

Sudden Death

Clinical Profile of Congenital Coronary Artery Anomalies With Origin From the Wrong Aortic Sinus Leading to Sudden Death in Young Competitive Athletes

Cristina Basso, MD, PhD,* Barry J. Maron, MD, FACC,† Domenico Corrado, MD,‡
Gaetano Thiene, MD*

Padua, Italy and Minneapolis, Minnesota

- OBJECTIVES** The purpose of this study is to characterize the clinical profile and identify clinical markers that would enable the detection during life of anomalous coronary artery origin from the wrong aortic sinus (with course between the aorta and pulmonary trunk) in young competitive athletes.
- BACKGROUND** Congenital coronary artery anomalies are not uncommonly associated with sudden death in young athletes, the catastrophic event probably provoked by myocardial ischemia. Such coronary anomalies are rarely identified during life, often because of insufficient clinical suspicion. However, since anomalous coronary artery origin is amenable to surgical treatment, timely clinical identification is crucial.
- METHODS** Because of the paucity of available data characterizing the clinical profile of wrong sinus coronary artery malformations, we reviewed two large registries comprised of young competitive athletes who died suddenly, assembled consecutively in the U.S. and Italy.
- RESULTS** We reported 27 sudden deaths in young athletes, identified solely at autopsy and due to either left main coronary artery from the right aortic sinus ($n = 23$) or right coronary artery from the left sinus ($n = 4$). Each athlete died either during ($n = 25$) or immediately after ($n = 2$) intense exertion on the athletic field. Fifteen athletes (55%) had no clinical cardiovascular manifestations or testing during life. However, in the remaining 12 athletes (45%) aged 16 ± 7 , certain clinical data were available. Premonitory symptoms had occurred in 10, including syncope in four (exertional in three and recurrent in two, 3 to 24 months before death) and chest pain in five (exertional in three, all single episodes, ≤ 24 months before death). All cardiovascular tests were within normal limits, including 12-lead electrocardiogram (ECG) pattern (in 9/9), stress ECG with maximal exercise (in 6/6) and left ventricular wall motion and cardiac dimensions by two-dimensional echocardiography (in 2/2).
- CONCLUSIONS** With regard to congenital coronary artery anomalies of wrong aortic sinus origin in young competitive athletes, 1) standard testing with ECG under resting or exercise conditions is unlikely to provide clinical evidence of myocardial ischemia and would not be reliable as screening tests in large athletic populations, 2) premonitory cardiac symptoms not uncommonly occurred shortly before sudden death (typically associated with anomalous left main coronary artery), suggesting that a history of exertional syncope or chest pain requires exclusion of this anomaly. These observations have important implications for the preparticipation screening of competitive athletes. (J Am Coll Cardiol 2000;35:1493–501) © 2000 by the American College of Cardiology

Although sudden death in young competitive athletes is a rare event, such catastrophes often assume a high public

profile because trained athletes may be regarded as the healthiest element of society. In this regard, a variety of structural cardiovascular abnormalities identifiable at autopsy have been implicated as the cause of athletic field deaths (1–10) although the prevalence of various lesions have differed somewhat in reports from the U.S. (1,2,5–9) and Italy (3,4,10).

While hypertrophic cardiomyopathy or arrhythmogenic right ventricular cardiomyopathy have been the most com-

From the *Department of Pathology and ‡Cardiology, University of Padua Medical School, Padua, Italy and †Minneapolis Heart Institute Foundation, Minneapolis, Minnesota. This study was supported by Veneto Region Research Project on Juvenile Sudden Death, Venice and MURST and CNR Projects on Myocardial Infarction, Rome, Italy, and by a grant from the Minneapolis Heart Institute Foundation.

Manuscript received October 1, 1999; revised manuscript received November 16, 1999, accepted January 7, 2000.

Abbreviations and Acronyms

ECG	= electrocardiogram
LMCA	= left main coronary artery
RCA	= right coronary artery

mon diseases in these surveys, a variety of congenital coronary artery anomalies (particularly those with wrong sinus origin) also consistently represent common causes of exercise-related sudden death in young athletes ≤ 35 years of age (3–5,8–10). The mechanism of sudden death is believed to be episodic myocardial ischemia (11–16). Nevertheless, these coronary anomalies are amenable to surgical correction (17), thereby emphasizing the crucial importance of timely identification during life. However, at present, there is a paucity of clinical information available in the literature regarding trained athletes with these coronary malformations. Therefore, we have reviewed two large registries of young competitive athletes who had died suddenly, to systematically analyze clinical markers that would promote detection during life of coronary artery anomalies of wrong aortic sinus origin.

METHODS

Selection of subjects. Cases of sudden death in competitive athletes resulting from coronary artery anomalies with wrong aortic sinus origin were retrospectively assembled based on the review of two large registries in the U.S. and Italy. First, since 1990, the Minneapolis Heart Institute Foundation has developed a U.S.-based registry of sudden cardiovascular deaths in young competitive athletes (6), consecutively identified (largely from news media accounts) and tracked in a systematic fashion.

Second, since 1979, a clinicopathologic target project on sudden death in the young has been carried out in the Veneto region of northeastern Italy (including the cities of Venice, Padova, Treviso, Verona and Vicenza), which has a population of over four million (10). All hearts from cases of sudden death in young people (including athletes) in this geographic region are systematically assessed at the University of Padova.

