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Enhanced Cardiovascular Risk Assessment in United States Subjects for Deployment to Antarctica

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ABSTRACT

Introduction: Coronary artery disease (CAD) is the leading cause of death in developed nations. Nearly half of asymptomatic CAD cases initially present as acute myocardial infarction (MI) or sudden cardiac death.Therefore, assessment of cardiovascular health is important in subjects who are deployed to remote stations with limited access to medical care, such as Antarctica. Effective screening strategies for detecting CAD and minimizing the risk of acute cardiovascular events in the deployed subjects are essential to mission success. Our study for the first time describes cardiovascular risk assessment in US subjects prior to their deployment to Antarctica. Methods: This report is a single center retrospective analysis of 135 subjects who underwent advanced cardiovascular screening from October 2013 to November 2017 prior to their deployment to Antarctica. Of the 135 subjects, 128 were assessed to be acceptable cardiac risk and were approved for deployment. However, only a total of 100 subjects proceeded for deployment to the South Pole. The deployment periods ranged from 6 to 324 days with a mean of 94.4 days (SD 73.8). All deployed subjects were exposed to the harsh cold climate in Antarctica. Primary outcomes include cardiovascular events such as acute myocardial infarction, unstable angina pectoris, congestive heart failure, cardiac arrhythmias, and sudden cardiac death. Results: None of the 100 subjects had cardiac events reported during their deployment. Conclusions: The current enhanced cardiovascular screening process, prior to deployment to US Antarctic Program stations, appears effective in identifying subjects with low risk of cardiac events.

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Introduction

Coronary artery disease (CAD) is the leading cause of death in developed nations. Screening and prevention of CAD are crucial as nearly half of asymptomatic cases initially present as an acute myocardial infarction (MI) or sudden cardiac death [1]. In subjects deployed to remote areas under harsh weather conditions, and limited access to medical care with hazardous and expensive evacuation, screening for CAD and prevention of acute CAD events are paramount to the success of the mission. Furthermore, subjects in Antarctica are exposed to extremely cold temperature and epidemiological studies show an association between cold temperatures and adverse cardiovascular events. In general, mortality is increased at lower temperatures [2]. Cardiovascular changes induced by cold stress may result in death from acute coronary events rather than chronic ischemic heart disease [3,4]. Although the impact of temperature on mortality is well documented, relatively few studies have evaluated the association of temperature with morbidity outcomes such as hospital admissions. In the current study, we describe the CAD screening strategies in subjects being deployed to Antarctica. The effectiveness of screening was assessed by retrospectively analyzing clinical data in 100 subjects for cardiac events and any other related morbidities during the deployment period.

Material and Methods

Our study was conducted after a full review and approval by the Institutional Review Board (IRB) at the University of Texas Medical Branch (UTMB), Galveston. Both subject identification and confidentiality were completely protected. The present report is based on a retrospective analysis of the enhanced screening of subjects considered to be potentially at risk of cardiovascular complications based on their initial screening. The data, obtained prior to and after deployment of subjects to Antarctica from October 2013 to November 2017, were analyzed. The deployment periods ranged from 6 days to 324 days with a mean of 94.4 days (SD 73.8). The screening process is described in the section below. Data collection included demographics, basic laboratory results, medications, resting ECG parameters, stress test results, echocardiographic measurements, and cardiac catheterization results.

UTMB in Galveston and the Center for Polar Medical Operations (CPMO) serve the National Science Foundation's US Antarctic Program (USAP). This collaboration obtains vital scientific research from the most remote places on Earth. The CPMO is responsible for the medical screening of all USAP participants who travel to Antarctica each year. All candidates for deployment, including National Science Foundation (NSF)-funded researchers and support personnel, undergo and pass a physical qualification

(PQ) process. The PQ process identifies any physical conditions that would threaten the health and safety of the candidate and that could not be effectively treated by the limited medical care capabilities in Antarctica, thus posing a risk in jeopardizing the accomplishment of the mission. It is well documented that the extremely cold temperature produces significant circulatory changes, thus adversely impacting any cardiovascular condition [5].

