# Sudden Death Associated With Anomalous Coronary Origin and Obstructive Coronary Disease in the Young

*Robert E. Eckart, DO,* Samuel O. Jones IV, MD,* Eric A. Shry, MD,† Paul D. Garrett, MD,† and Stephanie L. Scoville, DrPH‡*

**Abstract:** Sudden cardiac death in a young patient is a catastrophic occurrence. Anomalous coronary origin (ACO) is a significant cause of sudden cardiac death among individuals under the age of 35 years. We sought to define the premortem clinical and postmortem histopathologic findings in victims of sudden cardiac death resulting from either ACO or obstructive atherosclerotic coronary artery disease (CAD) among U.S. military recruits (ages 17–35 years). The autopsy records of all sudden cardiac deaths occurring among recruits during their basic military training period from 1977 through 2001 were reviewed. Twenty-one deaths were associated with ACO and 10 with CAD. Recruits with ACO were more likely to have prodromal symptoms of exertional syncope and/or chest pain (48% vs. 0%, $P = 0.011$). All sudden cardiac deaths resulting from ACO involved a left main coronary artery takeoff from the right coronary sinus with a course between the aorta and the right ventricular outflow tract and an otherwise normal distribution of the major epicardial coronary arteries. Myocardial fibrosis was seen equally in those with both CAD and ACO (30% vs. 20%, $P = 0.66$), but the finding of necrosis tended to be more common among recruits with CAD (50% vs. 15%, $P = 0.08$). In conclusion, review of autopsy data of sudden cardiac deaths among U.S. military recruits reveals myocardial fibrosis or necrosis occurred in 70% of cases with CAD and 35% of cases with ACO. Sudden cardiac deaths resulting from ACO were more likely to be associated with premortem exertional chest discomfort and/or syncope compared with deaths resulting from CAD.

**Key Words:** sudden cardiac death, coronary vessel anomalies, coronary arteriosclerosis, coronary disease, congenital heart defect

(*Cardiology in Review* 2006;14: 161–163)

From the *Brigham and Women's Hospital, Boston, Massachusetts; †Brooke Army Medical Center, San Antonio, Texas; and ‡U.S. Army Center for Health Promotion and Preventive Medicine, Aberdeen Proving Ground, Maryland.

The authors report no conflict of interest and have no financial disclosures to make as they apply to the research presented herein. The opinions and research contained herein are the private ones of the authors and are not to be considered as official or reflecting the views of the Department of the Army or the Department of Defense.

Reprints: Robert E. Eckart, DO, Cardiac Arrhythmia Service, Cardiovascular Medicine, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115. E-mail: robert.eckart@us.army.mil.



ISSN: 1061-5377/06/1404-0161
DOI: 10.1097/01.crd.0000197965.99826.b2

The finding of anomalous coronary origin (ACO), although rare in the population at large, is an acknowledged cause of sudden cardiac death (SCD) in adolescents and young adults.[1–4] Recent work has clearly defined ACO as a leading cause of sudden death among military recruits.[5] Of 64 sudden cardiac deaths identified among 6.3 million recruits undergoing basic military training from 1977 through 2001, most (61%) were attributed to coronary artery pathology. Among these, slightly more than half (54%) were the result of ACO.

Patients with ACO may report syncope or chest discomfort with exertion, but they usually have normal electrocardiograms and normal cardiac stress tests.[3] Although myocardial damage has been infrequently shown in young subjects with either ACO or atherosclerotic coronary artery disease (CAD), the relative contributions of recurrent myocardial injury, myocardial scarring, and cell death in the pathophysiology of SCD in these subjects is uncertain at this time.[2,3]

## METHODS

Nontraumatic deaths were identified through the Department of Defense Recruit Mortality Registry in the Medical Mortality Surveillance Division at the Office of the Armed Forces Medical Examiner.[6,7] Deaths were eligible for study if the fatal incident occurred while in an enlisted status before completion of basic military training in the U.S. Air Force, Army, Marine Corps, or Navy from 1977 through 2001. Deaths were included in this analysis if they were categorized as a SCD, had identifiable coronary artery pathology at autopsy that was considered to be contributory to their deaths, and had no evidence of other significant structural heart disease.

Sudden death was recognized as an event resulting in death or terminal life support within 1 hour of the inciting event. Deaths were considered cardiac in origin if there was autopsy documentation of cardiac pathology along with an appropriate clinical scenario.

The presence of a coronary artery anomaly, coronary atherosclerosis with the degree of luminal obstruction, and histologic abnormalities on cardiac microscopic examination were abstracted from autopsy reports and Armed Forces Institute of Pathology consultative reports. Measurements and histopathology were unavailable for only 1 death (which was the result of ACO).