Inclusion criteria. For inclusion into the study group, each patient fulfilled the following criteria (6,10): 1) a diagnosis at autopsy of congenital coronary anomaly of wrong aortic sinus origin—with an absence of other cardiac and noncardiac causes of death—based either on direct examination of the heart or analysis of a complete and detailed autopsy report; 2) a competitive athlete at the time of death—one who participated in an organized team or individual sport that required systematic training and regular competition against others and that placed a high premium on athletic excellence and achievement (18); 3) an age of ≤ 35 years at time of death; and 4) no evidence of drug or alcohol abuse

upon the postmortem toxicologic examination of blood and urine.

Clinical information. Clinical data reported here were derived differently from the U.S. and Italian registries. Among U.S. athletes, medical evaluation and testing were stimulated by symptoms suggestive of cardiac disease and were not part of systematic preparticipation screening programs.

Italian athletes were clinically evaluated as part of the longstanding and systematic national preparticipation screening program for competitive athletes (10). Standard 12-lead electrocardiograms (ECGs) and limited exercise testing (step test) are routinely obtained as part of this program. Other cardiovascular testing, including maximal exercise stress ECG, may be obtained if judged to be clinically indicated. Myocardial perfusion imaging was not part of the evaluation of any patients in this study.

Statistical analysis. Continuous variables are expressed as mean $\pm$ SD. Chi-square or Fisher exact test were used to assess the significance of differences between subgroups. Two-tailed *p* values < 0.05 were regarded as statistically significant.

RESULTS

Study patients. Twenty-seven competitive athletes comprised this study group by virtue of sudden cardiac death from a congenital coronary anomaly characterized by wrong aortic sinus origin (and course between the aorta and pulmonary trunk). These coronary anomalies included origin of the left main coronary artery (LMCA) from the right aortic sinus (*n* = 23) and origin of the right coronary artery (RCA) from the left sinus (*n* = 4).

Demographics. Of the 27 athletes, 22 were men and 5 were women; ages ranged from 9 to 32 years (mean 16 ± 5). Racial distribution was 16 whites (60%), 9 African Americans (33%) and 2 Asians (7%). Most athletes were competing either in junior high school (12; 44%) or high school (11; 41%); the remainder were professional (*n* = 3) or collegiate (*n* = 1) athletes. The athletes had participated in a variety of sports: basketball (*n* = 8), soccer (*n* = 7), football (*n* = 3), track-sprinting (*n* = 2), distance running (*n* = 2), as well as ice hockey, rugby, softball, cross-country and swimming (one each).

Each athlete died during (*n* = 25) or after (*n* = 2) intense exertion on the athletic field; 16 died during training, and 11 during organized competition. In 12 athletes (44%) the physical effort immediately before death was not only strenuous but also continuous and prolonged (> 30 min). Nineteen of the 27 sudden deaths (70%) were clustered between 3 PM and 9 PM, corresponding to the peak time for participation in most competitive sports; only eight deaths (29%) occurred during the remaining 18 h of the day.

Table 1. Demographic Data in 27 Competitive Athletes Who Died Suddenly of Wrong Aortic Sinus Coronary Artery Anomaly

	No Clinical Data During Life	Clinical Data During Life
No. of athletes	15	12
Gender (M/F)	12/3	10/2
Age (yrs)	9–20 (15 ± 3)	11–32 (17 ± 6)
Nationality	US = 15	US = 6
	Italy = 0	Italy = 6
Race	Black = 5	Black = 4
	White = 8	White = 8
	Asian = 2	
Sport	Basketball = 4	Basketball = 4
	Football = 3	Soccer = 4
	Soccer = 3	Hockey = 1
	Cross-country = 1	Track sprinting = 1
	Distance-running = 1	Rugby = 1
	Softball = 1	Distance-running = 1
	Swimming = 1	
	Track sprinting = 1	
Level of competition	JHS = 5	JHS = 7
	HS = 9	HS = 2
	College = 1	Professional = 3
Coronary anomaly	LMCA = 14	LMCA = 9
	RCA = 1	RCA = 3

HS = high school; JHS = junior high school; LMCA = left main coronary artery; RCA = right coronary artery.

Clinical data. Of the 27 athletes, 15 had no clinical manifestations or testing performed (Table 1, Fig. 1); however, clinical information was available for the remaining 12 patients (Table 2). These two groups did not substantially differ with respect to demographic parameters (Table 1).

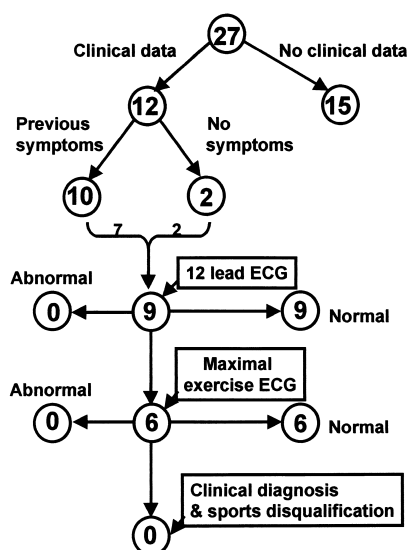


Figure 1. Flow-chart showing clinical data available and findings in the present study group of athletes who died of wrong aortic sinus coronary artery anomalies.

