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Long-term Mortality in NFL Professional Football Players:

No Significant Increase, but Questions Remain

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The many positive health benefits of regular exercise, including longer lifespan, outweigh the risks of being physically active from both an individual and a population standpoint. Although the risks of extreme sports and other activities with inherent risks are tolerated by participants and fans, there has been a resurgence of interest in the health of those who participate in contact sports, notably professional American football, as well as hockey, lacrosse, soccer, rugby, and other sports in which concussion or other traumatic brain injury (TBI) is more likely to occur.[1] While separated shoulders, torn ligaments, and broken ankles are tolerated as the "breaks of the game," the realization that both adverse short-term (concussion) and long-term (cognitive, neuromuscular, or movement disorder) consequences occur, coupled with intense public and media attention, have elevated concern about mortality among professional athletes.

Prior studies comparing the general US population with National Football League (NFL) players indicated that there was no difference in mortality.[2] In this issue of *JAMA*, Venkataramani and colleagues[3] used a historical anomaly to identify what they considered was a better comparison population. The authors reasoned that NFL players do not have the same mortality risk as the general population, by virtue of both risk-lowering factors (exercise and training, nutritional education and practice, and regular access to health care) and risk-increasing exposures (to drugs, excess weight, and possibly early death from cardiac or neurodegenerative diseases).

The authors also reasoned that it was not appropriate to compare seasoned veterans who may have played 4 years of high school, 4 years of college, and then perhaps 5 to 10 years of professional football vs the average man in the US population. Instead, the investigators identified an interesting comparator group—replacement players who played briefly (3 games) during the 1987 NFL players strike—to compare the mortality of these players with

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the mortality of long-time NFL players. Their rationale was that the replacement players had many of the same exposures in high school and college football, but less exposure to both the traumas of professional football and to other factors, such as illegal drugs. The cleverly conceived cohort of replacement players had a much lower “dose” of head trauma and other factors related to a career in the NFL than long-time professional players and presumably returned to much less physically demanding jobs after their participation as NFL replacement players.

To achieve adequate numbers of the replacement players’ contemporaries, the authors included all NFL players who were in the league in roughly the same period: 5 years before and 5 years after the 1987 NFL players’ strike. The authors also were extremely diligent about tracking down all the regular NFL players who played between 1982 to 1992 and matching them with the comparison group of replacement players. They grouped players by positions considered to be at similar risk. Description of the cases and the rationale for the statistical analyses were carefully done, using a complex design and multiple considerations about which participants to include and which analyses were appropriate to use.

The study population included 3812 men (mean [SD] age at first NFL activity, 23.4 [1.5] years), of whom 2933 were career NFL players (median NFL tenure 5 seasons [interquartile range {IQR}, 2–8]; median follow-up, 30 years [IQR, 27–33]) and 879 were NFL replacement players (median NFL tenure, 1 season [IQR, 1-1]; median follow-up, 31 years [IQR, 30–33]).[3]

Results revealed that the mortality among long-term NFL players was not significantly different than the mortality among the much more briefly exposed replacement players. At the end of follow-up, 144 NFL players (4.9%) and 37 replacement players (4.2%) were deceased (adjusted absolute risk difference, 1.0% [95% CI, −0.7% to 2.7%]; $P = .25$).[3] The adjusted mortality hazard ratio for NFL players relative to replacement players was 1.38 (95% CI, 0.95 to 1.99; $P = .09$).[3] These findings were consistent with earlier results that showed no mortality decrease when long-time players were compared with a matched nonplayer population.[2]

Causes of death among the deceased players (Table 3 and eTable 2 in the Supplement of the article[3]) showed some differences between the groups, but the numbers of cases were too small to consider them significant. There was, however, a notable numerical difference in neurodegenerative disorders, in that 7 deaths were categorized as neurodegenerative, and these occurred only in the long-term players. All of these 7 deaths were categorized as due to amyotrophic lateral sclerosis (ALS), a prevalence rate far higher than the 4.3 cases per 100 000 people in the general population (and that statistic is based on the oldest age group, >70 years).[4] The finding of excess ALS cases has been reported previously in studies of NFL players compared with the general population.[2,5] However, no dementia cases were reported as the cause of death in this 1982–1992 cohort despite concerns about chronic traumatic encephalopathy (CTE), which had not become a recognized issue in football until a little more than 10 years ago.[6–8] In addition, the oldest men in both cohorts would have been in their mid to late 50s when the data for this analysis were obtained.

