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American-Style Football and Cardiovascular Health

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To achieve success, whatever the job we have, we must pay a price.

—Vince Lombardi

American-style football (ASF) is the most popular organized team sport in the United States, with ≈1 million high school,[1] 70 000 collegiate,[2] and 2000 professional participants annually.[3,4] Although youthful competitive athletes are classically regarded as the paradigm of health and vitality, uncertainties surrounding the long-term health implications of ASF participation have recently become a topic of considerable interest and controversy.[5,6] Specifically, concerns about the impact of ASF participation on cardiovascular and neurocognitive health[7] have generated lively debates in the scientific literature, in the mainstream media, and within governing bodies that oversee ASF rules and regulations.

The physiology inherent in ASF participation is complex and differs from most other popular forms of sport. Factors including high loads of static hemodynamic stress, relatively low amounts of aerobic conditioning, deliberate body mass gain, psychological stress, and routine NSAID[8] use carry potential implications for cardiovascular health. In healthy nonathletic populations, early onset cardiovascular risk and attendant subclinical pathology at ages typical of ASF athletes predict later life cardiovascular morbidity and mortality.[9–11] Although this phenomenon has not been firmly established among ASF participants, a growing body of observational data documents associations among large body mass,[12,13] early life hypertension,[12,14] and subclinical pathologic cardiovascular phenotypes[15–18] in ASF athletes. In addition, epidemiologic outcomes data from former professional ASF athletes suggest accelerated cardiovascular mortality among former lineman-position players.[19,20] The precise relationship between early life ASF participation and subsequent cardiovascular health remains incompletely understood; however, multiple lines of evidence suggest that ASF participation may impart increased risk for the development of cardiovascular disease.

This review was constructed to delineate our contemporary understanding of cardiovascular health among ASF participants, a population that is commonly encountered in clinical cardiovascular practice. To do so, a comprehensive and broad scientific literature search targeting ASF and cardiovascular health was conducted. Studies matching this description were reviewed in detail and referenced in this review. The basic physiology accompanying ASF participation is initially discussed. Next, prior studies of high school, collegiate, and professional ASF cohorts that describe cardiovascular risk factor profiles, cardiovascular phenotypes, and outcomes data are detailed, along with an emphasis on key limitations of the currently available data. Finally, a framework for future research imperatives and clinical strategic approaches for cardiovascular specialists is proposed.

Basic Physiology of ASF Participation

The American College of Cardiology and American Heart Association physiologic sports classification algorithm defines ASF as a class 2B sport, a designation that implies a combination of moderate static and dynamic hemodynamic stress.[21] However, unlike most other team sports in which all athletes perform similar athletic tasks during training and competition and thus experience similar cardiovascular physiology, ASF athletes are a heterogeneous group. Simplistically, ASF athletes can be dichotomized by field position into men who play lineman field positions (ie, offensive center, guards, and tackles and defensive tackles and ends) and men who

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play nonlineman field positions (ie, receivers, running backs, quarterbacks, linebackers, cornerbacks, safeties, and kickers), with cardiovascular physiology during training and competition varying significantly as a function of this division. ASF athletes at the lineman field positions engage almost exclusively in short repetitive bursts of intense static activity both on the playing field (ie, tackling and blocking) and in the weight room. In contrast, nonlineman ASF athletes experience comparatively higher loads of dynamic physiology on the playing field and are more likely to include a high degree of aerobic conditioning during training. Divergent myocardial remodeling patterns that reflect the impact of these differences have been documented.[22,23]

Physiologic factors relevant to the cardiovascular health of ASF athletes extend beyond basic exercise physiology. Repetitive blunt trauma caused by player-to-player impact (ie, tackling and collisions) is an inherent component of ASF participation. To what degree the attendant deceleration forces within the thorax affect the cardiovascular system, particularly with respect to the aorta and adjacent great vessels, has not been rigorously examined. In addition, factors including the routine use of NSAIDs[8] and opioid-based analgesics, surreptitious use of performance-enhancing agents including but not limited to androgenic–anabolic steroids (AAS), and deliberate body weight gain[24] using high-calorie diets[25] are common within the ASF culture and remain incompletely understood with respect to cardiovascular health and disease. The potential impact of deliberate weight gain and long-term maintenance of high body mass, attributable to variable combinations of lean muscle mass and adipose tissue, is of particular interest. At the collegiate and professional levels of sport, lineman are substantially larger than their nonlineman counterparts, with body weights that routinely exceed 300 pounds.[12]