The USAP medical guidelines call for initial cardiovascular risk stratification in certain participants during the PQ process. Current standard screening procedures prior to deployment to the South Pole include history, physical examination, basic laboratory tests and a stress test. Participants over the age of 50 years, deploying to any USAP station during any season, except for Antarctica winter deployment, are required to undergo an exercise treadmill stress test if their Framingham risk score (FRS) is calculated at greater than 30%. For Antarctica winter deployment, participants aged 50-60 years old must complete an exercise stress test every other year, while participants aged > 60 years complete an annual stress test. Based on the initial risk stratification, if the subjects are considered non -physical qualified (NPQ) and eligible for waiver consideration, they are referred for enhanced evaluation by an experienced cardiologist. The present report is based on a retrospective analysis of the enhanced screening of NPQ subjects considered to be potentially at risk for cardiovascular complications based on their initial screening.

Statistics

The data were analyzed for the 135 subjects referred for enhanced screening. For the categorical variables, the absolute and relative frequencies were obtained, and the averages and standard deviation for the description of numerical variables with normal distribution were determined. The applied tests included Student-t test and U Mann-Whitney. The categorical variables were analyzed by the Chi-Square test, and exact test of Fisher. To determine the risk of cardiovascular disease FRS, Cox's regression model to 10-years was applied [6]. The level of significance used in all of the inference tests was 0.05.

Results

During the period from October 2013 to November 2017, a total of 135 subjects were referred for enhanced cardiovascular assessment. There were 111(82.2%) men and 24 (17.8%) women. The mean age was 48 ± 14.7 years. Of the total cohort, 9 (6.7%) subjects had known CAD, including 1 subject with previous coronary bypass surgery and 3 with previous percutaneous coronary intervention. The distribution of traditional risk factors for CAD included 24 (17.8%) subjects with known history of hypertension; 2 subjects (1.5%) with diabetes type 2; and 27 (20%) subjects with hyperlipidemia (HLD). There were a total of 13 (9.6%) current smokers and 31(23%) former smokers. Other important medical problems included a history of atrial fibrillation in11(8.1%) subjects, obesity, defined as BMI>30% in 38 (28.1%) subjects, and significant valvular abnormalities in 2 (0.01%) subjects. Clinical characteristics are shown in Table 1. Baseline laboratory tests showed mean values for hemoglobin 14.9 g/dl, creatinine 0.93 mg/dl, glycosylated hemoglobin 5%, total cholesterol level 187.1 mg/dl, LDL 107 mg/dl, triglycerides 111 mg/dl and HDL 57.1 mg/dl. Important baseline medications included statins in 23 (17%) subjects, ACE inhibitors in 18 (13.3%) subjects, aspirin 17 (12.6%) subjects, beta-blockers 14(10.4%) subjects, anti-arrhythmic agents 4(3%) subjects, and anticoagulation 2 (1.5%) subjects.

Table 1: Clinical Characteristics of 135 Subjects

Clinical Characteristics	n	%
Male	111	82.2
Female	24	17.8
Mean age	48 ± 14.7	n/a
CAD	9	6.7
History of CABG	1	0.7
Prior PCI	3	2.2
HTN	24	17.8
HLD	27	20.0
Current smokers	13	9.6
Former smokers	31	23.0
Atrial fibrillation	11	8.1
Obesity	38	28.1
Valvular abnormalities	2	1.5
CKD	1	0.7
Prior stroke	1	0.7
Obstructive Sleep Apnea	3	2.2

CAD = coronary artery disease; CABG = coronary artery bypass graft surgery; PCI = Percutaneous coronary intervention; HTN = Hypertension; HLD = Hyperlipidemia; CKD=chronic kidney disease

Using the FRS, a 10-year risk for cardiovascular disease was calculated. Risk score of <10% was considered low, 10% to 20% intermediate, and > 20% high. The risk score was low in 102 (75.6%) subjects, intermediate in 29 (21.5%), and high in 4 (3%), as shown in Figure 1. All females had a score of <10%, and males had a high score after age 52 years. Figure 2 shows that the CVD risk for women had a linear relationship and in men exponential.