Symptoms. Ten athletes (37%) were known to have experienced, before death, symptoms considered to be cardiovascular in origin. Four of these athletes had a previous syncopal episode, three occurring during physical exertion and one under sedentary circumstances. Of note, syncope occurred only 11 to 24 months before death and was recurrent in two athletes (both with a history of five episodes in the previous 1 to 2 years).

Episodes of chest pain (either typical or atypical of angina) had occurred in five athletes, including three during physical exertion. Each of these athletes experienced single episodes, which occurred a few days to 24 months before death. Two other athletes reported palpitations unrelated to physical activity, and one other experienced dizziness and palpitations with exertion. None of the athletes with symptoms had a family history of premature sudden cardiac death or cardiovascular disease.

Clinical testing. Standard 12-lead ECGs were performed at rest in nine athletes, 6 to 18 months (mean 11 ± 3) before their sudden deaths. Electrocardiogram patterns, including voltages, intervals and T wave morphology, were within normal limits for each (Fig. 2A). Two of these athletes, however, had isolated (one and two) premature ventricular complexes.

A maximal stress test ECG was available for six athletes (treadmill for three athletes from U.S. and bicycle for three from Italy), performed 6 to 18 months (mean 10 ± 4) before sudden death, and each was judged to be within normal limits. All athletes reached Stage V

Table 2. Demographic and Clinical Data in 12 Athletes With Wrong Sinus Coronary Artery Origin and Clinical Manifestations or Diagnostic Testing During Life

Age at Death	Gender	Nation	Race	Sport	Level	Site	Activity	Circumstances of Death	Prior Symptoms	Time From Symptoms to Sudden Death
11	M	Italy	W	Soccer	JHS	Field	Game	During effort	No	—
12	M	U.S.	B	Basketball	JHS	Field	Practice	During effort	Chest pain	7 days
12	M	U.S.	W	Hockey	JHS	Hotel	Sedentary	After effort	Syncope*, chest pain*	15 mo
12	M	U.S.	B	Basketball	JHS	Field	Practice	During effort	Syncope*†	14 mo
14	M	Italy	W	Soccer	JHS	Field	Game	During effort	No	—
15	M	Italy	W	Soccer	JHS	Field	Game	During effort	Syncope*	11 mo
15	F	U.S.	W	Tracksprint	HS	Field	Practice	During effort	Dizziness, palpitations*	15 mo
15	M	U.S.	B	Basketball	JHS	Field	Practice	During effort	Syncope†, chest pain	24 mo
16	M	U.S.	B	Basketball	HS	Field	Game	During effort	Chest pain*	8 mo
22	M	Italy	W	Soccer	Pro	Field	Game	During effort	Palpitations	12 mo
29	M	Italy	W	Rugby	Pro	Field	Practice	During effort	Palpitations	13 mo
32	F	Italy	W	Running	Pro	Field	Game	During effort	Chest pain*	9 mo

*During physical exertion; †recurrent episodes; ‡coronary artery anatomy was not investigated; — = data not available.

HS = high school; JHS = junior high school; LMCA = left main coronary artery origin from right aortic sinus; mo = month; pro = professional; PVC = premature ventricular complex; RCA = right coronary artery origin from left aortic sinus; U.S. = United States.

on the standard Bruce protocol with appropriate blood pressure and heart rate response during exercise and recovery. ST segment and T wave changes, arrhythmias and cardiac symptoms were absent. Also, a limited exercise test (step-test) was available in the six Italian athletes, and none showed abnormalities.

A two-dimensional echocardiogram was performed in two athletes and was normal with regard to left ventricular thickness and cavity dimension as well as segmental and global wall motion. These echocardiograms had not been interpreted prospectively with regard to coronary artery origin from the aorta.

When clinical and demographic variables were compared for athletes with an anomalous LMCA or an anomalous RCA, a statistically significant difference between the two subgroups was evident with respect to the prior occurrence of the major symptoms of syncope and chest pain ($p = 0.04$), which occurred exclusively in patients with an anomalous LMCA.

Pathologic findings. Each heart was characterized by both an acute angled take-off of the anomalous coronary artery, with a slit-like lumen at its point of origin from the wrong aortic sinus, and a proximal course between the aorta and pulmonary trunk (Fig. 2B). Heart weights were 240 to 410 g (mean 312 ± 87). Atherosclerotic narrowing of the major extramural coronary arteries (>50% of the cross-sectional area) was absent. Only one heart showed gross evidence of myocardial scarring suggestive of prior infarction.

Heart specimens were available for reexamination in 6 of

the 27 athletes (all Italian), including three with anomalous LMCA and three with anomalous RCA. In three of these hearts, based on histologic examination, the course of the proximal portion of the anomalous coronary artery (LMCA in two, RCA in one) was documented to be intramural, i.e., contained completely within the aortic wall (Fig. 3, A and B), so that the coronary artery and the aorta shared the same media without an interpositioned adventitia. In addition, in each of the six hearts, the region of myocardium supplied by the anomalous coronary artery showed evidence of acute ischemia with contraction band necrosis, wavy fibers and early neutrophilic infiltrate (Fig. 3C), and focal evidence of chronic myocardial ischemic damage with patchy replacement-type fibrosis was present in three (Fig. 3D).

