ORIGINAL RESEARCH

Echocardiographic Findings in NATO Pilots: Do Acceleration (+Gz) Stresses Damage the Heart?

AGARD Aerospace Medical Panel Working Group 18

Echocardiographic findings in NATO pilots: do acceleration ($+G_z$) stresses damage the heart? **Aviat Space Environ Med 1997;68:596–600.**

Background: Based on physiologic considerations, observations in animal experiments and the results of a preliminary French study, there has been an aeromedical concern that repeated exposure to high sustained G-forces might have a deleterious effect on the heart. The AGARD Aerospace Medical Panel initiated a multi-national study to address the question. ***Hypothesis:*** The study addressed the null hypothesis that "there is no difference in cardiac chamber dimensions, wall thickness or echocardiographic functional parameters between pilots who fly high sustained G (HSG) aircraft and pilots who fly primarily rotary wing or transport aircraft." ***Methods:*** The study was a cross-sectional design comparing echocardiographic parameters in NATO active duty male pilots of HSG aircraft with a control group of transport and rotary wing pilots (CNTL). Some 13 NATO nations participated using a detailed protocol which included specific echocardiographic technical instructions, and procedures for collecting quantitative data on demographic variables including exercise, smoking and flying hours. Data was forwarded on a specially-designed software program to a central data registry. Careful quality control was carried out. ***Results:*** Comparing data from 289 HSG pilots with 254 CNTL pilots, when corrected for the covariates, there were no differences for any of 16 echocardiographic parameters including right and left ventricular dimensions and wall thickness, aortic and left atrial dimensions, and tricuspid and mitral inflow velocities. ***Conclusions:*** The results support the null hypothesis. The conclusions are limited to the resolution of the technology employed and to the flight envelopes and $+G_z$ exposure in the current generation of fighter aircraft.

THERE IS AN AEROMEDICAL concern that repetitive exposure to high radial acceleration forces ($+G_z$) as experienced by fast jet aircrew may have a deleterious effect on the heart. This concern evolved both from theoretical analysis of potential effects of repetitive large changes in cardiac pre-load and afterload resulting from $+G_z$ exposure and anti-G protective measures, as well as from animal experiments including observations of subendocardial hemorrhages in miniature swine exposed to high levels of $+G_z$ (3,4). Although these findings were later found to be largely due to the catecholamine stress of handling and restraint, animals subjected to repeated acceleration over 6 mo showed suggestive evidence of myocardial scar-tissue (2,12). In 1985, French investigators reported echocardiographic findings of increased right ventricular dimensions in Mirage 2000 pilots compared with a control group of transport pilots (10), a finding lent credence by the observation of high right ventricular pressures in instrumented miniature swine exposed to acceleration stresses (20).

These concerns led the Aerospace Medical Panel (AMP) of the Advisory Group for Aerospace Research and Development (AGARD) to initiate a multi-national echocardiographic study of NATO pilots to determine whether there are structural or functional cardiac differences between transport and fast-jet pilots detectable by echocardiography. AGARD Working Group 13 developed a standardized protocol for the study (7), which was then undertaken by Working Group 18.

This paper reports the results of this multi-national study.

METHODS

Study Design/Subjects

The study was a cross-sectional design which compared echocardiographic parameters in fast-jet pilots with a control group of transport or rotary wing pilots. Subjects/participants were active duty male military pilots from 13 NATO countries including Belgium, Canada, Denmark, France, Germany, Greece, Italy, Norway, Portugal, Spain, Turkey, the United Kingdom, and the United States. Female pilots were not included because of the small numbers assigned to fast jets and the fact that many NATO countries do not employ women in fighter operations. Human research issues were the responsibility of each participating country. Both retrospective data and prospective data were collected for Working Group 18, but only prospective data are reported here (i.e., studies done specifically for the current echocardiographic investigation). Pilots were recruited for the study in various ways. In some countries, echocardiography is included as part of routine periodic screening. In other countries, pilots were asked to volunteer during flight medicals, during G-training programs, or during special visits by the investigators to flying units to recruit subjects for the AGARD study.

The null hypothesis of the study was "there is no difference in cardiac chamber dimensions, wall thickness or echocardiographic functional parameters between pilots

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who fly high sustained G (HSG) aircraft and pilots who fly primarily rotary wing or transport aircraft."