**TABLE 1.** Coronary Artery Pathology Seen at Autopsy of 39 Sudden Cardiac Deaths

| | |
|---|---|
| Anomalous coronary artery | 21 (54) |
| Obstructive atherosclerotic coronary artery disease | 10 (26) |
| Coronary artery hypoplasia | 3 (8) |
| Coronary artery aneurysm | 2 (5) |
| Coronary artery bridging | 2 (5) |
| Spontaneous coronary artery dissection | 1 (3) |

Values expressed as counts and percentages (in parentheses). Percentages do not total 100 as a result of rounding.

Descriptive statistics were calculated for continuous and categorical variables. Student *t* test was used to compare normally distributed continuous variables and the Kruskal-Wallis test was used for nonparametric data. Significant differences were considered if the *P* value was $<0.05$. Analysis was performed using JMP Professional (SAS Institute, Cary, NC).

## RESULTS

There were 39 deaths attributed to coronary artery pathology (Table 1). Most were the result of ACO (54%) and CAD (26%). There was a significant difference in the median age of recruits who died of CAD compared with ACO (26 vs. 19 years, $P = 0.006$) (Table 2). Recruits with ACO were more likely to have had prodromal symptoms than those with CAD ($P = 0.011$), although there was no statistically significant difference in the timing of death from the onset of military training. Of those identified with prodromal symptoms, chest pain was present in 6 (from 2 hours to 2 weeks before death) and/or syncope was present in 4 (from 48 hours to 6 years before death).

**TABLE 2.** Demographic and Clinical Characteristics of 31 Sudden Cardiac Deaths

| | Atherosclerotic CAD (n = 10) | Anomalous Coronary (n = 21) |
|---|---|---|
| Age, years (median)* | 26 | 19 |
| Range | 18–35 | 17–31 |
| Gender, male | 10 (100) | 19 (90) |
| Race | | |
| White | 5 (50) | 14 (67) |
| Black | 3 (30) | 7 (33) |
| Filipino | 2 (20) | 0 (0) |
| Height, cm* | 168 ± 9 | 180 ± 9 |
| Body mass index, kg/m$^2$* | 26.7 ± 3.6 | 23.6 ± 2.5 |
| Days in training† (median) | 25 | 32 |
| Range | 13–59 | 6–78 |
| Prodromal symptoms, present* | 0 (0) | 10 (48) |

*$P \leq 0.02$, otherwise $P > 0.05$.

Height and body mass index are expressed as mean ± standard deviation (and were calculated from measurements of 30 deaths resulting from the unavailability of these data for one death resulting from ACO); other values are expressed as counts and percentages (in parentheses).

CAD indicates coronary artery disease; ACO, anomalous coronary origin.

All SCDs resulting from ACO involved a left main coronary artery takeoff from the right coronary sinus with a course between the aorta and the right ventricular outflow tract and an otherwise normal distribution of the major epicardial coronary arteries. In all cases of SCD due to CAD, obstructive disease (>70%) of the left anterior descending artery was present. Four of the 10 recruits with CAD had multivessel disease. Myocardial fibrosis was seen equally in those with both CAD and ACO (30% vs. 20%, $P = 0.66$), but the finding of necrosis tended to be more common among those with CAD (50% vs. 15%, $P = 0.08$).

## DISCUSSION

Coronary artery aberrancy was associated with 33% of SCDs with identifiable cardiac structural abnormality in U.S. military recruits from 1977 through 2001.[5] This is an increase compared with the previous finding of 16% resulting from coronary anomalies among U.S. Air Force recruits from 1965 through 1985.[8] Anomalous coronary anomaly has been considered as the etiology in 5% to 35% of SCD in this population, although its incidence is less than 0.3% to 0.8% in populations undergoing catheterization.[9–13] We identified 21 cases with SCD and ACO, all of which were the left coronary arising from the right sinus of Valsalva with a course between the pulmonary artery and aorta. Of these recruits, 10 (48%) had prodromal symptoms of exertional syncope and/or chest pain identified during review of postmortem records. Although symptoms have previously been reported in association with ACO in angiographic series, causality has not been established.[10] Basso et al reported that in 27 sudden deaths resulting from ACO, 12 (44%) had documented clinical evaluation before the event. Of these, 10 (37%) were shown to have had either syncope or chest pain in the 2 years preceding the SCD.[3] Prior series of sudden death in athletes reported only 3% sought medical attention for cardiovascular symptoms before experiencing sudden death.[14]

The discovery that all of our cases of ACO and SCD were associated with the left main coronary arteries arising from the right coronary sinus is in concert with previously reported studies. In the largest study to date, Taylor et al reviewed clinical and pathologic records from 242 patients with isolated ACO (age 0–87 years). They discovered that in the 140 cases in which the anomalous artery originated in the aorta, the origin of the left main coronary artery from the right coronary sinus (49 of 140) was most often associated with SCD.[4] In the cases in which the left main arose from the right coronary cusp, the majority of the patients were younger (less than 30 years) and half of the patients had documented prodromal symptoms before SCD.[4]