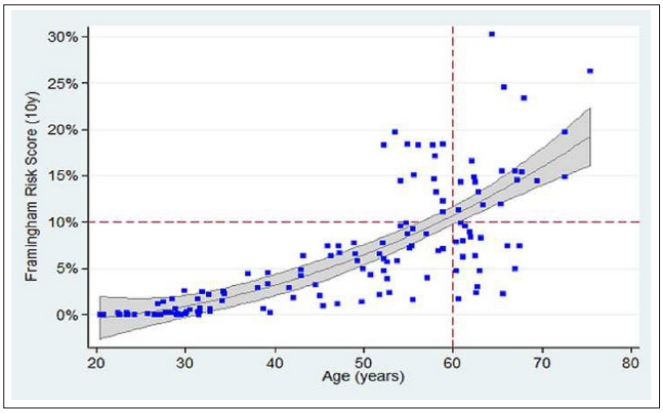

Figure 1: Framingham risk score by age

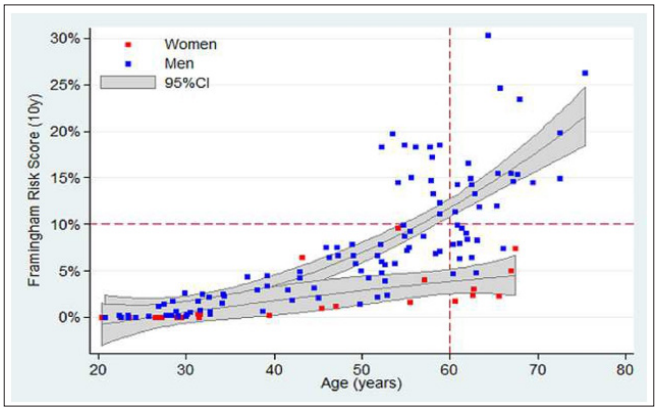

Figure 2: Framingham risk score by sex

Enhanced cardiac evaluation by an expert cardiology consultant was recommended for various reasons listed in Table 2, that included review of available data including cardiovascular history, physical examination, EKGs, laboratory data, and in some cases echocardiograms and stress tests. Sixty-six subjects were approved for deployment and in 69 (51.1%) subjects, further testing was recommended. Table 3 shows the additional tests and consults performed.

Table 2: Reasons for Enhanced Cardiology Screening Consult

Reasons for Enhanced Cardiology Screening Consult	n	%
Abnormal:		
EKG	88	66.1
Stress test	19	14.07
Echocardiogram	2	1.48
EKG with non-diagnostic stress test	2	1.48
EKG and history of Aortic valve replacement	1	0.74
Holter monitor	2	1.48
Stress test with Arrhythmias	1	0.74
History of:		
Supraventricular tachycardia	2	1.48
Atrial fibrillation	8	5.93
CAD and prior revascularization	5	5.74
Mitral valve prolapse	1	0.74
Non-ischemic cardiomyopathy	2	1.48
Syncope and bradycardia	1	0.74
Syncope and frequent PVC's	1	0.74
Total	135	100

PVC = Premature ventricular contraction; MR = Mitral regurgitation

Table 3: Additional Tests and Consults Performed

Additional Tests and Consults Performed	n	%
Echocardiogram	18	24.7
Exercise stress echocardiogram	11	15.1
Exercise stress echocardiogram – recommended but not done	3	4.1
Exercise ECG stress test	6	8.2
Coronary angiogram	2	2.7
Holter monitor	2	2.7
Nuclear stress test	4	5.5
Nuclear stress test recommended but not done	4	5.5
Saline contrast study	1	1.4
Electrocardiogram	15	20.5
Consultation with Electrophysiologist	6	8.2
Review of echocardiographic images for the presence of an intracardiac shunt	1	1.4
Total	73	100.0

Twenty-eight stress tests were requested, including exercise ECG stress test, exercise echocardiogram and nuclear stress test, in subjects with risk factors for CAD and/or an abnormal resting ECG or an inconclusive previously performed stress test. All completed stress tests (21 subjects) were normal. Among the 7 subjects that did not complete the stress test, 2 subjects were approved for deployment by their primary cardiologist and 5 were neither approved nor deployed. Two coronary angiograms were requested that revealed non- obstructive CAD.

The regression models did not show predictive value for further testing during the screening process for any of the variables including FRS, p=0.401. Furthermore, FRS was not predictive of the final clearance status for deployment, p=0.454.