DISCUSSION

Background and prevalence. Sudden death in young competitive athletes is often caused by previously unsuspected congenital cardiovascular disease (1–10). The prevalence of athletic field deaths has been estimated to be 0.5:100,000 per year in high-school-age athletes in the U.S. (19) and 1.6:100,000 per year in competitive athletes in Italy (10). In most U.S. autopsy-based series, hypertrophic cardiomyopathy is the most common cause of young athletic field deaths (1,2,5–9). By contrast, in Italy hypertrophic cardiomyopathy is an uncommon cause of such deaths, probably largely because of effective preparticipation screening and disqualification from sports; as a consequence, arrhythmogenic right ventricular cardiomyopathy has become the most common cause of these catastrophes in Italy (3,4,10).

Table 2. Continued

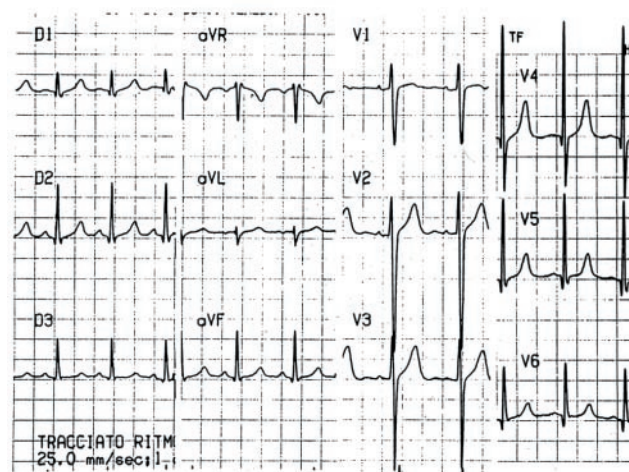
12-lead ECG Pattern	Maximal Stress ECG	2-D Echo	Coronary Anomaly (Autopsy)
Normal	—	—	LMCA
—	—	—	LMCA
Normal	Normal	Normal‡	LMCA
Normal	Normal	Normal‡	LMCA
Normal	—	—	RCA
Normal	Normal	—	LMCA
Normal	Normal	—	LMCA
—	—	—	LMCA
—	—	—	LMCA
Normal; PVC (1)	—	—	RCA
Normal; PVC (2)	Normal	—	RCA
Normal	Normal	—	LMCA

Nevertheless, in each of these populations, a variety of congenital coronary artery anomalies have been reported as frequent causes for athletic field sudden death (up to about 20%) (3-5,8-10).

Among the congenital coronary malformations, coronary artery origin from the wrong aortic sinus (coursing between aorta and pulmonary trunk) appears to be the most common in young trained athletes dying suddenly. Indeed, we have previously reported that these malformations are associated with sudden death more commonly in competitive athletes than in non-athletes (10).

However, these anomalies are rarely suspected or identified during life and are usually first recognized at autopsy, largely because there is insufficient clinical suspicion as well as the difficulties implicit in routine examination or clinical testing for these malformations (10,20,21). Consequently, such coronary anomalies are not recognized during routine preparticipation screening (10,22,23). Therefore, we thought it would be important to develop a clinical profile and assess the utility of noninvasive testing in young competitive athletes who had died suddenly with anomalous coronary artery origin from the wrong aortic sinus. Previously published descriptions are largely represented by anecdotal case reports. Thus, we believe this study is unique because it represents the first consecutive series of young athletic field deaths due to these coronary malformations in which it is possible to systematically assemble clinical data collected during life.

Premonitory symptoms. Premonitory symptoms occurred not uncommonly during life among our study patients (in about one third). Syncope or chest pain occurred in seven athletes within 24 months of sudden death. In our athlete



A



B

Figure 2. A 15-year-old male Italian soccer player with a history of exertional syncope one year before death who died suddenly while running during the second half of a game. **(A)** A 12-lead ECG performed 10 months before death, as part of routine preparticipation screening, is within normal limits. **(B)** View of the aortic root; RCA arises normally from the right aortic sinus (arrow), and the LMCA arises anomalously from the right sinus with an acute angle take-off producing a slit-like lumen (arrowhead).

series, these major symptoms were limited to anomalous LMCA origin, while anomalous origin of the RCA proved to be clinically silent. Other authors have, however, reported a few patients with anomalous RCA who experienced either angina or syncope before death (24,25). Therefore, although sudden death is frequently the first manifestation in patients with wrong sinus coronary artery origin, premonitory symptoms occur in a substantial proportion of these individuals (20). In both types of wrong sinus coronary artery anomalies described here, the vast majority of clinical events were related to exertion. These observations emphasize the pressing need to raise the index of clinical suspicion in an effort to identify during life any wrong aortic sinus coronary artery origin in young, physically active individuals (10).

