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# SUDDEN CARDIAC DEATH IN THE MOUNTAIN ENVIRONMENT

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## Abstract

Sudden cardiac death (SCD) is responsible for a considerable number of fatalities in the mountain environment. Victims are often middle aged men with risk factors for coronary artery disease (CAD). Deaths tend to occur during, or immediately after exercise and may be exacerbated by sympathetic stimulation triggered by factors such as anxiety, poor sleep, intercurrent infection, inadequate food intake and dehydration. Myocardial ischaemia, coronary artery spasm and the rupture or erosion of an atherosclerotic plaque have all been cited as potential causes for SCD in the mountain environment. Any strategy intent on reducing the risk of SCD will need to focus upon developing recommendations for those with CAD as well as the larger population who have risk factors for the disease. In addition to preventative strategies, popular ski centres and mountain resorts should also be capable of providing basic care for those who develop an acute coronary syndrome (ACS) and direct victims to appropriate treatment with the utmost urgency.

***Key words**: sudden cardiac death, altitude, exercise, acute coronary syndrome, myocardial ischaemia, coronary spasm*

*That sunny dome! Those caves of ice!*
*And all who heard should see them there,*
*And all should cry, Beware! Beware!*

*Excerpt from "Kubla Khan" by Samuel Taylor Coleridge*

## Introduction

Each year approximately 100 million people visit mountainous regions for recreation (1). Given these large numbers and the activities they undertake, it is inevitable that a number of fatalities occur. Whilst the majority of these deaths are the result of traumatic injuries, significant numbers of sudden cardiac deaths (SCD) occur (2-9). SCD can be defined as an, "unexpected natural death from a cardiac cause within a short time period, generally <1 hour from the onset of symptoms, in a person without any prior condition that would appear fatal" (10). SCD is the most common fatal manifestation of cardiac disease. Of 719,456 deaths due to cardiac disease identified in the USA in 1998, 456,076 (63.3%) were defined as SCD (11). In men, it has been estimated that approximately 6-17% of all SCD's are associated with vigorous exercise (10,11). SCD has been shown to be responsible for the deaths of up to 52% of downhill skiers and 30% of hikers (4,8). Although SCD's due to congenital abnormalities have been reported in young adults in the mountain environment the vast majority occur in sedentary, middle aged men during, or immediately following, exercise (4,8). Whilst many studies have estimated the risk of SCD during a wide range of physical activities, only a small number have focused upon the incidence of SCD in the mountain environment (4,7,8). These studies have demonstrated that one SCD occurs for every 0.1-2.6 million hours of skiing and 0.3-1.3 million hours of mountain hiking (4,7,8). Compared to the overall risk of SCD, the incidence of SCD during mountain activities is significantly greater. Amongst men aged over 34 years, the risk of SCD has been shown to increase by a factor of 4.3 during mountain hiking and 2.1 during downhill skiing (8). The intention of this review is to identify the risk factors associated with SCD in the mountain environment, outline the pathophysiology that underlies this process and propose a potential strategy that may reduce SCD's from occurring in the future.

## Risk Factors for SCD in the Mountain Environment

For many people, regular visits to the mountains form part of an active, healthy lifestyle. Indeed, regular physical activity has been shown to be effective in the

prevention of a number of conditions, including coronary artery disease (CAD) (12). However the benefits of exercise are not universal. In one of the earliest studies to address this issue, Thompson et/al found that joggers in Rhode Island were seven times more likely to die whilst jogging than during sedentary activities (13). Subsequent studies have shown that the incidence of acute cardiovascular events for every 10,000 person hours of physical activity is 0.3-2.7 in men and 0.6-6.0 in women (12). This represents a 7-14 fold increase in the risk of SCD during strenuous exercise compared to sedentary activities (14,15). Post mortem examinations have revealed that atherosclerotic coronary artery disease (CAD) is responsible for the vast majority of adult SCD's that occur during, or immediately following, episodes of vigorous exercise (16-18). Although only 1 SCD occurs for approximately 1.51 million episodes of physical activity, the incidence of SCD increases markedly in those with risk factors for CAD (19,20). SCD during, or immediately following exercise, is most commonly seen in middle aged and elderly males (21). In a prospective study examining deaths reported to the coroner in Birmingham and Solihull over a five year period, 52 were found to have occurred within six hours of sporting activity (18). Of these, 48 (92.3%) occurred in males and 42 (80.8%) were in those aged over 40 years. In 43 (82.7%) of these deaths, CAD was found to be responsible, with 40 (93.0%) suffering from previously undiagnosed triple vessel disease. In a study of 60 deaths that occurred within six hours of playing squash, 51 (85%) were attributed to CAD following post mortem examination (16). Of these, 32 (62.7%) had at least one risk factor for CAD, including 25 (49.0%) who had smoked more than 10 cigarettes a day, 18 (35.3%) with a family history of early myocardial infarction (<55 years) and 14 with a history of hypertension (27.5%). Low levels of physical activity are also associated with a greater incidence of myocardial infarction and SCD during vigorous exercise (22,23). The Physician's Health Study revealed that in those who undertook four episodes of exercise each week there was a lower relative risk of SCD during vigorous activity than those who exercised once a week or less (10.9 vs 74.1 $P<0.05$) (19).