NATO aircraft were classified as A, B or C. Type A aircraft are those capable of high sustained G, arbitrarily defined as designed to maintain greater than $+7G_z$ for at least 15 s. Examples include the F-15, F-16, F-18, Mirage 2000, and Hawk. Type B aircraft are other fast jets, not designed to be capable of HSG. Type C aircraft are rotary wing or transport aircraft including tankers and bombers.

NATO pilots were classified based on their flying experience as HSG pilots (i.e., those who had greater than 75% of their flying hours in Type A aircraft) and control (CNTL) pilots, who had greater than 75% of total flying hours in Type C aircraft. Other pilots with mixed transport/fast jet flying experience or the majority of flying hours in Type B aircraft are not included in this analysis. To allow for training hours which for most NATO pilots includes some fast jet exposure, actual hours flown in flying training was subtracted from each pilot's total flying hours, or 300 h if actual training hours were not known.

Participants were excluded for the following reasons:

- presence of known cardiovascular disease or referral for cardiovascular evaluation;
- use of cardiovascular drugs except lipid-lowering agents;
- clinically diagnosed pulmonary disease;
- lack of a flying history;
- lack of a quantified exercise history;
- female;
- age less than 18 or more than 55 yr;
- concurrent transport and fighter flying;
- no flying in the past 36 mo.

Data Collection

The protocol for data collection was detailed in an AGARD publication (7) which was followed by all investigators. Information was collected from each participant on a standardized questionnaire. Demographic and biographic data included age, smoking history, cholesterol, height, weight, and blood pressure. Details of the subjects' exercise patterns over the previous 6 mo were acquired in both a qualitative (slight, mild, moderate, heavy) and quantitative degree. The quantitative exercise history listed a wide variety of activities and acquired data as to the average number of hours per week and number of weeks in the past 6 mo in which the individual had engaged in the activity. From this information, the average number of kilojoules of energy expended per week on exercise was calculated using standard tables (7).

M-mode and two-dimensional echocardiograms and Doppler studies were completed on all pilots using standard American Society for Echocardiography techniques for obtaining images and measurements (8). Overall, 36 parameters were measured and additional information was collected about valvular and wall motion abnormalities.

Both the historical data from the questionnaires and the echocardiographic parameters were entered by each investigator in a software data collection program (PILOTES) designed specifically for this study (7). Data were forwarded on floppy disks to a central data facility at the Armstrong Laboratory, Brooks AFB, TX. Data management and statistical analysis was carried out at the Armstrong Laboratory.

Quality Control

Investigators forwarded videotaped copies of completed echocardiographic studies to the Project Coordinator at Brooks AFB. A cardiologist in the Internal Medicine Branch, Armstrong Lab reviewed and remeasured echo parameters in 5% of studies, or a minimum of 10 from each country. In addition, each investigator re-read a minimum of 5 studies in a blind fashion, and forwarded the duplicate results to Brooks to assess intra-observer variability.

Data Analysis

The 16 echo and Doppler parameters identified for statistical analysis are found in **Table I.**

Statistical Methods

Data were evaluated by *t*-tests for unadjusted comparisons and analysis of covariance (6,9) for adjusted comparisons. Resampling techniques were used to further adjust analysis of covariance p-values for multiple testing (19).

Analyses of covariance were performed using the SAS GLM (16,17) procedure. The sources of variation and associated degrees of freedom are found in **Table II.** Logarithms of smoking and exercise variables were used to control for extreme skewing.

The set of p-values adjusted for multiple-testing by bootstrap methods (in addition to being adjusted for the covariates) was computed from 10,000 bootstrap samples. These help control the Type I error rate that has been elevated due to performing numerous tests of significance.

RESULTS

A total of 543 prospective studies contained complete data sets for HSG and CNTL pilots. There were 289 HSG pilots (53%) and 254 CNTL pilots (47%) in the data set. Values for covariate and other demographic data are given in **Table III.**

The HSG pilot group was younger than the CNTL group by a mean of 1.9 yr which was statistically significant ($p < 0.001$). As anticipated, the CNTL pilots (mainly transport) had significantly more flying hours. There were no statistically significant differences in the other demographic/covariate data.

