Asymptomatic Wolff-Parkinson-White Pattern ECG in USAF Aviators

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INTRODUCTION: Wolff-Parkinson-White (WPW) pattern is occasionally found in asymptomatic aviators during routine ECGs. Aeromedical concerns regarding WPW pattern include risk of dysrhythmia or sudden cardiac death (SCD), thus affecting the safety of flight. The purpose of this study was to determine the prevalence and outcomes of aviators with asymptomatic WPW pattern and assess for risk factors that contribute to progression to dysrhythmia or symptoms.

METHODS: The U.S. Air Force (USAF) ECG library database containing over 1.2 million ECGs collected over the past 68 yr was used to identify 638 individual aviators with WPW pattern. Demographic, medical history, and outcome data were obtained by medical record review. Aviators who developed high risk features defined as symptoms, arrhythmia, or ablation of a high risk pathway, were compared to those who remained asymptomatic.

RESULTS: Prevalence of WPW pattern was 0.30% among all USAF aviators. Of the 638 individuals, 64 (10%) progressed to the combined endpoint of SCD, arrhythmia, and/or ablation of a high risk pathway over 6868 patient years, with average follow-up of 10.5 yr. There were two sudden cardiac deaths (0.3%). Annual risk of possible sudden incapacitation was 0.95% and of SCD 0.03%. Those that progressed to high risk were significantly younger, had lower diastolic blood pressure, lower total cholesterol, and better physical fitness testing scores.

DISCUSSION: WPW pattern on ECG found in asymptomatic aviators confers $<$ 1% annual risk of arrhythmia or incapacitating events with the highest risk in the younger, healthier, and most fit populations.

KEYWORDS: pre-excitation, WPW syndrome, aviation, catheter ablation.

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Wolff-Parkinson-White (WPW) syndrome was first described in 1930 by Drs. Wolff and White as an ECG pattern of "bundle branch block" with short PR interval in healthy young people prone to paroxysmal tachycardia.[1,3] Many years later, from anatomical and electrophysiological observations, the mechanism was established as a reentrant circuit, including the normal AV node-His axis and one or more bypass tract(s). The characteristic electrocardiogram (ECG) pattern for WPW syndrome includes a shortened PR interval, slightly widened QRS complex(es), and a delta wave due to pre-excitation of the ventricle via bypass tract with competing normal AV nodal ventricular activation.[1,3] Asymptomatic WPW pattern refers to ECG findings consistent with WPW in an individual who has no symptoms or arrhythmia. This is also sometimes referred to as isolated ventricular pre-excitation.[1]

Unfortunately, sudden cardiac death can occasionally be the presenting symptom for people with WPW syndrome.[4] The two typical mechanisms of arrhythmia are orthodromic atrioventricular reentrant tachycardia, which is due to retrograde AV conduction via an accessory pathway and anterograde conduction via the normal AV node-His-Purkinje pathway, and atrial fibrillation with rapid anterograde conduction via the accessory pathway, bypassing the normal AV node-His-Purkinje axis; either mechanism can lead to ventricular fibrillation.[1,3] Thus, for people with high-risk occupations such as those in aviation, WPW remains an important concern which goes beyond an abnormal ECG pattern. The

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prevalence of WPW pattern in the general population is estimated to be between 0.1% and 0.3%.[1,3,5]

