Anticoagulation and antiplatelet therapy in contact sports: is it career limiting?

Asim Kichloo ,[1,2] Rawan Amir,[3] Farah Wani ,[2] Sukhbir Randhawa,[2] Benjamin Rudd,[2] David Rechlin[2]

[1]Internal Medicine, CMU Medical Education Partners, Saginaw, Michigan, USA
[2]Department of Family/Internal Medicine, Samaritan Medical Center, Watertown, New York, USA
[3]Internal Medicine, University of Maryland Baltimore, Baltimore, Maryland, USA

Correspondence to
Dr Asim Kichloo, CMU Medical Education Partners, Saginaw, MI 48602-5303, USA;
kichlooasim@gmail.com

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ABSTRACT

Medical conditions requiring treatment with anticoagulation (AC) or antiplatelet therapy have a huge burden on the average patient, but such conditions can have catastrophic effects on the careers of young, rising athletes, in particular those involved in contact sports at a professional level. Contact sports are defined as sports in which body-to-body contact is expected as part of the game such as football, basketball, soccer and hockey. The rates of injuries in these sports are high increasing the likelihood of bleeding event on AC. The main etiologies requiring AC and antiplatelets in athletes are venous thromboembolism and coronary artery disease, respectively. To date, there are no clear medical guidelines on the management of such conditions in athletes. Herein we review the traditional approach to treating such conditions afflicting athletes as well as more recently modified approaches to answer the ultimate question: should anticoagulation or antiplatelet therapy in contact sports be career limiting?

BURDEN OF VENOUS THROMBO-EMBOLI AND CORONARY ARTERY DISEASE IN ATHLETES

The burden of venous thromboembolism (VTE) in the general population is reported to be as high as 1 to 2 events per 1000 people.[1] The exact incidence in athletes in particular is not clear though. A retrospective review of injuries reported in male professional athletes of four major American sports leagues (National Hockey League (NHL), National Football League (NFL), Major League Baseball (MLB) and National Basketball Association (NBA)) from 1999 to 2016 revealed 55 VTE events.[2] These events were composed of 19 upper extremity deep venous thromboses (DVTs), 15 lower extremity DVTs, 15 pulmonary emboli (PE), and 6 combined DVTs and PEs. The average age of affected players was around 29 years and average time out of play was 6.7 months.[2] So, one might wonder, why are these young healthy athletes in their prime years suffering from VTEs? There are multiple theories behind this unfortunate health challenge which likely all contribute in varying degrees to this phenomenon. Some authors have postulated that increased travel in this profession contributes to VTE development, while others hypothesized that a VTE pre-disposition can be magnified by intense cardiovascular training, increased thrombogenic risk factors leading to a hypercoagulable status and ultimately VTEs in selected patients.[3 4] In addition, repeated traumas and immobilization after injuries also play a role in increased risk of VTEs in this population. Regardless of the exact pathogenesis, VTEs are a burden on these young athletes that can eventually lead to early retirement due to the associated risk of major bleed when maintained on anticoagulation (AC) and increased risk of VTE recurrence off AC. The high rate of injuries in these contact sports is of major concern as it increases the likelihood of major bleeding events on AC. The rate of injury during competitive soccer matches was found to be as high as 65.9 injuries per 1000 hours of exposure.[5] Another review of 2203 NFL players reported injuries of the ankle in 52.7%, shoulder 51.9%, knee 51.2%, spine 35.6% and hand 33.5%.[6] All these data exacerbate the fear of major bleeding events in professional athletes on AC. And despite increased awareness of VTE occurrence in athletes due to media coverage in more recent years, there are still no clear or comprehensive professional guidelines on how to approach this predicament. Traditional approach of AC as well as a modified approach which attempts to minimize impact of VTE on athletes' careers will be reviewed later.

In regards to antiplatelet therapy (APT), contrary to popular belief, athletes do suffer from coronary artery disease (CAD) requiring single antiplatelet therapy (SAPT) or dual antiplatelet therapy (DAPT). As a matter of fact, atherosclerotic CAD is the most common cause of sudden cardiac death (SCD) and acute myocardial infarctions in athletes above the age of 35 years.[5] Although the common conception that physical activity is associated with lower risk of cardiovascular disease is correct, intense physical exertion is puzzlingly associated with temporary increase in cardiovascular events and SCD.[6 7] Few reports concluded that elite athletes actually have higher coronary artery calcium scores than their counterparts.[8 9] Whether this has any correlation with CAD is not yet known as we lack any single or multicenter studies or any randomized controlled trials (RCTs). Just as

with AC, there are no clear guidelines on how to approach APT in athletes to date; however, some recommendations on how to tackle this dilemma were made by the American College of Cardiology (ACC) and the European Association of Preventive Cardiology (EAPC) which we will discuss in further detail later.[10 11]