After completion of the screening process, a total of 128 (94.8%) subjects were finally approved for deployment. However, only 100 (78.3%) subjects were deployed to Antarctica. Deployment time ranged from 6 to 324 days with a mean of 94.4 days (SD 73.8). There were no cardiac events reported during deployment in the group of subjects approved after enhanced screening. An event was reported on a subject who was not part of our enhanced screening cohort and based on a review of the medical record, the subject would not have been approved for deployment without undergoing further testing. This subject had a history of CAD with a reportedly "normal stress test" performed by the primary cardiologist in the field and the deployment was recommended without enhanced screening. The subject suffered an uncomplicated acute MI requiring evacuation from the South Pole.

Discussion

Antarctica and Deployment of US Subjects

The USAP manages science and logistics in Antarctica for the NSF. Due to the remote location and limited resources available, the program maintains a physical qualification (PQ) program designed to minimize the risks to the health of the participant and the costs and logistics associated with an emergency medical evacuation. The CPMO at UTMB Galveston provides logistical support for physical qualification and medical care on the Antarctic continent. The mission is to safely deploy all eligible participants based on a complete understanding of their health and wellness. The health conditions must be stable, having the capability to treat expected complications of the disease. The medical qualification process is frequently compared to that of astronaut qualification. Both operate in austere environments with limited resources and difficult evacuation processes.

Risk Assessment for Coronary Artery Disease

CAD is a leading cause of permanent withdrawal from flight status and non-accidental deaths in military and civil aviation flight crews [7-9]. In the aviation community, there is a broad consensus that the risk of cardiac incapacitation of a professional pilot should not exceed the event rate associated with cardiac mortality of a 60-yr-old man in Western Europe, which is approximately 1% per year [10-12]. Cardiovascular screening for the U.S astronauts is similar to Russian cosmonauts and includes a stress test on a bicycle ergometer or a treadmill, 12-lead ECG at rest and with hyperventilation, 24-hr ECG and BP monitoring, duplex ultrasound of major vascular structures and, when clinically indicated, cardiac catheterization and/or echocardiography [13]. Cardiovascular retention standards for active astronauts involve annual medical examinations with a resting ECG and symptom limited maximal stress tests. Bruce protocol treadmill tests are repeated at ages 30, 35, 40 and then yearly thereafter [13]. The usefulness of cardiovascular screening in reducing cardiovascular events in subjects deployed to South Pole has not been studied and the quantification of acceptable cardiac risk for deployment missions has not been clearly defined.

The USAP's screening program focuses on CAD screening, which manifests as myocardial infarction, angina pectoris, heart failure, and sudden cardiac death. USAP MEDEVAC (medical evacuation) data dating back to 2003, documents 34 cases where a cardiovascular cause was implicated. While this is a low number, given the overall number of participants who were deployed during this time, estimated at 15,000 subjects, program impact can be significant in terms of MEDEVAC costs and potential morbidity to the patient. The USAP clinics do have the capability of treating a) acute myocardial infarction with thrombolytic therapy and b) accessing expert consultation through telemedicine. However, the nearest catheterization laboratory to McMurdo Station at the South Pole is 8 hours away via LC-130 to Christchurch, NZ. Evacuations from Antarctica and Palmer Stations could expose patients to significant further delays. These potential program and patient issues illustrate the importance of identifying participants at risk for the development of coronary events.

The Framingham Heart study has contributed significantly to the understanding of the quantitative and additive nature of cardiovascular risk factors toward the cause and progression of coronary heart disease and stroke in U.S. populations [14]. There is a consensus that only about 50% of CAD events can be explained by the traditional Framingham risk factors. Therefore, Framingham risk score may not be a useful means of estimating CAD risk of an individual subject deployed to the South Pole. Hamilton et estimated the all-cause cardiac risk in US astronauts by calculating individual Framingham risk scores [13]. These investigators suggest that male and female astronauts have a 3 to 5% risk of developing cardiovascular disease (CVD) between the age of 40 and 50 years. The analysis provides only a risk estimate in this population and not an assessment of whether the astronauts are at an increased risk relative to other occupations. In a study of cardiovascular screening of Army personnel over 40 years of age, Wortham et al showed a combination of presence of fluoroscopic coronary calcification and a positive stress test was an excellent predictor of obstructive coronary artery disease [15]. Similar studies in subjects deployed to Antarctica are not available.