Table IV displays the non-adjusted (NONAD) and covariate adjusted (ADJCV) mean value for each echo parameter for HSG and CNTL pilots, with three different p-values: a) unadjusted (P-VAL NONAD); b) after adjustment for the five covariates age, body surface area, exercise, smoking and country of origin (P-VAL ADJCV); and c) after additional adjustment for multiple parameters examined (P-VAL ADJMT).

Unadjusted comparison of HSG and CNTL pilots yielded

TABLE I. ECHOCARDIOGRAPHIC AND DOPPLER PARAMETERS ANALYZED.

M-mode measurements from short axis view (2-D directed)		
1.	Right ventricular internal dimension (diastole)	MM-RV
2.	Left ventricular internal dimension (diastole)	MM-LV
3.	Inter-ventricular septal thickness (diastole)	MM-VS
4.	Posterior wall thickness (diastole)	MM-PW
5.	Aortic dimension (diastole)	MM-AO
6.	Left atrial dimension (systole)	MM-LA
2-D measurements (parasternal long axis except where indicated)		
7.	Right ventricular internal dimension (diastole)	2D-RV
8.	Left ventricular internal dimension (diastole)	2D-LV
9.	Inter-ventricular septum (diastole)	2D-IVS
10.	Posterior wall thickness (diastole)	2D-PW
11.	Aortic dimension (diastole)	2D-AO
12.	Left atrial dimension (systole)	2D-LA
13.	Maximum right ventricular dimension apical 4 chamber view (diastole)	RVMAX
14.	Right ventricular area apical 4 chamber view diastole	RV-AR
Doppler measurements		
15.	Mitral peak E and peak A	MV E/A
16.	Tricuspid peak E and peak A	TV E/A

six parameters that were statistically significant (Table IV). All four measurements of left ventricular wall thickness in both M-mode and 2-D were significantly greater in CNTL pilots ($p < 0.05$). However, all four mean values in both HSG and CNTL pilots were less than 1.0 cm, well within established norms (8). The 2-D left atrial dimension and the RVMAX were also significantly greater in CNTL pilots, but again the absolute mean values were well within established norms.

Covariate adjusted comparisons: After adjusting for the five covariates, only MM-VS and MM-AO values were significantly different. Again, the mean values for these two echo parameters were well within established normal values and the 2-D measurements were not significantly different.

Multiple parameters adjustment: After further adjustment for multiple parameters, there were no significant differences for any of the echo parameters between HSG and CNTL pilots.

Investigators were also requested to report other echocardiographic findings. These reported findings are shown in **Table V.**

Of the 543 pilots, only 5 (0.9%) were found to have mitral valve prolapse, and 8 (1.5%) had mitral leaflet thickening or redundancy without prolapse. Only 2 (0.4%) had a bicuspid aortic valve; 6 others (1.1%) were noted to have aortic valve thickening or calcification. There were no statistically significant differences between HSG and CNTL pilots with respect to these findings.

Valvular insufficiency was recorded as present or absent based on the echocardiographic observation of regurgitation considered to be clearly abnormal (significant) and not a physiologic normal variant. No HSG or CNTL pilots were reported to have significant mitral regurgitation. Among the 289 HSG pilots, none were reported as having significant aortic or tricuspid regurgitation, and only one was noted to have significant pulmonic regurgitation. Of the 254 CNTL pilots, 4 were recorded as having significant aortic regurgitation, and 1 had significant tricuspid regurgitation. These numbers were too small to derive any statistical significance.

With respect to diastolic function indices, there were

TABLE II. SOURCES OF VARIATION AND ASSOCIATED DEGREES OF FREEDOM WHERE "NR OF SUBJECTS" IS THE TOTAL NUMBER OF SUBJECTS WITH COMPLETE DATA FOR THE DEPENDENT VARIABLE AND ALL THE SOURCE LINES LISTED.

Source	Degrees of Freedom
Pilot type (XX vs. ZZ)	1
Nation of study	11
Source	1
Body surface area	1
Ln (1 + pack-years smoking)	1
Ln (average weekly energy expenditure)	1
Error	Nr of subjects minus 17

TABLE III. COVARIATE AND BIOGRAPHIC DATA IN HSG AND CNTL PILOTS (ALL VALUES ARE MEANS UNLESS OTHERWISE SPECIFIED).