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It has been known for nearly a century that athletes have a higher propensity for developing neurodegenerative syndromes. ALS is known as “Lou Gehrig disease,” after the iconic Yankee baseball player who developed ALS in his 30s. Both dementia and parkinsonism were described many years ago in boxers. The clinical and pathological findings of frequent head trauma have been known since the 1920s.[9,10] The pathology was demonstrated in boxers (without the benefit of the immunohistologic antibodies available today), accompanied by a list of boxers termed *punch drunk*.[10] While the term was initiated by Martland[10] in the medical literature, it was used by boxing promoters at that time, one of whom gave Martland a list of more than 20 boxers who he, the promoter, considered punch drunk. The literature since the 1920s has many studies of the harm boxing causes to the brain.[11] The disorder was first referred to as CTE by the British neurologist Macdonald Critchley,[12] a prescient designation because repetitive head injury can produce the same syndrome regardless of the sport played.

The recent upsurge in interest in TBI and concussion in sports, and in the study of neurodegenerative diseases in contact sports, was sparked by increasing evidence over the past 10 to 15 years that professional American football players, as well as professional athletes in most if not all contact sports, may develop short-term, career-threatening, and long-term brain diseases. The findings in professional American football ignited the current interest in concussions and long-term neurological disease.[6] That initial finding attracted attention both because it happened in an immensely popular sport and because the finding was challenged by authors associated with a professional football organization.[8] However, the initial case was followed quickly by a small series of cases[7,13] and subsequent overwhelming behavioral[14,15] and neuropathological[16,17] evidence of brain dysfunction.

More recently, concern has been levied not just at concussions, but also at the multiple subconcussive blows to the head associated with years of high school, college, and professional sport practices and games. These repetitive traumas appeared to be the cause of CTE,[18] and other neuropathological studies confirmed the widespread brain damage that could cause ALS and parkinsonism.[18] Thus began an intensive examination of the cognitive, neuropsychiatric, neuroimaging, and functional brain changes associated with multiple contact sports and the role of multiple related factors: biopsychosocial factors, such as anabolic steroids to gain strength and weight, illicit drugs possibly causing some of the behavioral symptoms, and preexisting learning disorders.[15]

Although the life expectancy of professional football players was not significantly reduced based on the current evidence, the health of professional athletes should remain a focus of future research. Clinicians and researchers should now turn to the pressing issues of understanding how such repeated trauma leads to manifestations of neurodegenerative disease (and sometimes overlapping cognitive, neuropsychiatric, and movement disorders such as parkinsonism, tremor, and depression) and why and how altered tau protein plays a role in CTE.[19] The field now has the capability to use a variety of biomarkers, such as neurofilament protein[20] or tau imaging,[21,22] as diagnostic aids, and may well use blood biomarkers and advanced neuroimaging techniques[22] to both confirm the diagnosis and monitor treatments as they are developed.

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Rules changes and better technology and equipment are emerging and will improve over time. Animal models continue to evolve to help define pathology, molecular changes, and evolution of TBI,[23–25] as do clinical and neuropathologic diagnostic criteria.[26] A complete understanding is challenging due to wide publicity about the large percentage of brains of symptomatic former players found to have evidence of CTE,[27] despite frequent cautions that the high prevalence in symptomatic players reflects selection bias and is not likely to be characteristic of most former players. There have been repeated calls for large longitudinal studies of former players. Some studies designed to address this issue are under way with the help and cooperation of former players. Such studies will help determine the actual incidence and prevalence of these neurodegenerative diseases and will provide both a perspective on the real risks associated with repeated subconcussive brain trauma and an understanding of the susceptibility to them. As the life expectancy of NFL players continues to be monitored over time, research into prevention and treatment of tauopathies, ALS, parkinsonism, and CTE may provide hope that the quality of life can be improved as well.

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