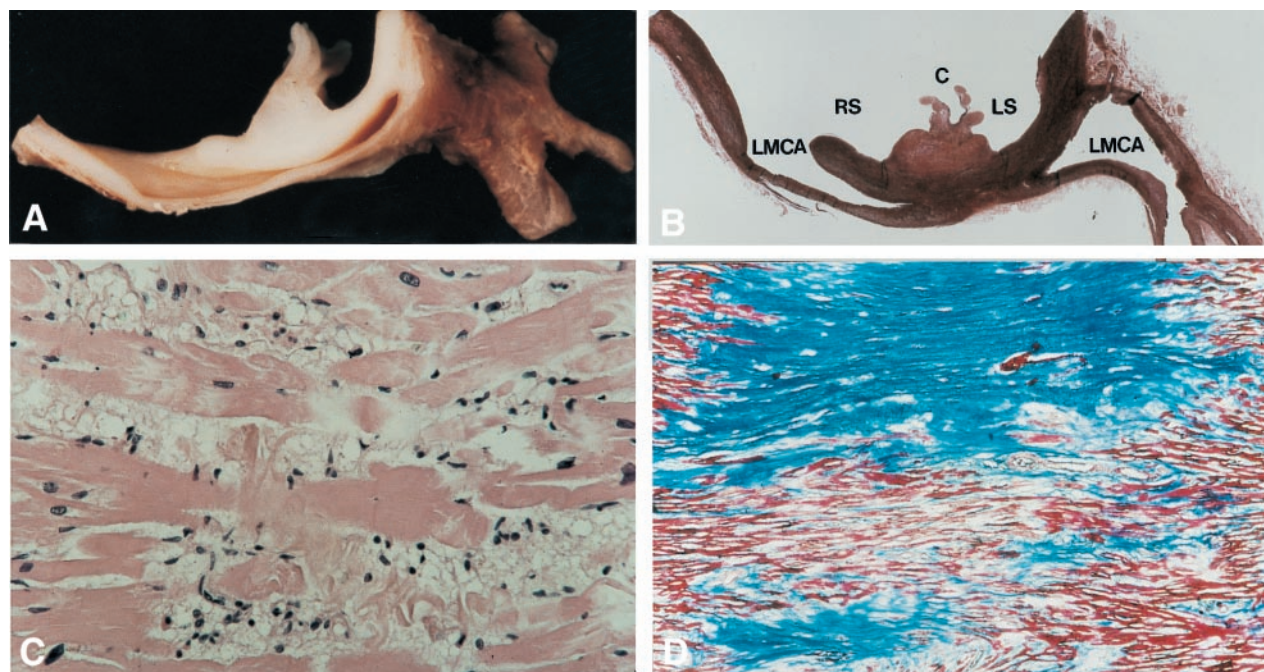


Figure 3. From the same Italian soccer player shown in Figure 2, with anomalous left main coronary artery (LMCA) and intramural course. **(A)** Transverse section of the aortic root at the commissural level. The anomalous LMCA shows an intramural aortic course just behind the commissure between the two coronary cusps. **(B)** Panoramic histology showing that the LMCA, which arises from the right sinus (RS) instead of from the left sinus (LS), and the aorta share the same media without an interpositioned adventitia, accounting for a collapsed coronary lumen (Weigert van Gieson stain, $\times 3$) (C = commissure). **(C)** Histologic section of the region of left ventricular myocardium supplied by the anomalous LMCA showing diffuse myocyte necrosis and neutrophilic infiltrates (Haematoxylin-Eosin stain, $\times 240$). **(D)** Multiple patchy areas of replacement-type fibrosis that stain blue are diffusely distributed throughout the myocardium (Heidenhain trichrome stain, $\times 30$).

Efficacy of ECG testing. In the present retrospective study of trained athletes, we showed that neither routine 12-lead ECG nor exercise stress tests were particularly informative for the diagnosis of congenital coronary anomalies. In particular, each of the nine ECGs recorded under resting conditions were within normal limits. These findings in our series of patients are consistent with that of several case reports in which an ECG was recorded (unassociated with symptoms) (21). In addition, exercise ECGs were available in six of our athletes, and each was within normal limits. In a review of the literature, we found 18 young patients (≤ 35 years) with wrong aortic sinus coronary artery anomaly and reported exercise stress test findings (Table 3), of whom only three were competitive athletes (11,14,26-38). A positive stress test ECG was present in only four of the 18 patients (22%), including two who were symptomatic (but none of the athletes). Thus, a negative even maximal-effort stress ECG does not exclude a potentially lethal coronary anomaly.

Pathophysiology of myocardial ischemia and sudden death. The clinical data available in this series suggest that myocardial ischemia in young athletes with wrong aortic sinus coronary artery anomalies probably occurs in infrequent bursts, which may be cumulative with time. This view

is supported by our data showing normal ECG patterns associated with pathologic evidence of acute myocardial ischemic damage and/or chronic ischemic injury with replacement-type fibrosis (in each of the six hearts available for morphologic reassessment). Thus, repetitive ischemic episodes may result in patchy myocardial necrosis and fibrosis, which could predispose to lethal ventricular tachyarrhythmias by creating an electrically unstable myocardial substrate. Considering the fact that these trained athletes had performed intense physical exercise many times before their fatal event (average age 16 years), it is most likely that critical impairment of coronary flow to the myocardium occurs only sporadically. Several potential mechanisms have been advanced to explain myocardial ischemia and sudden death in patients with wrong sinus coronary anomalies (11,12,16): the acute angle take-off and kinking of the coronary artery as it arises from the aorta; flap-like closure of the abnormal slit-like coronary orifice; compression of the anomalous coronary artery between the aorta and pulmonary trunk during exercise; and spasm of the anomalous coronary artery, possibly as a result of endothelial injury (39,40). Moreover, in three of the hearts we documented that, as previously described by others (11,39), the proximal portion of the anomalous coronary artery was essentially intramural (i.e., within the aortic tunica media), which