	HSG	CNTL
Age (yr)	29.8	31.7*
BSA (m^2)	1.96	1.96
Height (cm)	178.9	178.9
Weight (kg)	77.3	77.4
Systolic BP (mmHg)	124	125
Diastolic BP (mmHg)	78	77
Cholesterol (mg/dl^{-1})	207	206
HDL cholesterol (mg/dl^{-1})	53	52
Sports energy expenditure per week (Kj)	8098	10224
Smoking (pack yr)	2.6	2.9
Non-smokers (%)	62	67
Ex-smokers (%)	6	10
Current smokers (%)	32	23
Flying h	1347	2512*

* $p < 0.001$ Remaining comparisons N.S.

TABLE IV. VALUES FOR ECHOCARDIOGRAPHIC VARIABLES, NON-ADJUSTED (NONAD) AND ADJUSTED FOR COVARIATES (ADJCV) AGE, BSA, SMOKING, EXERCISE EXPENDITURE AND COUNTRY OF ORIGIN. P-VALUES COMPARING HSG AND CNTL GROUPS FOR EACH CONDITION ARE GIVEN. THE FINAL COLUMN GIVES p-VALUES AFTER ADJUSTMENT FOR MULTIPLE TESTS (p-VAL ADJMT).

	HSG NONAD	CNTL NONAD	p-VAL NONAD	HSG ADJCV	CNTL ADJCV	p-VAL ADJCV	p-VAL ADJMT
MM-RV	2.15	2.08	0.130	2.12	2.06	0.24	0.98
2D-RV	2.22	2.20	0.730	2.21	2.16	0.44	>0.99
MM-LV	5.07	5.07	0.940	5.09	5.10	0.93	>0.99
2D-LV	4.96	5.00	0.450	4.94	5.01	0.22	0.97
MM-VS	0.91	0.95	0.002*	0.92	0.95	0.04*	0.42
2D-VS	0.93	0.97	0.020*	0.93	0.96	0.19	0.95
MM-PW	0.85	0.89	0.001*	0.86	0.87	0.82	>0.99
2D-PW	0.92	0.96	0.004*	0.96	0.95	0.60	>0.99
MM-AO	3.01	2.99	0.350	3.02	2.95	0.03*	0.37
2D-AO	3.00	3.04	0.260	3.02	2.95	0.10	0.77
MM-LA	3.42	3.44	0.710	3.48	3.46	0.59	>0.99
2D-LA	3.22	3.33	0.010*	3.32	3.36	0.44	>0.99
RVMAX	3.50	3.62	0.030*	3.69	3.65	0.51	>0.99
RV-AR	19.00	19.80	0.100	19.50	20.10	0.20	0.96
MV E/A	1.62	1.64	0.640	1.62	1.62	0.86	>0.99
TV E/A	1.64	1.68	0.390	1.67	1.66	0.84	>0.99

CODE: MM = m-mode; 2D = two dimensional. All measurements in cm end-diastole except where indicated; RV = right ventricle; LV = left ventricle; VS = ventricular septum; PW = posterior wall; AO = aorta (end-diastole); LA = left atrium; RVMAX = maximum right ventricular dimension, apical 4 chamber view; RV = right ventricular area; MV E/A = mitral Doppler E wave/A wave ratio; TV E/A = tricuspid Doppler E wave/A wave ratio.

* $p < 0.05$.

no significant differences between HSG and CNTL pilots in E/A velocities for either the mitral or tricuspid valve.

DISCUSSION

Concern has been expressed for decades about the possible adverse cardiac effects of repetitive exposure to $+G_z$ forces. Data from an early study suggested a possible effect on the heart from flying HSG aircraft (10) although a later study did not find such an effect (18).

The results of this large, multi-center controlled study fail to detect any general cardiac structural or functional effect in pilots who fly either HSG or other military aircraft, and certainly show no echocardiographic differences between HSG and CNTL pilots. These results are strongly supportive of the null hypothesis on which the study was based.

There are several important outcomes from this study. First, it confirms that the large multi-national pool of NATO aircrew can be tapped to provide important epidemiologic evidence, allowing accumulation of statistically sufficient numbers in a relatively short period of time, a task which would be difficult if not impossible in any individual country. Second, it answers an important occupational concern as regards the lack of cardiac effects of repetitive exposure to $+G_z$ in serving HSG aircrew. Third, it serves as a template for future epidemiologic studies which might be undertaken to address other significant aeromedical concerns.