All recruits with SCD with CAD had obstructive lesions in the left anterior descending artery. There was a 70% occurrence of pathologic changes consistent with previous or ongoing myocardial damage in SCD with CAD. Interestingly, no corresponding symptoms were identified, which may be evidence of previous silent ischemia. Traditional risk factors for CAD were few, if present at all. There was a significant difference in the median age of recruits who died of CAD compared with ACO. However, the body mass index of these

young recruits was still well below those levels commonly associated with an increased independent risk for an adverse event.[15,16] Screening this population for coronary artery disease and coronary anomalies in the current era would be costly and time-consuming. Despite representing a leading cause of death in this young population, the incidence of coronary artery anomalies remains low. The diagnosis of ACO requires a high clinical index of suspicion in young persons with premonitory symptoms. Screening programs for the general population are not feasible given the extremely low prevalence of the condition. Our data emphasize the need to consider ACO as a cause of SCD in young persons.

Approximately half of the recruits with coronary anomalies were identified as having prodromal symptoms before sudden death, and these deaths occurred a median of 1 month after initiating military training (which includes strenuous exertion). Therefore, one needs to consider imaging to exclude an anomalous coronary artery in a young patient initiating an exercise program who presents with symptoms that may be referable to cardiovascular disease. Confirmatory imaging of the coronary artery ostium is of particular importance given the high false-negative rate of electrocardiography and maximal stress testing in identifying symptomatic patients who are at risk for death from anomalous coronary arteries.[3] Although transthoracic echocardiography can visualize the origins and proximal courses of the coronary arteries in some individuals, either computed tomography or magnetic resonance coronary angiography is a more sensitive and specific screen for ACO.[1,2]

## CONCLUSIONS

Young military recruits who died with ACO commonly presented with symptoms of exertional chest pain and/or syncope, providing the clinician with a diagnostic window of opportunity. Timely identification of ACO, particularly the left main coronary artery, may result in a curative surgical correction. The physician should have a high index of suspicion for this condition to avoid a potential devastating outcome.

## REFERENCES

1. Angelini P. Coronary artery anomalies—current clinical issues: definitions, classification, incidence, clinical relevance, and treatment guidelines. *Tex Heart Inst J*. 2002;29:271–278.
2. Davis JA, Cecchin F, Jones TK, et al. Major coronary artery anomalies in a pediatric population: incidence and clinical importance. *J Am Coll Cardiol*. 2001;37:593–597.
3. Basso C, Maron BJ, Corrado D, et al. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. *J Am Coll Cardiol*. 2000;35:1493–1501.
4. Taylor AJ, Rogan KM, Virmani R. Sudden cardiac death associated with isolated congenital coronary artery anomalies. *J Am Coll Cardiol*. 1992;20:640–647.
5. Eckart RE, Scoville SL, Campbell CL, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med*. 2004;141:829–834.
6. Gardner J, Cozzini C, Kelley P, et al. The Department of Defense Medical Mortality Registry. *Mil Med*. 2000;165(suppl 2):1–5.
7. Scoville SL, Gardner JW, Magill AJ, et al. Nontraumatic deaths during US Armed Forces basic training, 1977–2001. *Am J Prev Med*. 2004;26:205–212.
8. Phillips M, Robinowitz M, Higgins JR, et al. Sudden cardiac death in Air Force recruits. A 20-year review. *JAMA*. 1986;256:2696–2699.
9. Basso C, Corrado D, Thiene G. Congenital coronary artery anomalies as an important cause of sudden death in the young. *Cardiol Rev*. 2001;9:312–317.
10. Barriales Villa R, Moris C, Lopez Muniz A, et al. [Adult congenital anomalies of the coronary arteries described over 31 years of angiographic studies in the Asturias Principality: main angiographic and clinical characteristics]. *Rev Esp Cardiol*. 2001;54:269–281.
11. Felmeden D, Singh SP, Lip GY. Anomalous coronary arteries of aortic origin. *Int J Clin Pract*. 2000;54:390–394.
12. Dodge-Khatami A, Mavroudis C, Backer CL. Congenital Heart Surgery Nomenclature and Database Project: anomalies of the coronary arteries. *Ann Thorac Surg*. 2000;69(suppl):S270–S297.
13. Angelini P. Normal and anomalous coronary arteries: definitions and classification. *Am Heart J*. 1989;117:418–434.
14. Burke AP, Farb A, Virmani R, et al. Sports-related and non-sports-related sudden cardiac death in young adults. *Am Heart J*. 1991;121:568–575.
15. Van Itallie TB. Health implications of overweight and obesity in the United States. *Ann Intern Med*. 1985;103:983–988.
16. Rosenbaum M, Leibel RL, Hirsch J. Obesity. *N Engl J Med*. 1997;337:396–407.