Table 3. Previously Published Reports of Wrong Sinus Coronary Artery Anomalies in Persons Aged ≤ 35 Years in Whom ECG Data Were Available

Reference (#)	Year	Age, Gender	Anomaly	Symptoms	12-lead ECG	Exercise Stress Test	Myocardial Perfusion Scintigraphy	Athlete	Outcome ECG
Cheitlin et al. (11)	1974	14 M	LMCA	Syncope†	Normal	Normal	0	0	Alive (with surgery)
Pedal et al. (26)	1976	10 F	LMCA	Syncope	Normal	Normal	0	0	Sudden death
Benge et al. (27)	1980	25 M	RCA	Syncope	T wave inversion (II, III, aVF, V3-V6)	Normal	Not diagnostic	0	Alive
Mustafa et al. (28)	1981	12 M	LMCA	Syncope	Normal	Normal	Normal	0	Alive (with surgery)
Brandt et al. (29)	1983	35 M	RCA	Angina†	Inferior subendocardial MI	Normal	0	0	Alive (with surgery)
Donaldson et al. (30)	1983	* M	LMCA	Angina†	Normal	Positive (ventricular tachycardia)	0	0	Alive (with surgery)
Donaldson et al. (30)	1983	* M	LMCA	Angina†	Normal	Positive (subendocardial ischemia)	0	0	Alive (with surgery)
Donaldson et al. (30)	1983	* M	LMCA	Syncope†	Normal	Positive (subendocardial ischemia)	0	0	Alive (with surgery)
Barth and Roberts (31)	1986	14 M	LMCA	Syncope/angina†	Normal	Normal	0	0	Sudden death
Vander Sande et al. (32)	1989	14 F	LMCA	Syncope†	Normal	First degree atrioventricular block	0	0	Sudden death
Maron et al. (33)	1991	21 M	LMCA	Syncope†	LVI, T wave inversion (lateral leads)	Positive (sinus bradycardia, syncope)	0	0	Alive (with surgery)
Corrado et al. (14)	1992	22 M	RCA	Palpitations	Normal (PVC)	Normal	0	+	Sudden death
Amarasena et al. (34)	1993	18 M	LMCA	Syncope†	T wave inversion (I, aVL, V2-V3)	Normal	0	0	Alive (with surgery)
Jureidini et al. (35)	1994	12 M	LMCA	Syncope†	Normal	Normal	0	0	Sudden death
Van Son et al. (36)	1996	9 M	LMCA	Angina, syncope†	ST-T changes (II, aVF, V5-V6)	Normal	Normal	0	Alive (with surgery)
Phoon et al. (37)	1997	11 M	LMCA	Angina†	ST-T changes; PVC	Normal	Normal	0	Alive (with surgery)
Zeppilli et al. (38)	1998	17 M	RCA	None	Normal (PVC)	Normal	Normal	+	Alive
Zeppilli et al. (38)	1998	18 M	RCA	Dyspnea†	Incomplete RBBB	Normal	Positive (ischemia)	+	Alive

*Subjects aged ≤ 35 years but precise age of each individual patient uncertain; †on effort; 0 = absent; + = present.
LMCA = left main coronary artery; LVI = left ventricular hypertrophy; MI = myocardial infarction; PVC = premature ventricular complex; RBBB = right bundle branch block; RCA = right coronary artery.

could further aggravate the coronary obstruction, particularly with expansion of the aorta during exercise.

Strategies for clinical identification. On the basis of our findings, preparticipation screening, whether confined to standard history and physical examination or including 12-lead or exercise ECG (as is the practice in Italy), is limited in its power to identify coronary artery anomalies in young competitive athletes (10,22). Indeed, these lesions usually can be suspected only by prior symptoms such as syncope and angina, particularly if they occur during or immediately after exertion. Our observation that all 12-lead and exercise ECGs were within normal limits would seem to suggest that these tests are unlikely to provide clinical evidence of myocardial ischemia resulting from anomalous coronary artery origin, and they are therefore unreliable for clinical recognition of these coronary anomalies at preparticipation screening of competitive athletes (10).

A strategy for clinical identification of wrong sinus coronary artery anomalies in young athletes could be summarized as follows. If the index of suspicion is sufficiently high because of the presence of potential clinical markers such as exertional syncope or chest pain (even in the setting of both a normal 12-lead ECG and maximal exercise test), the anatomy of these malformations can be suspected or defined noninvasively by transthoracic or transesophageal echocardiography. Pelliccia et al. (41) demonstrated that echocardiographic imaging of left and right coronary arteries is feasible and reliable in a substantial proportion of young athletes (about 95%). Therefore, the failure to demonstrate that both the proximal left and right coronary arteries actually originate from their usual coronary sinuses in a young person with impaired consciousness or angina suggests the necessity of further anatomic definition with coronary arteriography (42) or possibly with magnetic resonance imaging (38,43,44) or computed tomography (45). An assessment of the diagnostic reliability of echocardiography in this regard for our patients was beyond the scope of the present paper. Two of our athletes had two-dimensional echocardiograms performed, but neither examination focused on the anatomy of coronary artery origin and course, as described by Pelliccia et al. (41).

