return to sports, return to work, and patient satisfaction are largely inconclusive [49]. There may be some patients that benefit, however, and decisions should be made on a case-by-case basis. In the training room, combined ice-compression units are commonly used to improve pain, and this may be most helpful in the lower extremities based on available evidence [50, 51].

Sleep and Perioperative Recovery

An overlooked consideration is sleep during recovery. For example, fracture healing time has been shown to increase following sleep deprivation in animal models [52]. Both pharmacological and non-pharmacological interventions can influence sleep. One consideration is the influence of light on circadian rhythms. Patients may benefit from exposure to light during the day to improve quality of sleep at night as this sets the sleep wake cycle [53]. In a related way, it would be useful to avoid artificial light towards the end of the day. In terms of pharmacology, avoidance of caffeine later in the day can help maintain sleep cycles.

Pharmacological interventions to improve sleep include benzodiazepines, zolpidem (Ambien) melatonin, and gabapentin. Benzodiazepines bind to GABA receptors at sites between α- and γ-subunits to increase receptor activity (and conduction of chloride ions). This inhibition relies on producing a negative voltage or clamping the membrane potential to that of GABA channels, which ultimately can promote sleep. Zolpidem binds to specific α1 subunits sites of GABA receptors, increasing the ability of the receptor to inhibit neural activity. Similar to benzodiazepines, it increases the ability to sleep by increasing the inhibitory influence of GABA [54]. Melatonin, produced by the pineal gland, can promote sleep by regulating the sleep wake cycle. Although it usually builds up during the day, taking additional melatonin can help to initiate the sleep part of the cycle. Gabapentin, discussed earlier as an analgesic can also influence sleep [55]. Its effects on calcium channels can increase slow wave sleep, which contributes to how effecting a period of sleep can be. Overall, these approaches to improving sleep can produce benefits in the healing process. Generally, non-pharmacological approaches are preferred, but when needed, pharmacological treatment can be added to improve a patient's ability to sleep as they heal.

Perioperative Nutrition Support

Nutrition must be maintained at a sufficient level when an athlete is injured. It is essential to find the right balance as their rigorous exercise routine is temporarily curbed. Lack of adequate energy will lead to fatigue and muscle depletion, whereas excess energy will generate fat [56].

The goal for an injured athlete during their time off from training is to minimize muscle loss, for which simultaneous protein and carbohydrate intake is essential [56]. Adequate protein intake provides the amino acids required for essential protein metabolism aimed at muscle protein synthesis. However, it is also important to maintain a baseline carb supply because insulin and leucine together produce a synergistic effect on protein synthesis [57]. In the absence of carbs, the body has to break down muscle glycogen to use for energy. In the presence of carbs, the body can break down carbs for energy and use protein to build muscle. Protein absorption in the body has many other benefits including healing wounds, repairing broken bones, building healthy blood cells, supporting immune system function. A non-training athlete should aim for 20–40 grams of protein intake every 3–4 hrs. It is favorable to consume proteins high in leucine for quick digestion during the day, and proteins high in casein for slow digestion prior to bed. Another area of interest related to protein balance is collagen supplementation [58]. Targeted supplementation with collagen peptides has been shown in some studies to affect collagen synthesis, reduce pain, and improve functional outcomes; however further controlled studies are needed to determine the role of collagen peptide supplementation in the perioperative period [59–62].

Nutrition also plays a significant role in wound-healing. The first phase of wound-healing is inflammation, which serves to eliminate toxic agents at the lesion and restore tissue homeostasis [63]. It is typically characterized by heat, redness, pain, swelling, and fever [64]. Athletes should incorporate foods high in omega-3 fatty acids, vitamin D, antioxidants, nitrate, and fluids to reduce inflammation through their diet. Experts may also recommend supplemental vitamins for specific types of injury. As previously mentioned, dietary protein sources high in leucine are commonly used in response to muscle injuries as it stimulates muscle protein synthesis and reduces muscle breakdown. Joint injuries are commonly treated with glucosamine and chondroitin which support growth and repair of connective tissue. In the case of tendon and ligament injuries, nitric oxide and vitamin C are used to stimulate collagen synthesis to speed healing of damaged soft tissue. Nutritional supplements for bone injuries include calcium to give bone structure and strength, and vitamin D to aid calcium absorption.