Research on asymptomatic WPW pattern is vast and varied. We first studied aviators with WPW pattern in 1968 using 320 ECGs on 128 aviators with up to 28 yr of follow-up and found that although 13% developed tachyarrhythmias, there were no known deaths attributable to cardiac etiology and, thus, WPW pattern was not thought to affect ability to perform flying duties.[2] Another study done by our group in 2001 on 228 military aviators over 4906 patient years with WPW pattern showed rates of SCD at 0.0002 per patient-year and annual risk of supraventricular tachycardia (SVT) of approximately 1%. Although there has been no conclusive evidence of greater than a 1% annual risk of sudden incapacitation in aviators, there were many studies done in 2003–2014 in nonaviators that showed SVT rates of 30–77% over 10 yr for an annual risk of 3–8% per year, well above that seen in aviators in the past.[9,10,11] These data prompted a new practice guideline for risk stratification for arrhythmic events in patients with asymptomatic pre-excitation.[1] The recommendations were based on nine studies, of which four were Italian studies done by the same group, with most patients from a single registry, none of whom were aviators. The recommendations for electrophysiology (EP) study in asymptomatic WPW pattern were based largely on one study of 2169 patients, of which 550 were actually symptomatic, median age was 19 yr old, and all malignant arrhythmias (V-fib) were age 32 or less with an average age of 12 yr old, only two were over 14 yr old, all were symptomatic prior to arrhythmia, and all were resuscitated, with no deaths. This study also showed the highest complication rate with ablation at 4%.[11] In the recently published 2015 ACC/AHA/HRS Guideline for management of adult patients with supraventricular tachycardia, they give a class IIA recommendation for all patients with asymptomatic WPW pattern to undergo EP study to risk-stratify arrhythmic events to be treated with catheter ablation if the EP study identifies high risk; however, they also give a IIA recommendation for observation without further evaluation. Most importantly, the same guideline gives a IIA recommendation to treat with ablation in "asymptomatic patients if the presence of pre-excitation precludes specific employment (such as with pilots)."[8] There were no data from high risk occupations such as pilots presented to support this last recommendation and, thus, we sought to answer the question: should asymptomatic WPW pattern without ablation "preclude specific employment…such as with pilots." The purpose of this study was to determine the prevalence of WPW pattern in U.S. Air Force (USAF) aviators, then compare those who remained asymptomatic to those who developed high risk features, defined as symptoms, arrhythmia [SVT and sudden cardiac death (SCD)], or ablation of high risk pathways.

METHODS

Data Collection

The study protocol was approved by the USAF 711th Human Performance Wing's Air Force Research Laboratory Institutional Review Board, Wright-Patterson Air Force Base, OH. All cardiac studies performed on aviators in the USAF are sent to the ECG library located at Wright-Patterson Air Force Base, OH. The ECG library started collecting data in 1957, at which time a screening ECG became required prior to entering aviation career fields, then periodically afterwards. In this database of just over 1.2 million ECGs, we found 729 past aviators, current aviators, and applicants who had WPW pattern on ECG. The Aeromedical Information Management Waiver Tracking System (AIMWTS) was queried using the diagnosis codes (ICD 9) 426.0 to 426.09 and 426.7 to 426.79, and the word queries "Wolff" and 'WPW.' This search of AIMWTS yielded a list of 216 aviators with the diagnosis. After combining the two lists and removing duplicate entries, 840 past and current aviators with a diagnosis of either Wolff-Parkinson-White pattern or syndrome were identified. Of these 840 individuals, 158 were excluded for insufficient follow-up data. Of the 682 remaining individuals, 44 were classified as having the diagnosis of WPW syndrome (based on high risk features) at the time of initial diagnosis and thus were excluded. From the remaining 638 individuals with an initial diagnosis of WPW pattern, there were 64 individuals who later had symptoms, SCD, arrhythmia, or ablation of a high risk pathway during the time they were followed by the Air Force.

The USAF's electronic medical record, AIMWTS, the USAF ECG library, and the Air Force Fitness Management System databases were used to obtain outcomes and risk factor data. For past aviators with no data history in the electronic medical record, AIMWTS, or Air Force Fitness Management System, all data was obtained from the ECG library.

The primary outcome was progression to symptoms, dysrhythmia, ablation of high risk pathway, or SCD. A pathway was considered high risk on EP study if there was a short refractory period (<250 ms), retrograde conduction, or multiple pathways. Secondary outcomes included dysrhythmia, ablation, SCD, coronary artery disease, and aeromedical disqualification. Variables assessed included physical fitness testing (PT) data, BMI, systolic blood pressure, diastolic blood pressure, heart rate, age, sex, total cholesterol, LDL cholesterol, HDL cholesterol, tobacco use, and alcohol use. Echocardiogram data included ejection fraction, evidence of left ventricular hypertrophy, and evidence of left atrial enlargement. Exercise treadmill test data included evidence of ischemia, WPW pattern at baseline, resolution of WPW pattern on surface ECG during testing, any arrhythmias during testing, and duration of the treadmill test in minutes. Holter monitor testing included average heart rate, WPW pattern or SVT on the Holter recording, and whether the Holter monitor was done prior to or after any ablation procedures. Electrophysiological and/or ablation testing data included location of the accessory pathway, refractory period of the accessory pathway, whether the accessory pathway had retrograde conduction, whether multiple accessory pathways were present, and the date of the study. The PT test information only included data from after 1 July 2010 because the test scoring changed at that time. We looked at total PT scores and aerobic PT scores.