Surgical management. Timely clinical identification of wrong sinus coronary artery anomalies in young trained athletes is crucial for two reasons. First, these coronary anomalies should result in exclusion from participation in intense competitive sports to reduce the risk of a cardiac event or sudden death (10,18). Second, and more importantly, wrong sinus coronary artery anomalies are surgically correctable (46). Indeed, operation is probably mandatory in any young person, particularly if symptomatic—with or without evidence of myocardial ischemia. Coronary artery bypass grafting remains the standard procedure for restoring normal distal coronary flow with good long-term results (46). An alternative surgical approach involves reimplantation of the anomalous vessel

in the proper coronary sinus, but the results are still preliminary (25). Recently, a new operative technique has been employed in the setting of a proximal aortic intramural course (such as described here), in which the ostium of the anomalous coronary artery is modified at the aorta by excising (“unroofing”) the common wall located between the aorta and the anomalous coronary artery (36,37,47).

Reprint requests and correspondence: Dr. Cristina Basso, Cardiovascular Pathology, University of Padua Medical School, Via A. Gabelli, 61, Padua, Italy.

REFERENCES

1. Maron BJ, Roberts WC, McAllister HA, et al. Sudden death in young athletes. *Circulation* 1980;62:218–29.
2. Maron BJ, Epstein SE, Roberts WC. Causes of sudden death in competitive athletes. *J Am Coll Cardiol* 1986;7:204–14.
3. Corrado D, Thiene G, Nava A, et al. Sudden death in young competitive athletes: clinicopathologic correlations in 22 cases. *Am J Med* 1990;89:588–96.
4. Thiene G, Nava A, Corrado D, et al. Right ventricular cardiomyopathy and sudden death in young people. *N Engl J Med* 1988;318:129–33.
5. Burke AP, Farb A, Virmani R, et al. Sports-related and non-sports-related sudden cardiac death in young adults. *Am Heart J* 1991;121:568–75.
6. Maron BJ, Shirani J, Poliac LC, et al. Sudden death in young competitive athletes: clinical, demographic and pathological profiles. *JAMA* 1996;276:199–204.
7. Maron BJ. Sudden death in young athletes. Lessons from the Hank Gathers affair. *N Engl J Med* 1993;329:55–7.
8. Libershon RR. Sudden death from cardiac causes in children and young adults. *N Engl J Med* 1996;334:1039–44.
9. van Camp SP, Bloor CM, Mueller FO, et al. Nontraumatic sports death in high school and college athletes. *Med Sci Sports Exerc* 1995;27:641–7.
10. Corrado D, Basso C, Schiavon M, Thiene G. Screening for hypertrophic cardiomyopathy in young athletes. *N Engl J Med* 1998;339:364–9.
11. Cheitlin MD, De Castro CM, McAllister HA. Sudden death as a complication of anomalous left coronary origin from the anterior sinus of Valsalva. A not-so-minor congenital anomaly. *Circulation* 1974;50:780–7.
12. Roberts WC. Major anomalies of coronary arterial origin seen in adulthood. *Am Heart J* 1986;111:941–63.
13. Taylor AJ, Rogan KM, Virmani R. Sudden cardiac death associated with isolated congenital coronary artery anomalies. *J Am Coll Cardiol* 1992;20:640–7.
14. Corrado D, Thiene G, Cocco P, Frescura C. Nonatherosclerotic coronary artery disease and sudden death in the young. *Br Heart J* 1992;68:601–7.
15. Basso C, Frescura C, Corrado D, et al. Congenital heart disease and sudden death in the young. *Hum Pathol* 1995;26:1065–72.
16. Frescura C, Basso C, Thiene G, et al. Anomalous origin of coronary arteries and risk of sudden death: a study based on an autopsy population of congenital heart disease. *Hum Pathol* 1998;29:689–95.
17. Cohen AJ, Grishkin BA, Helsel RA, Head HD. Surgical therapy in the management of coronary anomalies: emphasis on utility of internal mammary artery grafts. *Ann Thorac Surg* 1989;47:630–7.
18. Maron BJ, Mitchell JE. 26th Bethesda Conference: recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities. *J Am Coll Cardiol* 1994;24:845–99.
19. Maron BJ, Gohman TE, Aeppli D. Prevalence of sudden cardiac death during competitive sports activity in Minnesota high school athletes. *J Am Coll Cardiol* 1998;32:1881–4.
20. Cheitlin MD. Coronary anomalies as a cause of sudden death in the athlete. In: Estes NAM, Salem DN, Wang PJ, editors. Sudden