In addition to its importance to energy balance and muscle recovery, nutrition may also play a role with regard to pain and inflammation. Inflammatory pathways are mediated by omega fatty acids (FAs). In particular, Western diets tend to be higher in omega-6 FAs than omega-3 FAs [64]. Linoleic acid is the main fatty acid related to omega-6 and stimulates inflammation [65]. Therefore, dietary intake of foods containing the most potent omega-3 FAs (EPA & DHA) and supplementation with omega-3 FAs can be considered during the post-operative period for pain management [64, 65]. While mainly studied in chronic pain settings, a Mediterranean diet may be beneficial during this period as an adjunct for pain management [66, 67]. Vitamin deficiencies have also been implicated in pain perception. Low levels of vitamin D are associated with increased central hypersensitivities, and pain improvements have been shown with supplementation [68]. Therefore, in addition to evaluating vitamin D for the reasons mentioned above, it should also be evaluated and appropriately supplemented if low [69]. Deficiencies of vitamin B12 are also known to contribute to neurologic dysfunction and chronic pain [69]. While deficiency is uncommon with a Western or Mediterranean diet, vegetarians, vegans, those athletes with malabsorption problems such as celiac disease or Crohn's disease may need supplementation [70]. Ginger and curcumin (the active compound in turmeric) also have strong anti-inflammatory properties and work by disrupting the COX-2 pathway described above [71]. Dietary intake and supplemental forms can be considered during the post-op period as an adjunct to other methods of pain management [72, 73].

Finally, hydration is important to promote regular bowel movements and alleviate medication-induced constipation [74]. Additionally, there appears to be a correlation with hydration status and pain levels, related to central sensitization [75, 76]. These findings are preliminary and should be researched further.

Psychological Considerations in the Injured Athlete

While exercise and sport is expected to boost mood and self-esteem, athletes may face other factors that put them at risk for depression including injury, performance failure, and overtraining [77, 78]. The greatest limitation on studies that assess rates of depression among athletes is reliance on self-reporting. Literature comparing rates of depression symptoms between athletes and nonathletes thus far has not produced consistent results [79]. However, studies have shown significantly higher rates of depression symptoms in athletes following injury [79].

Athletes typically undergo a variety of emotional responses in response to being injured. These feelings include sadness, frustration, anger, lack of motivation, lowered self-esteem [80]. The stress can manifest itself as depression, as they have just had something they love to do taken away from them. Often the sport itself is an outlet and escape from other emotional stresses, so inability to participate can worsen the athlete's mental state. Fear and anxiety may set in, as the athlete worries about the uncertainty of their future and losing their competitiveness as they fall behind in training relative to their peers [81]. A comparative systematic review on mental health responses of collegiate athletes following either musculoskeletal or concussive injury sustained that athletes from both groups exhibited depressive and/or anxiety symptoms at various time points post-injury and returned to play before psychological symptoms returned to baseline [82].

There are challenges in access to mental health care for athletes. The first is the stigma attached to mental health within the sport context. Athletes are praised for their "mental toughness" and so may be less likely to engage in dialogue about their issues [75]. Even once an athlete comes forward, there may be limited access to resources. While Division 1 athletics departments commonly employ full-time athletic trainers, in-house sports medicine physicians, and dietitians, not many employ licensed psychologists [78]. Often this results in reliance on campus counseling centers, which typically do not have a psychologist with adequate training to meet a student athlete's specific needs. Furthermore, there is a lack of training models for mental health providers in the domain sport psychology as there are only few programs that offer graduate coursework in this area [79]. Sport organizations can begin to address such challenges by hiring more full-time mental health professionals embedded within the organization to work directly with athletes, coaches, and staff. An immersive experience is important for the licensed psychologist to better understand the external stressors, motivations, and dynamics within collegiate athletics and thus be better able to provide care [80–81]

In this time of psychological distress, the athlete requires social and emotional support. Maintaining confidence is crucial for the athlete, and this may require external support as confidence can easily plummet during injury. The Sport Psychology and Leadership team can work with athletes on adjusting expectations and setting achievable goals. This allows the athlete to have successes, which helps to boost confidence. The athlete should also focus on self-progress rather than comparison with others. Focusing on self-progress allows the athlete to feel themselves moving in a forward direction, closer to being back in the game [82]. The athlete may also try to practice imagery, a form of multi-sensory visualization. This is a tactic used to elevate confidence, in which the athlete tries to see, hear, and feel success. At the time of return to play, the athlete may feel significant pressure due to fear of not meeting both self-imposed and external expectations. Dale notes that a key component of managing this pressure is to train the athlete to be motivated to pursue success. He says it is not uncommon for athletes returning from injury to find themselves preoccupied with avoiding failure. This mindset results in tentative, poor performance. By contrast, an athlete who is motivated to pursue success typically exhibits a more aggressive, confident, and successful performance. This is a critical distinction between two mindsets for athletes who are returning to competition post-injury.