The individuals in the WPW pattern group may have had an EP study as this was not required in all cases; however, to return to flying duties ablation was required if the EP study showed high risk characteristics that would have predicted future arrhythmic events. High risk characteristics on EP study that required ablation included presence of retrograde conduction, multiple pathways, and/or fast antegrade pathway conduction manifested by a short refractory period or shortest pre-excited R to R interval during induced or spontaneous atrial fibrillation of less than 250 ms. For all those who received an ablation, their periods of follow-up, for the purposes of this study, ended at the time of their ablation as they were considered "cured."

Study Design

This is a retrospective case-control study. Cases consisted of aviators who initially had WPW pattern only on ECG and developed symptoms, arrhythmia, or ablation for high risk features during the follow-up period. Controls consisted of aviators who had WPW pattern only, but did not develop symptoms or undergo ablation. For the overall prevalence of WPW in the aviator population, cases consisted of aviators who had ever had either WPW syndrome or WPW pattern on ECG.

Statistical Analysis

Demographic statistics were derived from all primary and secondary endpoints and are listed in **Table I** and **Table II**. Chi-squared and Fisher exact tests were used to determine the difference in prevalence among the categorical variables listed in **Table III**. One-sided *t*-tests were used to compare means of continuous variables listed in Table II and **Table IV**. A significance level of 0.05 was used to determine prevalence and mean differences in all statistical tests.

RESULTS

There were 840 aviators with a diagnosis of WPW pattern or syndrome in the ECG database, which corresponds to a prevalence of WPW in our population of 0.298%. In the 638 who had appropriate follow-up, there were 44 individuals who had an initial diagnosis of WPW syndrome (thus high risk WPW) and an additional 64 who later met the primary outcome of high risk features for a total prevalence of "high risk WPW" of 0.038%. The demographics of those with initial diagnosis of asymptomatic WPW pattern compared to those with high risk WPW pattern/syndrome in the ECG library are in Table I.

Table I. Comparison of Participants' Demographics of Initial ECG Diagnosis of WPW Syndrome and WPW Pattern.

	WPW SYNDROME	TOTAL WPW PATTERN
Number of People	44	682
Age Range at Diagnosis	2–45	2–58
Mean Age at Diagnosis	21.3 yr	28.6 yr
Male (%)	36 (81.88%)	655 (96.0%)
Female (%)	8 (18.2%)	27 (4.0%)
Mean Years Follow-up	1.9 yr	10.5 yr

In the 638 individuals with WPW pattern, 574 remained with WPW pattern only, while 64 met the primary end point of progression to high risk. Table II compares the demographic information for those who remained asymptomatic to those who progressed to high risk (symptoms, ablation of high risk pathway, arrhythmia, or SCD). Those that progressed to high risk were significantly younger [$t(636) = -3.12$, $P = 0.001$] and less likely to have long-term follow-up since many were no longer allowed to continue aviation duties in the USAF. There was a nonsignificant trend for women to be more likely to progress to high risk than men; however, there were very few women in the study.

Comparison of variables, risk factors, and secondary endpoints between groups can be seen in Table III**.** Those that progressed to high risk had significantly lower LDL [$t(279) = -2.29$, $P = 0.0114$], total cholesterol [$t(287) = -2.95$, $P = 0.0017$], and diastolic blood pressure [$t(417) = -1.84$, $P = 0.0329$]. Those that progressed to high risk had significantly higher overall PT scores [$t(20) = 2.01$, $P = 0.0288$] and aerobic PT scores [$t(20) = 2.55$, $P = 0.0096$].

There was progression to symptoms, arrhythmia, and/or high risk features on EP study in 64 of the 638 individuals who started with only WPW pattern (10%). There was an average follow-up of 10.5 yr, which gives a 0.95% annual risk of possible sudden incapacitation in this population with asymptomatic WPW pattern.

DISCUSSION

This study found the prevalence of combined WPW pattern and syndrome in our population of USAF aviators to be 0.298% and the prevalence of WPW with high risk features to be 0.038%. The annual risk of someone in our population with WPW pattern going on to arrhythmia, SCD, or a high risk EP study requiring ablation is 0.95%, while risk of sudden cardiac death is 0.03% and younger, healthier aviators (lower lipids, lower blood pressure, and better PT test scores) have increased risk of arrhythmia.