Those who die from SCD during mountain activities share many of the same characteristics as those who succumb to the condition during exercise at lower altitudes. In a case control study that examined SCD amongst skiers, 94% of victims were male and 90% were aged over 40 (24,25). Amongst 179 hikers diagnosed with SCD in the Alps the average age was 60.6 years (26). In long distance skiers participating in the Vasaloppet races in Sweden, men aged between 51 and 70 years had the highest SCD standardised mortality rate (2). A questionnaire study of 2474 individuals aged between 2 and 90 found that 12.7% of hikers and 11.2% of skiers reported a history of hypertension, cardiac arrhythmias or ischaemic heart disease (26). In males aged over 34, factors such as a history of prior myocardial infarction, diabetes mellitus, known coronary artery disease, hypercholestrolaemia and hypertension were all shown to be independent risk factors linked to SCD during downhill skiing and mountain hiking (24,25). Meanwhile, regular exercise in the mountain environment appears to offer some degree of protection. In the Austrian Alps, the incidence of SCD was found to be lower in active hikers who undertook mountain sports for more than two weeks each year and skiers who completed more than one period of high intensity exercise each week (24,25). Similar results were also found in a study undertaken in the mountainous region of Veneto in northern Italy. Here, only 14% of SCD occurred in those who undertook regular physical exercise (7).

In addition to the demands of physical exercise, the mountain environment may also play a part in triggering SCD. Any ascent to altitude is accompanied by a fall in barometric pressure and a subsequent reduction in the partial pressure of inspired oxygen ($PIO_2$). The resulting fall in the arterial oxygen saturation ($SaO_2$) and oxygen content of arterial blood ($CaO_2$) clearly has the potential to reduce myocardial oxygenation. Historically, this was used in the Levy hypoxaemia test in order to identify those with CAD and to estimate the severity of their symptoms (27). Using hypoxic gas mixtures equivalent to 10,000-15,000 feet (3050-4575m) of altitude, significant ST depression (>0.5mm) was elicited in 26% of those with known CAD (28).

The fall in ambient temperature can also have an adverse effect on those with CAD (29-31). The incidence of SCD's is 60% higher in winter compared to summer months. This is thought to be largely due to the effect of the cold stimulating the sympathetic nervous system and increasing cardiac work (32). In the mountain environment an increase in sympathetic nervous system activity is common. Anxiety, poor sleep, intercurrent infection, inadequate food intake and dehydration can all result in greater physiological demands being placed upon the heart (33).

Clearly, CAD increases the likelihood of SCD in the mountain environment. What connects them together?

## The Pathophysiology of SCD in the Mountain Environment

Three pathological processes may explain the triggering of a SCD in the mountain environment:

***1. Rupture or Erosion of Atherosclerotic Plaque – Acute Coronary Syndrome***

Post mortem examinations of SCD victims who died during vigorous exercise tend to reveal widespread atherosclerotic CAD with critical obstruction of

two or more coronary trunks (>75% cross sectional area) (34,35). In the vast majority of cases there is clear evidence of a ruptured atherosclerotic plaque and extensive coronary thrombus. In a post mortem study of 141 SCD victims, the incidence of plaque rupture was found to be considerably greater in those who died during exercise (68%) than at rest (23%) (35). Importantly, these plaques differed from those that ruptured at rest, since they possessed a thinner fibrous cap and were often found to rupture in the centre of the cap rather than at the periphery. In these cases the rupture or erosion of an atherosclerotic plaque may be explained by the bending, twisting and flexing motions required of the coronary arteries during exercise and the resulting increase in shear forces that act upon vascular walls (12). In the mountain environment this could be compounded by the addition of sympathetic stimuli such as hypoxia, sleep deprivation, dehydration, missed meals, anxiety and extremes of temperature. Interestingly, it is not only the atherosclerotic plaque that may be vulnerable at altitude, but also the resulting coronary thrombus. Observational studies have demonstrated a high incidence of portal vein thromboses and ischaemic strokes in previously healthy Indian soldiers following prolonged stays at moderate altitudes (36,37). These findings are consistent with the increases seen in D-Dimer and prothrombin fragment 1 + 2 concentrations in those who travel to the mountains and suggest that in certain circumstances there is an imbalance between coagulation and fibrinolysis (38-40).