Conclusion

A multi-faceted approach is paramount to optimizing post-operative recovery in collegiate athletes. Implementing a multimodal pain management approach that includes peripheral nerve blocks, non-opiate medications such as NSAIDS, acetaminophen, and gabapentin, and non-pharmacologic interventions can help minimize reliance on opiate pain medication. Institutional resources should be harnessed to support athletes in their well-being from a nutritional, psychological, and sleep standpoint. Critical to success is communication among team members and with the athlete and family to address pain and stress management and encourage timely, safe return to play.

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Conflict of Interest

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References

[1] Allen LH. Causes of vitamin B12 and folate deficiency. Food Nutr Bull 2008; 29: 35–27

[2] Boyd C, Crawford C, Berry K et al. Conditional recommendations for specific dietary ingredients as an approach to chronic musculoskeletal pain: Evidence-based decision aid for health care providers, participants, and policy makers. Pain Med 2019; 20: 1430–1448

[3] Wang D, Rugg CM, Mayer E et al. Precollegiate knee surgery predicts subsequent injury requiring surgery in NCAA athletes. Am J Sports Med 2016; 44: 2023–2029

[4] Taree A, Charen D, Huang HH et al. Analysis of surgery rates among 25 national collegiate athletic association sports. Phys Sportsmed 2022; 50: 30–37

[5] Bleakley CM, McDonough SM, MacAuley DC et al. Cryotherapy for acute ankle sprains: a randomised controlled study of two different icing protocols. Br J Sports Med 2006; 40: 700–705

[6] Bischoff-Kont I, Fürst R. Benefits of ginger and its constituent 6-shogaol in inhibiting inflammatory processes. Pharmaceuticals (Basel) 2021; 14: 571

[7] Cashman JN. The mechanisms of action of NSAIDs in analgesia. Drugs 1996; 52: 13–23

[8] Chen J, Li L, Chen SR et al. The α2δ-1-nmda receptor complex is critically involved in neuropathic pain development and gabapentin therapeutic actions. Cell Rep 2018; 22: 2307–2321

[9] Baron JE, Khazi ZM, Duchman KR, Westermann RW et al. Risk factors for opioid use after patellofemoral stabilization surgery: A population-based study of 1,316 cases. Iowa Orthop J 2020; 40: 37–45

[10] Brady JE, Giglio R, Keyes KM et al. Risk markers for fatal and non-fatal prescription drug overdose: a meta-analysis. Inj Epidemiol 2017; 4: 24

[11] Cordain L, Eaton SB, Sebastian A et al. Origins and evolution of the Western diet: health implications for the 21st century. Am J Clin Nutr 2005; 81: 341–354

[12] Bauman NJ. The stigma of mental health in athletes: are mental toughness and mental health seen as contradictory in elite sport? BJSM 2016; 50: 135–136

[13] Basu P, Maier C, Basu A. Effects of curcumin and its different formulations in preclinical and clinical studies of peripheral neuropathic and postoperative pain: A comprehensive review. Int J Mol Sci 2021; 22: 4666

[14] Collier M. Understanding wound inflammation. Nurs Times 2003; 99: 63–64

[15] Lee LA, Posner KL, Domino KB et al. Injuries associated with regional anesthesia in the 1980s and 1990s: A closed claims analysis. Anesthesiology 2004; 10: 143–152

[16] Tran DQ, Salinas FV, Benzon HT et al. Lower extremity regional anesthesia: essentials of our current understanding. Reg Anesth Pain Med 2019. DOI:10.1136/rapm-2018-000019

[17] Neal JM, Barrington MJ, Brull R et al. The Second ASRA Practice Advisory on Neurologic Complications Associated With Regional Anesthesia and Pain Medicine: Executive Summary 2015. Reg Anesth Pain Med 2015; 40: 401–430