Cardiovascular Risk Factors Among ASF Participants

Among nonathletic cohorts, the prognostic implications of cardiovascular risk factors emerging early in life including obesity,[26] hypertension,[9,10] impaired glucose handling,[27] dyslipidemia,[28] and arterial stiffness[29] have been well established. Although comparable outcomes data among ASF participants are lacking, a growing body of literature describes analogous and, in some cases, more unfavorable cardiovascular risk factor profiles among similarly aged ASF athletes (Table 1).[30–34]

Obesity and Weight Gain

In normally active population cohorts, obesity is a strong independent predictor of incident cardiovascular disease.[35] In the general pediatric population, epidemiologic data obtained from separate cohorts of obese children and adolescents of various ethnicities and from separate geographic regions have also demonstrated increased cardiovascular disease mortality later in adulthood.[36–39] Similar to the observed data reported from adults, strong associations between increased body mass index (BMI; calculated as kg/m^2) and systolic blood

Table 1. Selected Studies Analyzing Cardiovascular Risk Among ASF Players

Study	Year	ASF Population	Participants, N	Key Findings
Baron and Rinsky[19]	1994	Retired Professional	6848	50% increased cardiovascular disease risk in linemen
George et al[30]	2003	Professional	52	34% prevalence of SDB (apnea–-hypopnea index ≥10)
Tucker et al[12]	2009	Professional	504	High prevalence of prehypertension and hypertension (75%)
Selden et al[31]	2009	Professional	69	Cardiometabolic syndrome prevalent among linemen
Hurst et al[32]	2010	Retired Professional	201	Presence of carotid artery plaque similar between retired players and BMI-matched healthy nonathletic controls
Rice et al[33]	2010	Professional	137	19% prevalence SDB (respiratory disturbance index ≥5)
Baron et al[20]	2012	Retired Professional	3439	50% increased cardiovascular mortality for those with playing-time BMI ≥30
Weiner et al[14]	2013	Collegiate freshman	113	High prevalence prehypertension and hypertension (61%) predicted by lineman position
Kim et al[16]	2015	Collegiate freshman	32	Seasonal longitudinal increase in central aortic pulse pressure
Crouse et al[34]	2016	Collegiate freshman	80	High prevalence of prehypertension and hypertension (74%)
Lin et al[17]	2016	Collegiate freshman	87	High prevalence of prehypertension and hypertension (63%)
Kim et al[18]	2017	Collegiate	40	55% prevalence of SDB (apnea–hypopnea index ≥5)

ASF indicates American-style football; BMI, body mass index; SDB, sleep disordered breathing.

pressure (SBP) have been demonstrated in large population-based pediatric studies such as NHANES III (Third National Health and Nutrition Examination Survey).[40]

Among ASF athletes at all levels of competition, the presence of BMI that, in the general population, would be characterized as obese (≥30) [41] is common as demonstrated by cross-sectional studies of high school[25] and collegiate ASF athletes.[42,43] In the largest reported cohort of professional ASF athletes (n=504), the mean BMI was 31.4 (95% confidence interval [CI], 31.3–31.6) with offensive linemen (37.8 [95% CI, 37.3–38.2]) and defensive linemen (35.7 [95% CI, 34.9–36.6]) demonstrating significantly higher BMI than athletes at nonlineman field positions.[12] A causal relationship between ASF participation and elevated BMI is suggested by several relatively short-duration longitudinal studies that consistently document weight gain, particularly among linemen, during a single season of collegiate ASF participation.[14,18] However, it must be emphasized that although BMI is a validated marker of cardiac risk in the general population, its prognostic significance among elite ASF athletes has not been similarly established. Further rigorous study designs focused on changes in body mass, as a function of both lean muscle and fat mass, will be necessary to determine the optimal anthropometric measures of body habitus that dictate cardiovascular risk among ASF athletes.