Unfortunately post mortem studies of SCD's in the mountain environment are limited. During the snowstorms that affected New Jersey, USA in 1996, 17 patients developed either a myocardial infarction or unstable angina whilst shovelling snow. Thirteen (76%) had evidence of a rupture of the coronary artery whilst 6 (35%) had evidence of extensive intramural thrombus (41). Closer to the mountains, work by Sherry and Cloud on downhill skiing fatalities revealed significant coronary occlusion in 13 out of 15 (87%) SCD's suggesting, somewhat tentatively, that a similar pattern is found in all forms of exercise, irrespective of the location in which they are undertaken (4).

***2. Myocardial Ischaemia***

An imbalance between oxygen delivery and demand can result in the triggering of ventricular arrhythmias, especially in those with pre-existing areas of peri-infarction, ischaemic tissue or myocardial scarring (12). At altitudes of up to 7100m the process of acclimatisation ensures that sea level $CaO_2$ is maintained (42). However on acute exposure $CaO_2$ falls since key haematological and respiratory adaptations often require several days or weeks to develop (42-44). In response to a low $CaO_2$ the sympathetic nervous system is stimulated (43). In healthy individuals this results in the dilatation of epicardial coronary arteries and arterioles and an increase in myocardial blood flow (45-46). However in those with CAD, there is evidence to suggest that diseased vessels are unable to dilate when exposed to catecholamine surges and at modest altitudes the expected increase in coronary blood flow is lost (46). Since heart rate and mean arterial pressure are higher during rest and sub-maximal exercise at altitude, cardiac work is increased throughout much of the time spent in the mountain environment (47,48). An imbalance between oxygen demand and delivery in those with CAD is therefore a very real possibility. Such a difference may be exaggerated following an abrupt cessation in exercise since many of the arterial beds remain dilated for some time and result in a reduction in venous return, cardiac output and coronary perfusion (12,49). In the mountains, this may be amplified further, since a fall in plasma volume is a key component of the acclimatisation process (46). It is therefore conceivable that the combination of a low level of $CaO_2$ and a reduction in myocardial perfusion may therefore prompt an ischaemic insult and trigger a fatal ventricular dysrhythmia.

***3. Coronary Vasospasm***

Whilst pre-existing CAD is found in the majority of SCD victims, in a small number of cases the coronary arteries are normal (4,9,11,13). Hultgren, the highly respected cardiologist and high altitude physician, highlighted the case of a patient who developed severe angina following an ascent to Keystone, Colorado (2796m) (27). Despite the presence of T wave inversion in the pre cordial leads of an electrocardiogram, a subsequent coronary arteriogram was normal. Hultgren argued that this may have been the result of coronary vasospasm triggered by a combination of sympathetic stimulation and respiratory alkalosis (27). Following exposure to high altitudes, the peripheral and central chemoreceptors trigger an increase in ventilation that results in a decrease in the alveolar partial pressure of carbon dioxide ($P_ACO_2$) and an increase in pH (43). Although bicarbonate excretion increases with acclimatisation, the pH tends to remain persistently high. This has been demonstrated recently on Mt Everest where the pH of four mountaineers at 8400m was found to lie between 7.45 and 7.60 (42). Although the link between coronary spasm and respiratory alkalosis is poorly understood, a short period of controlled hyperventilation has been shown to trigger spasm in up to 65% of those vulnerable to

the condition (50). In these cases, spasm has been linked to local changes in the ionised concentrations of electrolytes such as calcium, potassium and magnesium (51,52). The addition of a sympathetic stimulus has the potential to compound this process still further. Normally, blood vessel calibre is controlled by the continuous production of nitric oxide (53,54). However in those vessels deficient in NO, the constricting effect of α-adrenergic activity will be most strongly felt. In Tibetan, Indian and Bolivian high altitude populations, concentrations of NO in plasma and exhaled gas are consistently higher than those found in sea level residents who ascend to altitude (55-57). The difference between these groups may be explained, to some degree, by the over-representation of the 4b polymorphism in the endothelial nitric oxide synthase (eNOS) gene of high altitude natives. The absence of this genetic variation makes the enzyme susceptible to intracellular proteases and reduces NO production. At low altitudes the presence of the 4b polymorphism reduces the incidence of essential hypertension by 15% and could, in theory, provide some protection against coronary spasm (58).