Current guidelines show a high level of evidence and a class I recommendation that abrupt loss of conduction over a manifest pathway during exercise testing in sinus rhythm or intermittent loss of pre-excitation during ECG or ambulatory monitoring are useful to identify patients at low risk of rapid conduction over the pathway.[1] In our study, although half of the high risk WPW patterns resolved with exercise, the feature that classified all 10 of these as high risk was retrograde conduction across the pathway and none had inducible arrhythmia or rapid antegrade conduction (<250 ms) across the accessory pathway. Alternatively, we did have 21 patients who did not lose the WPW pattern with exercise who went on to low risk EP studies. There were no patients age 35 or older who had WPW pattern that was either intermittent or resolved abruptly with exercise testing who went on to high risk. In our review of the literature and given our current study results, there is no data to support EP study with or without ablation in adults age 35 or older with

Table II. Comparison of Participants' Demographics of Those Remaining in Low Risk WPW Pattern and Those Who Converted to High Risk WPW Pattern/Syndrome.

	WPW PATTERN HIGH RISK	WPW PATTERN LOW RISK	TEST STATISTIC	ONE-SIDED *P*-VALUE
Number of people	64	574		
Age range at Diagnosis	18–53	2–58		
Mean age at Diagnosis (SD)	25.9 yr (6.9)	29.4 yr (8.8)	−3.12‡	0.0010†
Male (%)	60 (93.8%)	559 (97.4%)	0.06*	0.1129
Female (%)	4 (6.3%)	15 (2.6%)	−0.06*	0.1129
Mean years of Follow-up (SD)	3.7 yr (5.0)	12.0 yr (13.3)	−4.90‡	<0.0001†
Total years of Follow-up	237.5 yr	6868.3 yr		

† Significance $P < 0.05$; ‡one-sided *t*-test; *one-sided Fisher Exact Probability test with phi statistic based on sex.

asymptomatic WPW pattern that is either intermittent or resolves abruptly with exercise testing.

There are some important limitations in this study. First, we defined high risk and WPW syndrome as arrhythmia, symptoms, ablation, or high risk EP study. Although there is ample evidence that arrhythmia and symptoms of palpitations are high risk, we do not know if all ablations were truly high risk and in those we were able to identify who got an EP study without ablation, we defined high risk as a short refractory period (<250 ms), multiple pathways, and/or retrograde conduction, of which the latter may not be considered high risk. However, including lower risk patients in the high risk category errs on the side of caution. Another limitation is that when reviewing records to see if a patient reported cardiac symptoms related to WPW, there was occasionally conflicting information from multiple providers and, thus, any symptom of palpitations at any time was considered symptomatic. Another possible limitation is the low number of PT data, which changed metrics in July of 2010. There was PT data available from 2004 to current, but we only used the data after July 2010 so that we would better be able to compare the data. Finally, not all individuals in the study had all the testing done or available for review and clinical provider notes were used when actual study data was missing. There is also very little data on female aviators secondary to aviation historically being a primarily male career field in the USAF.

Table III. High and Low WPW Pattern Risk Prevalence Comparison.

	WPW PATTERN HIGH RISK (%)	WPW PATTERN LOW RISK (%)	CHI-SQUARED STATISTIC	*P*-VALUE
Dysrhythmia, Ablation, or SCD	64/64 (100.0)	55/136 (40.4)	64.06	<0.0001†
Dysrhythmia	20/60 (33.3)	7/130 (5.4)	26.30	<0.0001†
Ablation	58/62 (93.5)	49/132 (37.1)	54.31	<0.0001†
SCD	2/62 (3.2)	0/130 (0.0)	-0.15	0.1031*
Symptomatic	36/60 (60.0)	14/132 (10.6)	52.25	<0.0001†
History of Tobacco use	16/61 (26.2)	36/203 (17.7)	2.14	0.2003
History of Alcohol use	49/61 (80.3)	153/202 (75.7)	0.55	0.5657
WPW Goes Away on Stress Test	10/20 (50.0)	35/56 (62.5)	0.95	0.4751
LVH on Echo	0/49 (0.0)	4/121 (3.3)	0.10	0.2653*
LAE on Echo	6/49 (12.2)	6/121 (5.0)	-0.13	0.0921*
CAD	1/60 (1.7)	4/174 (2.3)	0.02	0.6192*
Repeat Ablation Needed	9/57 (15.8)	7/49 (14.3)	0.05	1.0000
WPW Reoccurrence	9	6		
Aeromedical Waivers Granted	51/56 (91.1)	115/129 (89.1)	0.16	0.8875
Aeromedical Disqualifications	5/56 (8.9)	13/129 (10.1)	0.06	1.0000

† Significant $P < 0.05$; *Fisher Exact Probability Test with phi statistic (one-sided).
Echo = echocardiography, LVH = left ventricular hypertrophy, LAE = left atrial enlargement, CAD = coronary artery disease.