Impaired Glucose Tolerance

In the general population, obesity serves as an independent determinant of health outcomes and may simultaneously potentiate other risk factors including glucose intolerance and insulin resistance.[44] In contrast, it has also been well established that exercise training improves glucose tolerance both acutely and through chronic effects.[45] However, among ASF athletes, observational data characterizing glucose metabolism have produced mixed results. Small cross-sectional studies of collegiate ASF athletes report prevalence estimates of metabolic syndrome ranging from 9% to 49%, with obesity and participation at a lineman field position as independent risk determinants.[13,46,47] Cross-sectional prevalence studies of former professional ASF athletes also report higher fasting glucose levels among former linemen compared with nonlinemen and population-based controls.[48,49] Perhaps as a consequence of athletic training, a protective effect of active professional ASF participation is suggested by data from the previously referenced cross-sectional cohort study in which there was a lower prevalence of impaired fasting glucose among athletes compared with a control cohort derived from the CARDIA (Coronary Artery Risk Development in Young Adults) study (6.7% [95% CI, 4.6–8.7%] versus 15.5% [95% CI, 13.8–17.3%], $P<0.001$).[12]

Hypertension

Hypertension during young adulthood, the time period that coincides with competitive ASF participation, is a well-established independent risk factor for later life cardiovascular disease morbidity and mortality.[9,10,50] In the prospective Harvard Alumni Health Study of 18 881 male undergraduate participants, cardiovascular disease mortality was significantly associated with the participants' blood pressure as recorded at the time of university matriculation.[9] Importantly, the risk estimates remained relatively unchanged after adjustment for the presence of middle-aged hypertension.

Data characterizing ASF-associated hypertension commenced with the aforementioned study from Tucker and colleagues investigating the prevalence of cardiovascular risk factors in a cohort of 504 active professional ASF athletes.[12] In this cross-sectional analysis (first-year "rookie" players were excluded), hypertension (13.8% [95% CI, 11–16.7%]) and prehypertension (64.5% [95% CI, 58.3–70.7%]) were significantly more common in the ASF cohort compared with age-matched controls (5.5% [95% CI, 4.6–6.6%] and 24.2% [95% CI, 22.3–26.1%], respectively), despite 30% prevalence of active tobacco use among the controls. A strong association between ASF participation and incident hypertension was established in collegiate ASF athletes.[14,16,17] In a longitudinal, repeated-measures study of 113 freshman ASF athletes followed across seasonal training, there were significant increases in both SBP (116±8 versus 125±13 mm Hg, $P<0.001$) and diastolic blood pressure (DBP; 64±8 versus 66±10 mm Hg; $P<0.001$) from the pre- to postseason, with 61% of the cohort meeting criteria for either elevated blood pressure (SBP 120–129 mm Hg, DBP <80 mm Hg), stage 1 hypertension (SBP 130–139 mm Hg, DBP 80–89 mm Hg) or stage 2 hypertension (SBP ≥140 mm Hg, DBP ≥90 mm Hg) at the time of immediate postseason assessment.[14,51] Importantly, intraseason changes in SBP significantly correlated with increases in left ventricular (LV) mass ($R=0.46$, $P<0.001$) among the linemen. This finding suggests a mechanistic role of resting hypertension, perhaps complementing static exercise physiology, in the genesis of cardiac hypertrophy among ASF athletes. Despite the accumulation of observational data demonstrating the acquisition and presence of early hypertension among competitive ASF athletes, the impact of these findings on long-term health outcomes in this population remains uncertain.

Pharmaceuticals and Performance-Enhancing Drugs

Although the actual prevalence of NSAID use among ASF athletes remains unknown, limited data from collegiate ASF

athletes[8] and mainstream media reports[52,53] suggest the routine use of NSAIDs among ASF participants. NSAID use patterns among ASF athletes vary and include short-term use in the context of acute injury management, long-term use for the management of chronic pain syndromes, and pregame use, often at high doses, including injectable formulations. At present, the cardiovascular[54] and renal[55] implications of each of these NSAID utilization strategies among ASF participants are unknown; however, associations linking NSAID use with increases in blood pressure,[56] incident ischemic heart disease,[57] and cerebrovascular disease[58] in the general population underlie contemporary public health guidelines, which endorse only modest NSAID intake for short-term medical conditions.[59]