[18] Bear T, Philipp M, Hill S et al. A preliminary study on how hypohydration affects pain perception. Psychophysiology 2016; 53: 605–610

[19] Anderson BJ. Paracetamol (acetaminophen): mechanisms of action. Paediatr Anaesth 2008; 18: 915–921

[20] Ohashi N, Kohno T. Analgesic effect of acetaminophen: A review of known and novel mechanisms of action. Front Pharmacol 2020; 11: 580289

[21] Ramachandran A, Jaeschke H. Acetaminophen toxicity: Novel insights into mechanisms and future perspectives. Gene Expr 2018; 18: 19–30

[22] Allen LH. Causes of vitamin B12 and folate deficiency. Food Nutr Bull 2008; 29: 35–27

[23] Radi ZA, Khan KN. Cardio-renal safety of non-steroidal anti-inflammatory drugs. J Toxicol Sci 2019; 44: 373–391

[24] Nash DM, Markle-Reid M, Brimble KS et al. Nonsteroidal anti-inflammatory drug use and risk of acute kidney injury and hyperkalemia in older adults: a population-based study. Nephrol Dial Transplant 2019; 34: 1145–1154

[25] Ghosh N, Kolade OO, Shontz E et al. Nonsteroidal anti-inflammatory drugs (NSAIDs) and their effect on musculoskeletal soft-tissue healing: A scoping review. JBJS Rev 2019; 7: e4

[26] Duchman KR, Lemmex DB, Patel SH et al. The effect of non-steroidal anti-inflammatory drugs on tendon-to-bone healing: A systematic review with subgroup meta-analysis. Iowa Orthop J 2019; 39: 107–119

[27] Marquez-Lara A, Hutchinson ID, Nuñez F Jr. et al. Nonsteroidal anti-inflammatory drugs and bone-healing: A systematic review of research quality. JBJS Rev 2016; 4: e4

[28] Martinez V, Beloeil H, Marret E et al. Non-opioid analgesics in adults after major surgery: systematic review with network meta-analysis of randomized trials. Br J Anaesth 2017; 118: 22–31

[29] Gabriel RA, Swisher MW, Sztain JF et al. State of the art opioid-sparing strategies for post-operative pain in adult surgical patients. Expert Opin Pharmacother 2019; 20: 949–961

[30] Smith RV, Havens JR, Walsh SL. Gabapentin misuse, abuse and diversion: a systematic review. Addiction 2016; 111: 1160–1174

[31] Hah J, Mackey SC, Schmidt P et al. Effect of perioperative gabapentin on postoperative pain resolution and opioid cessation in a mixed surgical cohort: A randomized clinical trial. JAMA Surg 2018; 153: 303–311

[32] Secrist ES, Freedman KB, Ciccotti MG et al. pain management after outpatient anterior cruciate ligament reconstruction: A systematic review of randomized controlled trials. Am J Sports Med 2016; 44: 2435–2447

[33] Varga EV, Navratilova E, Stropova D et al. Agonist-specific regulation of the delta-opioid receptor. Life Sci 2004; 76: 599–612

[34] Kaye AD, Jones MR, Kaye AM et al. Prescription opioid abuse in chronic pain: An updated review of opioid abuse predictors and strategies to curb opioid abuse: Part 1. Pain Physician 2017; 20: 93–109

[35] Lyden J, Binswanger IA. The United States opioid epidemic. Semin Perinatol 2019; 43: 123–131

[36] Seth P, Scholl L, Rudd RA, Bacon S. Overdose deaths involving opioids, cocaine, and psychostimulants — United States, 2015–2016. MMWR Morb Mortal Wkly Rep 2018; 67: 349–358

[37] Gil JA, Gunaseelan V, DeFroda SF et al. Risk of prolonged opioid use among opioid-naïve patients after common shoulder arthroscopy procedures. Am J Sports Med 2019; 47: 1043–1050

[38] Moutzouros V, Jildeh TR, Khalil LS et al. A multimodal protocol to diminish pain following common orthopedic sports procedures: Can we eliminate postoperative opioids? Arthroscopy 2020; 36: 2249–2257

[39] Lawal OD, Gold J, Murthy A et al. Rate and risk factors associated with prolonged opioid use after surgery: A systematic review and meta-analysis. JAMA Netw Open 2020; 3: e207367