Cold Temperature and CAD

Atherosclerosis is an insidious and often a clinically silent process involving the deposition of mixed lipid and calcium plaque [16]. The primary mechanism leading to acute coronary syndromes (sudden death, myocardial infarction, unstable angina) is plaque rupture. The pathophysiological key to predicting acute coronary events is the identification of factors that result in the development of a "vulnerable" plaque [17]. The impact of temperature variations on human health in the context of systemic diseases has garnered immense concern. Epidemiological studies have shown an association between cold temperature and adverse cardiovascular events since the 1940s. In general, mortality is usually lowest around a certain temperature and will increase at lower or higher temperatures [2]. Potential mechanisms for the cold-induced increased risk for incident coronary events may include the stimulation of cold receptors in the skin leading to a rise in catecholamine levels and subsequent vasoconstriction, increased heart rate and blood pressure, which may precipitate myocardial ischemia and coronary plaque instability [18]. Men wintering in Antarctica have been found to develop changes in their response to a standard cold stress [19, 20]. Cold pressor stimulation has been shown to be effective as a noninvasive stress test during Thallium-201 myocardial scintigraphy [5]. Both the acute effects of cold temperature and the added exercisemay contribute to the higher morbidity and mortality in subjects with underlying CAD. Cardiovascular screening is therefore important for subjects being deployed to Antarctica [21-23].

Coronary Events in the Asymptomatic Population

Subclinical asymptomatic cardiovascular pathology might be present in subjects deployed to the South Pole. Guidelines for assessing cardiovascular risk in asymptomatic patients with CAD have resulted in conflicting recommendations. These recommendations include using Framingham risk score in intermediate or high-risk patients and computed tomography with calcium scoring in other patients. Indeed, studies assessing the incremental benefit of testing for subclinical atherosclerosis and their value in predicting clinical CAD are scarce and give inconsistent results [24]. These findings are important especially in subjects with an intermediate risk according to the classical risk factor scoring. A certain proportion of these subjects may be misclassified by traditional risk prediction, and subclinical atherosclerosis testing may help to re-classify some of them either into a low or a high-risk group [25]. Whether abnormal findings from subclinical atherosclerosis testing significantly changes the risk assigned to an individual is not clear. Based on our data from Antarctica, there is no evidence that the presence of asymptomatic cardiac dysrhythmias or left ventricular dysfunction resulted in clinical manifestation of cardiovascular disease during the deployment period. The lone subject with

acute MI during deployment to the south pole did not meet our enhanced screening criteria and was approved for deployment by his primary cardiologist. Furthermore, it is not known if the subject was compliant with the recommended medical management during the deployment period.

In comparison to the general US population, the incidence of CVD in our study population is low. According to a 2015 American Heart Association report, men and women between the ages of 45 years and 54 years have an incidence rate of 10.1 per 1000 for men and 4.2 per 1000 for women, for CAD, heart failure, stroke, or intermittent claudication [26]. The low incidence of CVD in subjects deployed to the Antarctica reported in the present investigation when compared to the general US population, suggests that our subject population represents a lower risk group.

Limitations

We did not evaluate the effectiveness of USAP medical guidelines used in the initial cardiovascular risk stratification of subjects under consideration for deployment to Antarctica. These USAP protocol-based evaluations were carried out by physicians at different centers and sites throughout the US. Our study focused on the group of subjects, referred for enhanced cardiovascular screening, and who were considered non-physical qualified (NPQ) based on their initial assessment. A retrospective analysis of the data confirmed the effectiveness of the enhanced screening performed at our site. None of the subjects approved after enhanced screening had an event. Whether our enhanced screening protocol will be effective in a higher risk group needs further study.

All follow up data during deployment were compiled from a review of the medical records. Ideally, a prospective follow up of the deployed subjects is needed for a more precise assessment.

Conclusion

Our report is the first description of the application of advanced screening protocol for subjects under consideration for deployment to Antarctica. The current primary screening process in the field relies heavily on the Framingham risk score and cardiovascular stress testing. Whether alternative techniques such as computed tomography with coronary calcium scoring should be applied in higher risk asymptomatic subjects is not clear at this time. The advanced screening process in selected subjects appears adequate in identifying those with low risk of cardiac events during deployment to USAP stations. The effectiveness of our protocol for advanced screening in a higher risk group of subjects needs further study. The role of future research in the adaptation of subjects with heart disease to a cold environment may help to further reduce the already low incidence of cardiac events in deployed subjects. Enhancement of treatment facilities for emergent cardiac events at the local Antarctic medical facility is also a desired option.

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