The health impact of performance-enhancing drugs, including illicit AAS use among ASF participants, remains incompletely understood largely because of the inherent challenges in the study of this topic. Nevertheless, the use AAS and other performance-enhancing drugs may be commonplace across elite competitive sports, including ASF, based on the ability of these drugs to increase strength, speed, and musculoskeletal recovery.[60] Recently, adverse cardiovascular implications of long-term AAS use have been described.[61,62] In a cross-sectional cohort study of 140 male weightlifters (86 AAS users versus 54 nonusers), AAS users demonstrated relative reductions in LV systolic function (ejection fraction: 52±11% versus 63±8%; $P<0.002$) and diastolic function (lateral wall relaxation velocity [E′]: 9.3±2.4 versus 11.1±2.0 cm/s; $P<0.001$) by echocardiography.[61] Of further concern was the observation of increased coronary artery plaque volume in the AAS users (median: 3 [interquartile range: 0–174] versus 0 [interquartile range: 0–69] mL^3; $P=0.012$), which was statistically associated with lifetime AAS dose.[61] Thus, it is plausible that longstanding AAS use contributes to cardiovascular disease burden among ASF athletes and should be considered a part of the differential diagnosis when pathologic cardiovascular phenotypes are discovered in active or former ASF athletes.

Cardiovascular Phenotypes Among ASF Participants

Healthy sport-specific cardiovascular adaptations occur in response to the hemodynamic stressors inherent in strenuous exercise training.[63] As detailed, ASF participants are exposed to considerable amounts of isometric hemodynamic stress with variable amounts of concomitant dynamic stress, as dictated by field position. Although the term isometric stress is classically, and most accurately, used to describe basic skeletal muscle physiology, it has been adopted in the cardiovascular literature as the descriptor of the short, intense, and repetitive bursts of physical activity that are characteristic of strength sports. From the perspective of the LV and central vasculature, static stress is characterized by surges in arterial blood pressure and relatively stable cardiac output, which equates to a relative "pressure challenge," thereby stimulating mild adaptive concentric LV remodeling. For the ASF athlete, emerging data suggest that this benign training-induced cardiac adaptation may be accompanied, or perhaps replaced, by pathologic cardiovascular remodeling (Table 2, Figure 1).

LV Structure

The development of concentric LV hypertrophy among ASF participants has been demonstrated by several longitudinal observational studies.[14,17,64] Weiner et al observed similar and significant increases in LV mass among collegiate ASF athletes with concentric LV hypertrophy (LV mass index >115 g/m^2 and relative wall thickness >0.42), occurring more frequently among linemen compared with nonlinemen (20/24 [83%] versus 1/12 [8%]; $P<0.001$).[14] The observation that the development of concentric LV hypertrophy was associated with intraseason changes in SBP and absolute postseason SBP suggests an element of subclinical hypertensive cardiac remodeling rather than simply benign exercise-mediated adaptive remodeling. The development of

Table 2. Selected Studies Analyzing Pathologic Cardiovascular Phenotypes Among ASF Players

Study	Year	ASF Population	Participants, N	Key Findings
Baggish et al[15]	2008	Collegiate freshman	24	Seasonal longitudinal decrease in echocardiographic measures of diastolic function
Weiner et al[14]	2013	Collegiate freshman	113	31% of linemen developed concentric LV hypertrophy, positive correlation with change in SBP
Kim et al[16]	2015	Collegiate freshman	32	Seasonal longitudinal increase in central aortic pulse pressure, PWV increased compared with older collegiate control group
Lin et al[17]	2016	Collegiate freshman	87	Collegiate linemen with concentric LV hypertrophy were associated with decrements in LV GLS
Kim et al[18]	2017	Collegiate	40	Athletes with SDB demonstrated significant correlation with reduced diastolic function and increased arterial stiffness

ASF indicates American-style football; GLS, global longitudinal strain; LV, left ventricle; PWV, pulse wave velocity; SBP, systolic blood pressure; SDB, sleep-disordered breathing.