TRADITIONAL APPROACH

Anticoagulation

Given the increased risk of major bleeds associated with AC, which is increased even further in the setting of contact sports, the traditional approach to athletes requiring AC was to simply remove them from active play as long as they were on AC. Typically, provoked VTEs were treated for 3 months while unprovoked VTEs required extended courses of AC. Athletes were encouraged to resume daily activities and non-contact light sports as early as 3 weeks post-VTE, while on AC. However, return to contact sports was never thoroughly studied and hence many players were automatically removed from play to avoid potential AC side effects. Although this method minimizes the risk of major bleeds and definitely puts physicians' minds at ease, it ends the futures of these young and ambitious athletes.

Antiplatelets

The approach to APT is also similar to AC where athletes were removed from play while on DAPT. In these patients with CAD, the degree of CAD activity also plays an important role in the decision of permanently side-lining players from the game.

MODIFIED APPROACH

Anticoagulation

In the past few years, the concept of intermittent AC was introduced as a means to allow athletes to resume play and practice sessions in contact sports during safer (lower) drug levels while maintaining higher drug levels in-between play.[12] This method allows lifelong AC without career limitation in these athletes. However, patients must be carefully selected for this regimen and, as we will outline in our discussion later, there are many knowledge gaps which need to be addressed before being able to safely implement this modified AC approach on a larger scale.

Patient selection

Intermittent AC is not an option for any and all players in contact sports. All players in the first 3 months post-VTE require full AC with no involvement in any contact sports. For athletes with provoked VTEs and no other indication for lifelong AC, contact sports can be resumed after completion of 3 months of AC with necessary VTE precautions to be taken. Athletes requiring lifelong AC will need to have a discussion with their physicians regarding different AC plans including traditional and modified regimens. The athlete's personal preference is the initial deciding factor, which route to take, yet there is much more than that which affects the decision of pursuing the modified AC route. Intermittent AC requires close follow-up with frequent blood draws requiring specific laboratory investigations; availability of these resources must be assured in order to even consider intermittent AC therapy. In addition, patients in contact sports with multiple weekly practices and games, such as those participating in American football, may not be candidates for this regimen due to lack of feasibility of discontinuing and resuming AC so frequently. Moreover, discussions will need to be made with athletes' team physician as well as their sponsors to assess their comfort level caring for an athlete on AC, as many are hesitant to accept such a non-traditional approach. All these factors influence one's ability to implement an intermittent AC regimen.

Drug selection

Classic vitamin K antagonists, such as warfarin, have a longer half-life and hence never allowed the introduction of the concept of intermittent AC; yet the quick on-and-off characteristics of direct oral anticoagulants (DOACs) have made this approach possible. No studies were done to favor a particular DOAC in such settings; however, a recent study concluded that prolonged thrombin inhibition was observed in patients taking 20 mg of rivaroxaban daily versus those on 10 mg of apixaban twice daily.[13] This may encourage physicians to use shorter-acting apixaban in intermittent AC regimens.

Individualized approach

The concept of intermittent AC is to have a player play at safer drug levels at which the risk of having a major bleed is equivalent to their athlete counterparts not on AC. Hence, it completely relies on identifying how long each athlete takes to clear the DOAC from their system. This can be identified using pharmacokinetic and pharmacodynamic (PK/PD) studies where athletes are instructed to take a DOAC and serial blood draws are done to monitor serum plasma drug levels (typically at hours 8, 12, 16 and 20); this in turn helps identify how long after taking a DOAC it takes the athlete to reach a drug level where bleeding risk is minimal and it is considered safe to partake in contact sports. It has been recommended to perform a second confirmatory PK/PD study due to observed intra-individual drug concentration variability, particularly with dabigatran.[12] Based on the results of PK/PD studies, an individualized AC regimen can be created for each athlete where lowest drug concentrations are targeted around play time, minimizing bleeding risk, and therapeutic drug levels are achieved immediately with resumption of AC once play and risk of trauma are over.