Despite the limitations, this is the largest WPW pattern study of asymptomatic adult individuals in the aviation career field with just over 6868 patient years of follow-up. Our data supports current USAF policy. All personnel interested in aviation careers in the USAF have an initial flight exam which includes an ECG. A diagnosis of WPW pattern or syndrome is disqualifying, but the person may be eligible for a waiver to begin flight training;[6] the Federal Aviation Administration and U.S. Navy also allow for ongoing flight duties.[4,7] Given the younger age of pilot applicants (average age 21 yr), the USAF requires an EP study in addition to exercise treadmill test, Holter monitor, and an echocardiogram. An ablation is required if the applicant is considered to have high risk characteristics on EP testing. High risk characteristics include retrograde conduction, multiple pathways, short refractory period, or inducible arrhythmia utilizing the accessory pathway. For aviators already trained with a new ECG showing WPW pattern, the USAF will require a cardiology consultation, Holter monitor, and treadmill testing. They do not necessarily require an EP study unless the aviator is deemed to be at high risk for WPW syndrome based on arrhythmia, symptoms, lack of abrupt termination of the pattern with exercise, or structural heart disease. This information is sent to the Aeromedical Consult Service to review and make a recommendation to the approval authority for the waiver. For those with WPW syndrome or high risk features as above, ablation is required. For individuals who undergo ablation, follow-up noninvasive testing is done at 3 mo post ablation and, if normal, then waiver is usually recommended with regular follow-up at 1–3 yr intervals.

Per the literature review, we believe this is the largest study to date on aviators with WPW pattern. This study found that the prevalence of WPW pattern in USAF aviators is very similar to that of the general population. We also found that for our population, there is a 0.95% annual risk for someone with WPW pattern to develop high risk features worrisome for sudden incapacitation. With less than 1% annual risk of going from WPW pattern to syndrome, the majority of aviators can be evaluated with noninvasive testing and followed clinically. The youngest and healthiest aviators may benefit from an EP study to better define risk. Future prospective studies are needed to evaluate this. Results from this

Table IV. High and Low WPW Pattern Risk Comparison.

	WPW PATTERN HIGH RISK *N* (%)	WPW PATTERN HIGH RISK MEAN (SD)	WPW PATTERN LOW RISK *N* (%)	WPW PATTERN LOW RISK MEAN (SD)	*t* STATISTIC	ONE-SIDED *P*-VALUE
HDL	60 (93.8)	50.3 (13.9)	226 (39.4)	49.7 (13.9)	0.29	0.3874
LDL	60 (93.8)	98.7 (34.4)	221 (38.5)	110.3 (34.8)	−2.29	0.0114†
Total Cholesterol	61 (95.3)	166.1 (33.4)	228 (39.7)	182.8 (40.7)	−2.95	0.0017†
Systolic BP	64 (100.0)	124 (10.3)	355 (61.8)	124 (12.4)	−0.36	0.3615
Diastolic BP	64 (100.0)	74 (9.0)	355 (61.8)	76 (9.1)	−1.84	00,329†
Mean Heart Rate	59 (92.2)	68 (11.4)	205 (35.7)	70 (11.6)	−1.18	0.1202
BMI	64 (100.0)	25.2 (2.7)	481 (83.8)	25.2 (2.8)	−0.08	0.4664
PT Score	9 (14.1)	97.2 (3.0)	13 (2.3)	94.0 (3.8)	2.01	0.0288†
Aerobic PT Score	9 (14.1)	58.6 (1.4)	13 (2.3)	55.2 (3.6)	2.55	0.0096†

† Significant $P < 0.05$.

HDL = high density lipoprotein; LDL = low density lipoprotein; BP = blood pressure; BMI = body mass index; PT = physical testing.

study can be used to help support policy regarding individuals with asymptomatic WPW pattern on ECG who want to pursue a career in aviation or other high risk occupation.

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