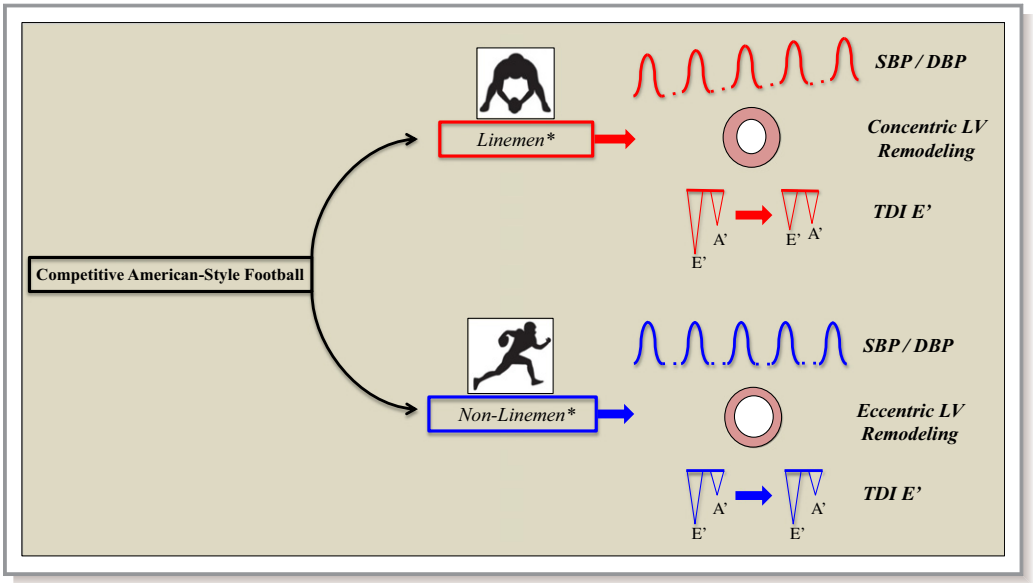

Figure 1. Generalized differences in American-style football cardiovascular phenotypes by player position. *Lineman positions are offensive tackles, guards, and center and defensive tackles and ends; nonlineman positions are quarterback, running backs, receivers, defensive backs, linebackers, and special teams. A′ indicates late mitral annular relaxation velocity; DBP, diastolic blood pressure; E′, mitral annular early relaxation velocity; LV, left ventricle; SBP, systolic blood pressure; TDI, tissue-Doppler imaging.

concentric LV hypertrophy among ASF linemen has since been reproduced in several distinct longitudinal collegiate cohorts and has been associated with relative myocardial functional impairment[17] and vascular dysfunction,[16] as discussed below. In addition, cross-sectional data examining LV structure in active professional ASF athletes report 23% incidence of LV hypertrophy with predominantly concentric geometry.[65] The persistence of this phenotype, particularly among former ASF athletes who played a lineman field position, has been documented well into the fifth decade of life.[66]

Among nonathletic populations, concentric LV hypertrophy present at youthful ages is associated with increased risk of later life coronary heart disease and stroke.[11] Consequently, the development of ASF-associated concentric LV hypertrophy, a process that appears to be driven at least in part by acquired hypertension, may be pathologic rather than adaptive, with attendant implications for later life cardiovascular risk. At present, this concept remains hypothetical and is deserving of future, confirmatory study.

LV Function

Exercise-induced cardiac remodeling, common among endurance and team sport athletes, is associated with augmentation of LV systolic and diastolic function. Data documenting LV function among ASF participants are comparatively sparse but instructive. The first longitudinal study examining the relationship between LV structure and function among collegiate ASF athletes demonstrated a surprising relationship between LV remodeling and diastolic function. Specifically, among 24 freshman ASF athletes followed over a single season of competitive ASF participation, there was a highly significant inverse relationship between change in LV mass and change in LV early diastolic relaxation (R^2=0.79), as measured by tissue-Doppler echocardiography, with ≈1 cm/s decline in E′ for each 10 g/m^2 increase in LV mass.[15] In addition, concentric LV remodeling was coupled with a significant decrease in diastolic function, as measured by echocardiographic tissue velocity imaging in the lateral (preseason versus postseason E′: 11.6±1 versus 10.2±1 cm/s) and septal (preseason versus postseason E′; 10.3±2 versus 9.6±2 cm/s; P<0.05 for both) points mitral annulus.[15]

The first study examining LV systolic function among ASF athletes was conducted by Abernethy et al, who documented normal LV ejection fractions among 156 participants but noted that 39% of this cohort had ejection fractions at the lower limits of normal, as defined by a range of 50% to 55%. More recently, speckle-tracking echocardiography has enabled the ability to measure strain, a more sensitive measure of LV systolic function that has emerged as a highly reproducible technique with powerful prognostic implications in numerous clinical populations. Among older and comorbid patient populations, for example, reduced global longitudinal strain correlates significantly with both pathologic increases in SBP and the development of concentric LV hypertrophy.[67,68] The first application of strain echocardiography utilized among ASF

athletes was reported recently. Specifically, Lin et al reported an association between the development of concentric LV hypertrophy and concomitant reductions in longitudinal strain among collegiate ASF freshman linemen after a single season of ASF training.[17] In this analysis, 90% of linemen (27/30) acquired either prehypertension or overt hypertension, demonstrated concentric LV remodeling, and experienced a corollary mean reduction in global longitudinal strain of 1.1% by the postseason measurement time point. Multivariate predictors of reduced global longitudinal strain included lineman field position, postseason weight, SBP, relative wall thickness, and absolute LV wall thickness.