Timing of holding and resuming AC

As can be concluded from the discussion earlier, there is no clear-cut rule on when to discontinue or resume AC in athletes participating in contact sports. AC discontinuation relies heavily on athlete-specific PK/PD studies. When to resume AC is also a difficult question in this scenario as one cannot clearly distinguish when the risk of bleed is normalized post-trauma. Generally, it is considered acceptable to resume AC 1–2 hours after play without significant trauma; however, in the presence of trauma during play, AC therapy resumption will have to be delayed and expert opinion should be sought.[14]

Risk of recurrent VTE

The major concern with such an AC approach is recurrent VTE. When patients (non-athletes) with unprovoked VTEs were followed over time, it was estimated that the risk of developing recurrent VTE off AC was 10.4% in the first 6 months.[15] Fatal VTEs occurred at a rate of 0.3 per 100 patient-years in patients off AC.[16] Hence, it was extrapolated that the risk of recurrent non-fatal and fatal VTEs in athletes off AC were low at rates of 1 per 3500 per day and 1 per 100,000 per day, respectively.[14] Therefore, risk of non-fatal and fatal VTE recurrence in athletes on intermittent AC is expected to be very low. Although this looks favourable, but still without multicentered RCTs, the exact safety of this approach is not clear. However, risk of recurrent VTE in players with back-to-back games requiring prolonged holding of AC is unclear, and the safe duration for holding AC has not been identified.

Challenges with intermittent AC

The main challenge faced with intermittent AC lies in identifying "safe drug levels" where bleeding risk is minimal. This safe drug level has, in reality, not been identified due to lack of studies and RCTs. In addition, identifying this "safe drug level" will present a real challenge, if at all possible, due to large variabilities in interindividual drug processing and clearance. Reports of rivaroxaban's drug half-life ranged from 5.2 to 14.3 hours at a dose of 20 mg daily in healthy male volunteers, from 4.4 to 32 hours at a dose of 10 mg daily in healthy male volunteers, and from 6.9 to 11.7 hours at a dose of 10 mg daily in healthy male and female volunteers.[17 18] This large difference in drug half-life highlights the need for individual PK/PD studies and the inability to rely on a one-fit-for-all method in intermittent AC. The large amount of medical resources required to adequately plan and execute an individualized intermittent AC regimen per athlete presents a second challenge, making this method less feasible and more difficult to implement on a larger scale.

Antiplatelets

Unfortunately, there are extremely limited data published regarding antiplatelet therapy (APT) approach in athletes in general, let alone athletes participating in contact sports in particular. What we do know is that in this select patient population, APT, and even more so, underlying CAD, greatly impacts the decision to return to play.[10 11]

Current recommendations

Over the past few years, the ACC and EAPC published some general recommendations for the approach to CAD in athletes; luckily, these recommendations briefly addressed APT as well.[10 11] Current recommendations suggest that athletes should avoid contact sports while on DAPT. Yet after DAPT is complete, the decision to return to play is greatly based on the athlete's preference and risk category. If the athlete is deemed low risk for a recurrent cardiac event with normal exercise capacity, normal ejection fraction and no inducible ischemia or arrythmia, then return to any sport is allowed. However, if the athlete is considered high risk, such as those with inducible ischemia, abnormal left ventricular function, arrhythmias or significant myocardial fibrosis, then activity should be limited to low-intensity sports.

In regard to timeline of de-escalation of DAPT, newer data are shifting the approach from 12 months of DAPT post–percutaneous coronary intervention () to merely 1 month of DAPT post-PCI. In the non-inferiority randomized trial, there was a reduced risk of bleeding with no increase in ischemic events in patients who received prasugrel for 1 month only post-PCI versus those who completed a full year.[19] We suggest that this strategy be followed when treating professional athletes post-PCI as well to minimize bleeding risk and time out of play.

Reports are present of professional athletes who resumed play once stable on SAPT. Although we lack statistics identifying the number of professional athletes taking aspirin for secondary prevention of CAD, what we do know is that aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) are commonly taken by professional athletes for anti-inflammatory effects. In a review of 144 rising athletes in the National Collegiate Athletic Association (NCAA), 80% reported using ibuprofen while 71% reported using aspirin for pain relief.[20] Another review of 494 Finnish elite athletes revealed that 8.1% regularly use NSAIDs.[21] Despite the increased bleeding risk with these agents, the use of aspirin and/or NSAIDs has yet to be addressed by any specialized sports physician task force. And although risk of bleed on SAPT is lower than that on DAPT, there still is a need for RCTs to assess the safety of playing contact sports on SAPT.

CONCLUSION

AC and antiplatelet therapy have always presented a challenge when used in athletes, particularly those participating in contact sports. The traditional approach of removing athletes from active play has slowly seen a few developments, with the introduction of more modified methods of approaching these therapeutic regimens, particularly AC. The real question remains: should AC and APT in contact sports be career limiting? Put simply, the answer is still not clear. With the major advancements we are making in medicine, the need for an athlete to be on an anticoagulant or antiplatelet may not have to limit their career in contact sports. However, there is a dire need for trials to fill in the major gaps of knowledge before being able to safely and confidently allow athletes to return to contact sports on AC or APT.

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ORCID iDs
Asim Kichloo http://orcid.org/0000-0003-4788-8572
Farah Wani http://orcid.org/0000-0002-4683-6845

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