Individuals with a history of underlying cardiovascular disease may be particularly vulnerable to the effects of coronary vasospasm since many will have extensive microvascular disease. Despite normal coronary arteries, those with significant left ventricular hypertrophy (LVH) have a reduction in their maximal coronary blood flow compared to healthy individuals (59). Instead of stenotic vessels being to blame, the high pressure in the left ventricle damages layers of the endocardium and impairs perfusion through the arterioles and capillaries (60). At altitude, this may be compounded by changes in the microcirculation that trigger a slowing in the flow of blood through the smallest blood vessels. Using sidestream dark-field imaging, researchers at University College London have recently identified a reduction in red blood cell flow through small (<25μm) and medium (26-50μm) sized blood vessels following ascent to 4900m.

Examples of this phenomenon can be seen at: http://www.sdfimaging.net/dsmsealevelmicrocirc.wmv and http://www.sdfimaging.net/dsm6400metermicrocirc.wmv. Although the reasons behind this change are unclear, the rise in haematocrit concentration has been cited as a likely explanation for this delay (61).

**A Strategy for Reducing SCD in the Mountain Environment**

SCD in the mountains tends to occur in those with established CAD. Whilst there is little direct evidence to support a strategy reducing SCD in this environment, there are a number of interventions that have sound physiological reasons behind their use.

A history of CAD is the single greatest risk factor for SCD in the mountain environment. In a study comparing matched controls, those who suffered a SCD during mountain hiking were more likely to have had either a prior myocardial infarction (17% vs 0.9% $p<0.001$) or a known history of CAD without prior myocardial infarction (17% vs 4% $P<0.001$) (62). In addition, many of those who die from SCD during vigorous exercise display symptoms in the weeks and months prior to their fatal event. In all, some 50% of joggers, 75% of squash players and 81% of long distance runners experience symptoms prior to SCD, however only a small proportion undergo investigations or treatment (12,16). Leading high altitude physicians such as Herb Hultgren and Peter Hackett, advise a cautious approach in the management of those with CAD intending to venture into the mountains (63,64). This involves a thorough process of investigation and treatment, a lengthy programme of graded exercise prior to any ascent and a prolonged period of acclimatisation prior to episodes of modest exercise.

Unfortunately, guidance for those with only risk factors for CAD is far less clear. The American College of Cardiology and the American College of Sports Medicine recommend that those, "individuals who appear to be at greater risk of having underlying CAD should be considered for exercise testing before beginning a vigorous exercise training programme" (12). However there are limitations to this approach. Firstly, risk factors for CAD are commonplace in those who venture into the mountains. In a questionnaire study of 737 male skiers and hikers, 16.3% reported a history of hypertension (26). Clearly, exercise testing such a large population would be problematic. Secondly, the sensitivity of exercise testing remains in question since it relies upon the presence of flow limiting coronary lesions in order to identify "at risk" individuals (12). In most cases, SCD's during vigorous exercise are the result of atherosclerotic plaque breakdown in previously asymptomatic individuals and therefore stenotic lesions are often absent. An alternative approach to identifying those at risk from CAD is to calculate the risk of developing the condition from the presence of, "unfavourable levels of blood cholesterol and blood pressure, smoking, diabetes and adverse dietary habits" (65). Whilst evidence supporting the use of formal risk scores in CAD prediction is limited, addressing these risk factors is undoubtedly of benefit (65,66).

Whilst many of those who are at risk of CAD can be identified before they head into the mountain environment, there is evidence to suggest that a considerable proportion of SCD's occur in those with previously unsuspected CAD. It is therefore vital that adequate emergency facilities are available in popular ski cen-

tres and mountain resorts in order to treat those with acute coronary syndrome (ACS). As a minimum, the American Heart Association recommend that health fitness facilities should be able to, "perform pre-entry screenings, to have written emergency policies, to conduct regular emergency drills and cardiopulmonary resuscitation practice, to have automatic external defibrillators available for immediate use by trained personnel and to establish a "hotline" to summon emergency medical services" (67).

## Conclusion

Although many of us obtain enormous benefits from exercise in the mountain environment, a considerable number are at risk of SCD. Since the majority of those who will suffer a SCD have underlying CAD, any strategy that intends to address this in the mountain environment will need to focus upon: (i) recommending an appropriate management plan for those with CAD (ii) reducing the advancement of CAD in those with risk factors for the condition and (iii) successfully treating those who develop complications of CAD.

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