Vascular Structure and Function

Central arterial stiffness, as estimated by pulse wave velocity and the central aortic pulse pressure, is an important mechanistic precursor to the development of hypertension and has emerged as an independent, validated marker of cardiovascular disease risk.[69–71] In a small multischool cohort of 32 freshmen collegiate ASF athletes, longitudinal increases in central aortic pulse pressure (27±4 versus 34±8 mm Hg; $P<0.001$) were observed in combination with increases in SBP following a season of competitive ASF participation.[16] Compared with a nonathletic undergraduate student control cohort (n=47), postseason pulse wave velocity was also increased among ASF athletes (6.2±0.9 versus 5.6±0.7 m/s, $P=0.002$). Although subclinical in absolute measure, the observed increases in pulse wave velocity values within the ASF cohort approximated the upper limits of normal[72] and were driven by athletes participating at lineman field positions. Data characterizing central arterial function among active and former professional athletes are lacking, and thus the natural history of vascular function across and beyond the entirety of an ASF career remains to be defined; however, a recently published cross-sectional study of former professional ASF athletes (mean age: 57.1±10.3 years) documents high rates of ascending aortopathy.[73] Specifically, former ASF athletes demonstrated larger ascending aortic diameters (38±5 mm) than population-based control participants from the Dallas Heart Study 2 (34±4 mm), a difference that retained statistical significance after adjustment for age, race, body surface area, SBP, history of hypertension, tobacco use, diabetes mellitus, and lipid profiles.[73] Importantly, former ASF athletes were twice as likely than controls (odds ratio: 1.99 [95% CI, 1.14–3.44]) to have aortic dimensions >40 mm, and a striking 9% of former ASF athletes had ascending aortic dimensions >45 mm.[73] Although it may be hypothesized that cumulative exposure to ASF-associated hypertension and vascular stiffening underlie these findings, mechanistic explanations remain speculative.

Sleep-Disordered Breathing

Sleep-disordered breathing (SDB) appears to be highly prevalent among collegiate and professional ASF athletes.[18,30,33] The prevalence of SDB among ASF athletes, as in other nonathletic populations, is driven to a large extent by body habitus, with increasing BMI representing a powerfully predictive risk factor. Recent data derived from the study of ASF athletes has begun to clarify important interactions between SDB and cardiovascular physiology. In a recent analysis of 40 collegiate ASF athletes from 2 National Collegiate Athletic Association (NCAA) programs, ASF participants with SDB (22/40, 55%), as defined by an apnea–hypopnea index ≥5, demonstrated relative impairments in LV diastolic and vascular function, as reflected by lower lateral E′ (14±3 versus 17±3 cm/s; $P=0.007$) and septal E′ (11±2 versus 13±2 cm/s; $P=0.009$) in tissue and higher pulse wave velocity (5.4±0.9 versus 4.8±0.5 m/s, $P=0.02$) compared with those athletes without SDB.[18] Although similar pathologic cardiovascular phenotypic relationships have been demonstrated in older, more comorbid members of the general population with SDB,[74–76] these data are the first to document an association between SDB and abnormal ventriculoarterial coupling patterns in youthful and relatively healthy athletic participants. At present, data defining the prevalence, physiologic correlates, and corollary clinical outcomes among active and former professional ASF athletes with SDB are unavailable.

Longevity Among ASF Athletes

Sudden Cardiac Death

Sudden cardiac death (SCD) during sport is a rare, tragic, and well-established phenomenon. Risk factors for SCD include male sex, black ethnicity, and sport type, with ASF representing one of the highest risk sports.[77] Data derived from an NCAA database during the decade spanning 2003 to 2013 identified 18 SCD events during collegiate ASF participation, which translated into an SCD risk of 1 in 8988 over a 4-year collegiate career.[77] Of the 16 autopsy reports obtained from these 18 ASF cases, 9 of 16 (56%) athletes were black, and the most common etiologies reported were sudden or unexplained (n=4) and structural (n=5) cardiomyopathy (K.G. Harmon, unpublished data, 2015). Statistics from the National Center for Catastrophic Sport Injury Research suggest that most football-related SCD cases occur at the high school level, but accurate estimates of risk in this population are lacking.[78] At present, the specific disease processes responsible for SCD among ASF athletes and the relative weight of congenital/genetic versus acquired cardiovascular processes in SCD etiology remain largely unknown. Further work requires more rigorous and complete case cataloguing and inclusion of high school ASF athletes in the analysis.