Pilots of HSG aircraft are exposed to rapid and dramatic cardiovascular changes related to the hydrostatic effects of $+G_z$ exposure, and to the countermeasures used to prevent G-induced loss of consciousness. These countermeasures include respiratory anti-G straining maneuvers (AGSM) and now positive pressure breathing (PPG) the aim of which is to increase intrathoracic pressure and hence intracranial arterial pressure. Anti-G suits have been in use for over 50 yr to improve tolerance to $+G_z$, both by improving preload but also by increasing arterial resistance below the chest, helping to maintain cerebral perfusion.

These repetitive changes in preload and afterload might well be expected to have an effect on cardiac structure and function. Weight lifting also involves respiratory straining maneuvers similar to the aircrew AGSM with maximal voluntary muscular contraction combined with forced exhalation against a closed glottis. In a recent study of the physiologic changes during a weight lifting exercise in healthy young men, Lentini et al. demonstrated dramatic changes in intrathoracic pressure with resultant large pressure transients in systolic blood pressure (to 270 mmHg) and diastolic blood pressure (to 183 mmHg). Weight lifters exhibit different left ventricular dynamics than aerobic exercisers during exercise, with increased left ventricular thickness during both systole and diastole (1). Competitive weight lifters repetitively train with such exercises and changes in cardiac structure or function might be expected. Echocardiographic left atrial and right ventricular cavity enlargement have been found in weight lifters and body builders compared with controls (5).

TABLE V. OTHER ECHOCARDIOGRAPHIC DIAGNOSES.

	HSG		CNTL	
Diagnosis	Number	Percent	Number	Percent
MVP	3	1.0	2	0.8
BAV	0		2	0.8
MVT/RED	6	2.1	2	0.8
AVT/CA	1	0.3	5	2.0

MVP = mitral valve prolapse; BAV = bicuspid aortic valve; MVT/RED = mitral valve thickening or redundancy without prolapse; AVT/CA = aortic valve thickening or calcification.

Since fighter aircrew perform repetitive straining maneuvers similar to weight lifters, changes in cardiac structure or function might be expected to occur. The lack of cardiac structural effects in serving active duty pilots in this large, controlled study is reassuring. A corollary question is why is there no cardiac effect of repetitive high sustained $+G_z$ exposure? This study does not directly address this question but may provide clues. The intuitive answer is that there is not sufficient sustained G-dose with simultaneous countermeasures to cause a cardiac effect in a normal flying career. Many fast jet missions, such as intercept or patrol, involve little exposure to HSG. Of the total flying hours logged by the HSG pilots in our study, only a small percentage were attributed to "air-to-air" combat in which $+G_z$ exposure might be expected to be substantial.

The incidence of other echocardiographic cardiac anomalies in this study is remarkably low. The explanation for this may be that this aircrew population is highly selected and regularly screened with periodic physical examinations in every country, and echocardiographic examination in some. Aircrew with even apparently benign murmurs are often referred for further evaluation, and so the incidence of clinically undetected echocardiographic abnormalities such as mitral valve prolapse would be expected to be low in this population. Referral for cardiovascular evaluation, or a known cardiac anomaly, was an exclusion criteria for this study. Hence, the low incidence of valvular abnormalities and regurgitation reported in this study should not be interpreted to reflect the prevalence of these findings in all aviators. These data are from a select population which has met specific exclusion criteria, including the absence of suspected cardiac disease.

This large study shows no evidence at all of a structural or functional cardiac effect of flying military aircraft. The careful control of covariates and particularly exercise history in this study may account different result from the study by Ille et al. (10).

These data are valid only in current aircrew flying the current generation of fighter aircraft. Development of the next generation of fighters is well underway with concurrent evolution of more advanced life support equipment. Tomorrow's fighter pilots may expect significantly greater G forces, both negative and positive, with more rapid onset. Life support equipment is being redesigned to meet these challenges with simultaneous PPG and redesigned anti-G garments with increased bladder coverage, all of which translates into ever greater changes in preload and afterload and resultant cardiovascular stress. The question addressed by this study will have to be answered again for the aircrew flying such aircraft.

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