[40] Veliz P, Epstein-Ngo Q, Austic E et al. Opioid use among interscholastic sports participants: an exploratory study from a sample of college students. Res Q Exerc Sport 2015; 86: 205–211

[41] Johnson MI. Resolving Long-standing uncertainty about the clinical efficacy of transcutaneous electrical nerve stimulation (TENS) to relieve pain: A comprehensive review of factors influencing outcome. Medicina (Kaunas) 2021; 57: 378

[42] Martimbianco ALC, Porfírio GJ, Pacheco RL et al. Transcutaneous electrical nerve stimulation (TENS) for chronic neck pain. Cochrane Database Syst Rev 2019; 12: CD011927

[43] Vance CG, Dailey DL, Rakel BA et al. Using TENS for pain control: the state of the evidence. Pain Manag 2014; 4: 197–209

[44] Elboim-Gabyzon M, Andrawus Najjar S, Shtarker H. Effects of transcutaneous electrical nerve stimulation (TENS) on acute postoperative pain intensity and mobility after hip fracture: A double-blinded, randomized trial. Clin Interv Aging 2019; 14: 1841–1850

[45] Forogh B, Aslanpour H, Fallah E et al. Adding high-frequency transcutaneous electrical nerve stimulation to the first phase of post anterior cruciate ligament reconstruction rehabilitation does not improve pain and function in young male athletes more than exercise alone: A randomized single-blind clinical trial. Disabil Rehabil 2019; 4: 514–522

[46] Mahure SA, Rokito AS, Kwon YW. Transcutaneous electrical nerve stimulation for postoperative pain relief after arthroscopic rotator cuff repair: a prospective double-blinded randomized trial. J Shoulder Elbow Surg 2017; 26: 1508–1513

[47] Rakel BA, Zimmerman BM, Geasland K et al. Transcutaneous electrical nerve stimulation for the control of pain during rehabilitation after total knee arthroplasty: A randomized, blinded, placebo-controlled trial. Pain 2014; 155: 2599–2611

[48] Van den Bekerom MP, Struijs PA, Blankevoort L et al. What is the evidence for rest, ice, compression, and elevation therapy in the treatment of ankle sprains in adults? J Athl Train 2012; 47: 435–443

[49] Hubbard TJ, Denegar CR. Does cryotherapy improve outcomes with soft tissue injury? J Athl Train 2004; 57: 278–279

[50] Kunkle BF, Kothandaraman V, Goodloe JB et al. Orthopedic application of cryotherapy: A comprehensive review of the history, basic science, methods, and clinical effectiveness. JBJS Rev 2021; 9: e220. 00016

[51] Xu X, Wang R, Sun Z et al. Trehalose enhances bone fracture healing in a rat sleep deprivation model. Ann Transl Med 2019; 7: 297

[52] Tamrat R, Huynh-Le MP, Goyal M. Non-pharmacologic interventions to improve the sleep of hospitalized patients: a systematic review. J Gen Intern Med 2014; 29: 788–795

[53] Wisden W, Yu X, Franks NP. GABA receptors and the pharmacology of sleep. Handb Exp Pharmacol 2019; 253: 279–304

[54] Lo HS, Yang CM, Lo HG et al. Treatment effects of gabapentin for primary insomnia. Clin Neuropharmacol 2010; 33: 84–90

[55] Papadopoulou SK. Rehabilitation nutrition for injury recovery of athletes: The role of macronutrient intake. Nutrients 2020; 12: 2449

[56] Figueiredo VC, Cameron-Smith D. Is carbohydrate needed to further stimulate muscle protein synthesis/hypertrophy following resistance exercise? J Int Soc Sports Nutr 2013; 10: 42

[57] Shaw G, Serpell B, Baar K. Rehabilitation and nutrition protocols for optimising return to play from traditional ACL reconstruction in elite rugby union players: A case study. J Sports Sci 2019; 37: 1794–1803

[58] Shaw G, Lee-Barthel A, Ross ML et al. Vitamin C-enriched gelatin supplementation before intermittent activity augments collagen synthesis. Am J Clin Nutr 2017; 105: 136–143

[59] Praet SFE, Purdam CR, Welvaert M et al. Oral supplementation of specific collagen peptides combined with calf-strengthening exercises enhances function and reduces pain in Achilles tendinopathy patients. Nutrients 2019; 11: 76