- Cardiac Death in the Athlete. Armonk, NY Futura Publishing, 1998;379.
21. Chu E, Cheitlin MD. Diagnostic considerations in patients with suspected coronary artery anomalies. *Am Heart J* 1993;126:1427-38.
22. Maron BJ, Thompson PD, Puffer JC, et al. Cardiovascular preparticipation screening of competitive athletes. *Circulation* 1996;94:850-6.
23. Maron BJ, Bodison SA, Wesley YE, et al. Results of screening a large group of intercollegiate competitive athletes for cardiovascular disease. *J Am Coll Cardiol* 1987;10:1214-21.
24. Roberts WC, Siegel RJ, Zipes DP. Origin of the right coronary artery from the left sinus of Valsalva and its functional consequences: analysis of 10 necropsy patients. *Am J Cardiol* 1982;49:863-8.
25. Ghosh PK, Agarwal SK, Kumar R, et al. Anomalous origin of the right coronary artery from left aortic sinus. *J Cardiovasc Surg* 1994;35:65-70.
26. Pedal I. Aortale urprungsanomalie einer koronararterie. *Dtsch Med Wochenschr* 1976;101:1601-4.
27. Bengt W, Martins JB, Funk DC. Morbidity associated with anomalous origin of the right coronary artery from the left sinus of Valsalva. *Am Heart J* 1980;99:96-100.
28. Mustafa I, Gula G, Radley-Smith R, et al. Anomalous origin of the left coronary artery from the anterior aortic sinus: a potential cause of sudden death. *J Thorac Cardiovasc Surg* 1981;82:297-300.
29. Brandt B, Martins JB, Marcus ML. Anomalous origin of the right coronary artery from the left sinus of Valsalva. *N Engl J Med* 1983;309:596-8.
30. Donaldson RM, Raphael M, Radley-Smith R, et al. Angiographic identification of primary coronary anomalies causing impaired myocardial perfusion. *Cathet Cardiovasc Diagn* 1983;9:237-49.
31. Barth CW, Roberts WC. Left main coronary artery originating from the right sinus of Valsalva and coursing between the aorta and pulmonary trunk. *J Am Coll Cardiol* 1986;7:366-73.
32. Vander-Sande JH, Vandermaast MF, Amsel BJ, et al. Cardiac arrest due to aberrant left coronary artery originating from the right sinus of Valsalva in a young girl. *Intensive Care Med* 1989;15:135-6.
33. Maron BJ, Leon MB, Swain JA, et al. Prospective identification by two dimensional echocardiography of anomalous origin of the left main coronary artery from the right sinus of Valsalva. *Am J Cardiol* 1991;68:140-2.
34. Amarasekera NL, Pillai RP, Forfar JC. Atypical ventricular tachycardia and syncope with left coronary artery origin from the right coronary sinus. *Br Heart J* 1993;70:391-2.
35. Jureidini SB, Eaton C, Williams J, et al. Transthoracic two-dimensional and color flow echocardiographic diagnosis of aberrant left coronary artery. *Am Heart J* 1994;127:438-40.
36. Van Son JAM, Haas GS. Anomalous origin of left main coronary artery from right sinus of Valsalva: modified surgical treatment to avoid neocoronary ostial stenosis. *Eur J Cardiothorac Surg* 1996;10:467-9.
37. Phoon CK, van Son J, Moore PA, et al. Aberrant left coronary artery arising from the right sinus of Valsalva with a right coronary arteriovenous malformation. *Pediatr Cardiol* 1997;18:385-8.
38. Zeppilli P, Dello Russo A, Santini C, et al. In vivo detection of coronary artery anomalies in asymptomatic athletes by echocardiographic screening. *Chest* 1998;114:89-93.
39. Taylor AJ, Byers JP, Cheitlin MD, Virmani R. Anomalous right or left coronary artery from the contralateral coronary sinus: "high-risk" abnormalities in the initial coronary artery course and heterogeneous clinical outcomes. *Am Heart J* 1997;133:428-35.
40. Maddoux GL, Goss JE, Ramo BW, et al. Angina and vasospasm at rest in a patient with an anomalous left coronary stem. *Cathet Cardiovasc Diagn* 1989;16:95-8.
41. Pelliccia A, Spataro A, Maron BJ. Prospective echocardiographic screening for coronary artery anomalies in 1,360 elite competitive athletes. *Am J Cardiol* 1993;72:978-9.
42. Serota H, Barth CW, III, Seuc CA, et al. Rapid identification of course of anomalous coronary arteries in adults: the "dot and eye" method. *Am J Cardiol* 1990;65:891-8.
43. McConnell MV, Ganz P, Selwyn AP, et al. Identification of anomalous coronary arteries and their anatomic course by magnetic resonance coronary angiography. *Circulation* 1995;92:3158-62.
44. Post JC, van Rossum AC, Bronzwaer JGF, et al. Magnetic resonance angiography of anomalous coronary arteries. A new gold standard for delineating the proximal course? *Circulation* 1995;92:3163-71.
45. Mousseaux E, Hernigou A, Sapoval M, et al. Coronary arteries arising from the contralateral aortic sinus: electron beam computed tomographic demonstration of the initial course of the artery with respect to the aorta and right ventricular outflow tract. *J Thorac Cardiovasc Surg* 1996;112:836-40.
46. Thomas D, Salloum J, Montalescot G, et al. Anomalous coronary arteries coursing between the aorta and pulmonary trunk: clinical indication for coronary artery bypass. *Eur Heart J* 1991;12:832-4.
47. Daliento L, Fasoli G, Mazzucco A. Anomalous origin of the left coronary artery from the anterior aortic sinus: role of echocardiography. *Int J Cardiol* 1993;38:89-91.