Cardiovascular Disease Mortality

The first seminal analysis evaluating mortality outcomes in former professional ASF players was conducted in 1994 by the National Institute for Occupational Safety and Health.[19] Among 6848 former players, all-cause mortality was reduced by 46% among ASF athletes compared with matched members of the general population. Cardiovascular disease mortality, however, was increased by 52% among men who had played at a lineman field position, and mortality in this group was primarily attributable to hypertensive heart disease and coronary artery disease. In a 2012 follow-up study also conducted by Baron and colleagues, similar results were obtained.[20] Of 3439 former players (seasons played between 1959 and 1988), all-cause player mortality was significantly decreased (standardized mortality ratio: 0.53 [95% CI, 0.48–0.59]) compared with US men stratified by age, race, and calendar year. Former defensive linemen, however, had increased risk of cardiovascular disease mortality (standardized mortality ratio: 1.42 [95% CI, 1.02–1.92]) and cardiomyopathy (standardized mortality ratio: 5.34 [95% CI, 2.30–10.5]) compared with controls. In addition, former ASF participants with a BMI ≥30 during years of active play had close to twice the risk of cardiovascular disease mortality compared with other former players (hazard ratio: 2.02 [95% CI, 1.06–3.85]).

Several limitations of the available epidemiologic data characterizing mortality among ASF participants are noteworthy. First and most important, it is possible that selection bias was introduced through a "healthy worker effect" and that use of the general population as the control group was inappropriate for causal inferences with regard to all-cause mortality. Future epidemiologic studies of ASF participant longevity may be better served by the use of other former elite, non-ASF athletic cohorts as controls. Second, the mantra that modern ASF athletes are "bigger, stronger, and faster" than their historical counterparts is accurate.[79] As such, the impact of factors related to modern training methods and changes in body composition on long-term health measures are not known and should not be underestimated. The recognition that 21st century ASF athletes are different compared with ASF athletes from prior eras suggests that epidemiologic estimates may not be static in nature and that follow-up assessments engaging contemporary ASF athletes will be necessary to understand the potential risks and benefits of ASF participation.

Future Directions

Despite important advances in our understanding of how competitive ASF participation affects cardiovascular health, key areas of uncertainty remain that set the stage for future work. First, the specific mechanistic factors inherent in ASF participation that underlie the development of cardiovascular risk factors and pathologic phenotypes remain incompletely understood. Although deliberate increases and long-term maintenance of high body mass appear contributory,[14,17,18] it is unlikely that body habitus functions in isolation. Instead, this is likely a complex and multifactorial process in which other factors including intense static exercise training coupled with a relative dearth of dynamic or aerobic conditioning, extensive use of NSAIDs for pain and injury,[8] dietary food intake, and surreptitious use of cardiotoxic performance-enhancing drugs[61] work in synergistic fashion to potentiate cardiovascular risk and pathologic phenotypes (Figure 2). Future studies designed to characterize, isolate, and ultimately manipulate these candidate mechanisms are required. In addition, while practical control groups may be challenging to construct, athletes involved in pure isometric sporting disciplines (ex, weight lifters, track and field throwers, wrestlers) likely represent the most ideal athletic groups necessary for appropriate comparison to ASF lineman in future studies.

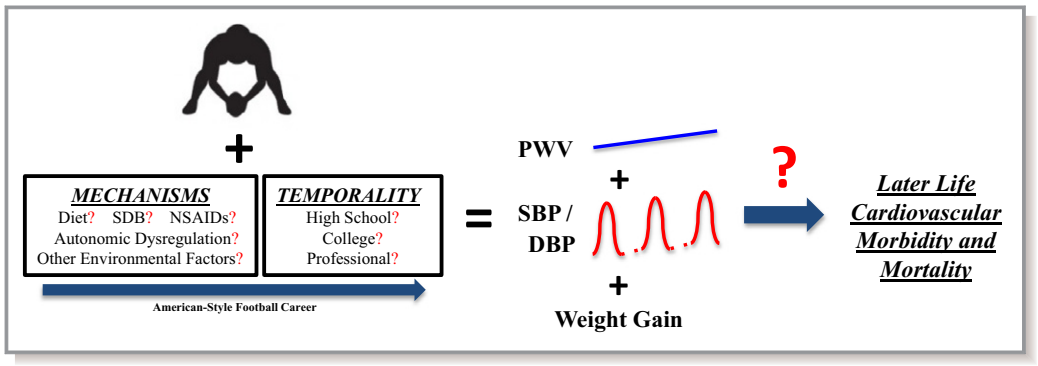

Figure 2. Proposed mechanisms and unknown temporality of cardiovascular pathology associated with American-style football participation. DBP indicates diastolic blood pressure; PWV, pulse wave velocity; SBP, systolic blood pressure; SDB, sleep-disordered breathing.