[60] Zdzieblik D, Oesser S, Gollhofer A et al. Improvement of activity-related knee joint discomfort following supplementation of specific collagen peptides. Appl Physiol Nutr Metab 2017; 42: 588–595

[61] Dressler P, Gehring D, Zdzieblik D et al. Improvement of functional ankle properties following supplementation with specific collagen peptides in athletes with chronic ankle instability. J Sports Sci Med 2018; 17: 298–304

[62] Cordain L, Eaton SB, Sebastian A et al. Origins and evolution of the Western diet: health implications for the 21st century. Am J Clin Nutr 2005; 81: 341–354

[63] Dragan S, Șerban MC, Damian G et al. Dietary patterns and interventions to alleviate chronic pain. Nutrients 2020; 12: 2510

[64] Ramsden CE, Faurot KR, Zamora D et al. Targeted alteration of dietary n-3 and n-6 fatty acids for the treatment of chronic headaches: a randomized trial. Pain 2013; 154: 2441–2451

[65] Field R, Pourkazemi F, Turton J et al. Dietary interventions are beneficial for patients with chronic pain: A systematic review with meta-analysis. Pain Med 2021; 22: 694–714

[66] Sköldstam L, Hagfors L, Johansson G. An experimental study of a Mediterranean diet intervention for patients with rheumatoid arthritis. Ann Rheum Dis 2003; 62: 208–214

[67] Ghai B, Bansal D, Kanukula R et al. Vitamin D supplementation in patients with chronic low back pain: An open label, single arm clinical trial. Pain Physician 2017; 20: 99–105

[68] Julian T, Syeed R, Glascow N et al. B12 as a treatment for peripheral neuropathic pain: A systematic review. Nutrients 2020; 12: 2221

[69] Pawlak R, Parrott SJ, Raj S et al. How prevalent is vitamin B(12) deficiency among vegetarians? Nutr Rev 2013; 71: 110–117

[70] Zhang YM, Shen J, Zhao JM et al. Cedrol from ginger ameliorates rheumatoid arthritis via reducing inflammation and selectively inhibiting JAK3 phosphorylation. J Agric Food Chem 2021; 69: 5332–5343

[71] Gaffey A, Slater H, Porritt K et al. The effects of curcuminoids on musculoskeletal pain: a systematic review. JBI Database System Rev Implement Rep 2017; 15: 486–516

[72] Zhu Q, Sun Y, Yun X et al. Antinociceptive effects of curcumin in a rat model of postoperative pain. Sci Rep 2014; 4: 4932

[73] Prichard D, Norton C, Bharucha AE. Management of opioid-induced constipation. Br J Nurs 2016; 25: 8–11

[74] Carr C, Davidson J. Mind, Body and Sport: The psychologist perspective. NCAA. Available from: https://www.ncaa.org/sports/2014/11/3/mind-body-and-sport-the-psychologist-perspective.aspx. Accessed August 4, 2021

[75] Parker J, Heinking KP, Kappler RE. Efficacy of osteopathic manipulative treatment for low back pain in euhydrated and hypohydrated conditions: A randomized crossover trial. J Am Osteopath Assoc 2012; 112: 276–284

[76] Putukian M. The psychological response to injury in student athletes: A narrative review with a focus on mental health. Br J Sports Med 2016; 50: 145–148. Epub 2015

[77] Purcell R, Gwyther K, Rice SM. Mental health in elite athletes: Increased awareness requires an early intervention framework to respond to athlete needs. Sports Med Open 2019; 5: 46

[78] Wolanin A, Gross M, Hong E. Depression in athletes: Prevalence and risk factors. Curr Sports Med Rep 2015; 14: 56–60

[79] Tracey J. The emotional response to the injury and rehabilitation process. J Appl Sport Psychol 2003; 15: 279–293

[80] Rondanelli M, Faliva MA, Miccono A et al. Food pyramid for subjects with chronic pain: foods and dietary constituents as anti-inflammatory and antioxidant agents. Nutr Res Rev 2018; 31: 131–151

[81] Sabol J, Kane C, Wilhelm MP et al. the comparative mental health responses between post-musculoskeletal injury and post-concussive injury among collegiate athletes: A systematic review. Int J Sports Phys Ther 2021; 16: 1–11

[82] Smith RV, Havens JR, Walsh SL. Gabapentin misuse, abuse and diversion: a systematic review. Addiction 2016; 111: 1160–1174