Conceptually, in combination with the study of proposed environmental factors, the analysis of ASF-associated cardiovascular risk also requires an intricate, multisystem approach. As a primary example, the association between pathologic central nervous system processes as a consequence of repetitive head trauma and cardiovascular pathology is a compelling but speculative realm in need of testing. To date, among ASF athletes, the acute and long-term effects of postconcussive autonomic dysregulation[80] and sympathetic nervous system overstimulation on cardiovascular parameters have not been explored. A second intriguing unknown worthy of study is the impact of NSAID use on both cardiovascular and renal physiology. As mechanistic studies include larger cohorts of ASF athletes, the analysis should not be limited to cardiovascular phenotyping but rather designed to define the complex multiorgan system interactions that ultimately determine how ASF participation affects health in both favorable and adverse ways.

Second, the temporal sequence of the development and progression of cardiovascular risk and pathology among ASF athletes remains largely undefined. It must be acknowledged that the majority of the available longitudinal phenotypic data have been derived from relatively short-duration studies of collegiate athletes. Similar work focusing on high school ASF athletes (the largest ASF athlete population[1]) and both active and former professional ASF athletes are needed. Studies of former professional ASF athletes should begin data capture at time points that coincide with ASF career completion to differentiate the impact of ASF participation from unrelated postcareer factors that may have a significant impact on player health. It is possible, if not probable, that post-ASF career lifestyle changes—both healthy and unhealthy—are more important determinants of later life cardiovascular health than actual ASF exposure among former ASF athletes.

Third, additional epidemiologic outcomes data will be required to delineate the potentially positive and negative health attributes of the contemporary sport. Optimally, future studies should incorporate both active and former professional ASF athletes as well as former high school and collegiate ASF athletes who did not advance to professional careers. As discussed, careful control population selection will be required to ensure appropriate causal inference from these data. Participant recruitment and retention for this work may prove challenging and will best be accomplished by collaborative efforts between the organizations that oversee the welfare of active and former players and members of the scientific community with the requisite expertise.

Finally, work designed to address these knowledge gaps should be coupled with enhanced cardiovascular care of ASF participants. At the “grassroots” level, team-based sports medicine and sports cardiology practitioners should consider the development of clinical protocols aimed at identifying and closely monitoring players deemed high risk from a cardiovascular standpoint (eg, linemen, players with significant weight gain, players with preseason prehypertensive or hypertensive blood pressures). In practice, clinicians should be aware of the potential cardiovascular risks associated with ASF participation and should use individualized clinical monitoring plans if appropriate. Although the vascular, metabolic, and cardiac structure and performance changes associated with exposure to ASF develop in response to unique physiological stressors, many of these conditions are well-established determinants of cardiovascular health among the general population and are amenable to interventions proven to reduce morbidity and mortality. As such, the initiation of lifestyle modifications, pharmacotherapy, and other treatment modalities (eg, continuous positive airway pressure) among ASF athletes should be considered on a case-by-case basis, as defined by clinical guidelines and clinician expertise. The design and implementation of clinical trials tracking regression and improvement of these phenotypes among active and former ASF athletes are of paramount importance.

Conclusions

Concerns regarding the impact of long-term ASF participation on cardiovascular health have led to observations of cardiac risk and pathologic cardiovascular phenotypes among ASF athletes, particularly the lineman-position players. Although the impact of these findings on long-term health outcomes in this population remains incompletely characterized, the development of risk stratification and clinical management algorithms specific to ASF athletes represents important future research directions. In addition, because the clinical management of most ASF-associated cardiovascular conditions is primarily evidenced-based and unlikely to dramatically alter sport participation, ongoing ASF cardiovascular research efforts continue to represent a public health opportunity to improve clinical outcomes in a youthful and uniquely at-risk population.

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None.

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