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The role of cardiovascular CT in occupational health assessment for coronary heart disease: An expert consensus document from the Society of Cardiovascular Computed Tomography (SCCT).

Ahmad M Slim

Emilio Fentanes

Michael K Cheezum MD
Parkview Health, Michael.Cheezum@parkview.com

Iain T Parsons

Christopher Maroules

See next page for additional authors

Authors

Ahmad M Slim, Emilio Fentanes, Michael K Cheezum MD, Iain T Parsons, Christopher Maroules, Billy Chen, Suhny Abbara, Kelley Branch, Prashant Nagpal, Nishant R Shah, Dustin M Thomas, Todd C Villines, Ron Blankstein, Leslee J Shaw, Matthew Budoff, and Ed Nicol

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Guidelines

The role of cardiovascular CT in occupational health assessment for coronary heart disease: An expert consensus document from the Society of Cardiovascular Computed Tomography (SCCT)

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Preamble

In response to the increasing application of cardiovascular computed tomography (cardiovascular CT), the Society of Cardiovascular Computed Tomography (SCCT) guidelines committee has produced this document to guide the use of cardiac CT in the risk assessment of coronary artery disease (CAD) in occupational health evaluation. The purpose of this document is to support quality care given to individuals who undergo occupational health evaluation for the diagnosis of CAD. This document reviews evidence regarding the prevalence of coronary artery disease (CAD), the incidence of major adverse cardiac events (MACE), and the recommendations for enhanced cardiovascular screening and investigation for CAD evaluation amongst safety sensitive occupations. This document examines occupation risk categories where cardiac CT may be appropriate to investigate for CAD and evaluates available testing strategies for risk assessment.

1. Introduction

Cardiovascular disease (CVD) is one of the commonest causes of incapacitation and death globally; it remains the leading cause of mortality in the United States (US) where it accounts for one in every three deaths.[1] On a global scale, CVD is the leading cause of death with an estimated death toll of 17.9 million accounting to 31% of all-cause mortality in 2016.[2] Using the US as an example, over 130 million adults are employed, representing 55% of the adult population. The evaluation of CVD and cardiovascular risk factors are essential when considering occupational health and safety. The influences of health on work, and work on health, are well established and the impact of CVD morbidity and mortality is estimated to account for $120 billion in lost productivity in the workplace in the US alone.[3] Unfortunately, widespread variation remains in occupational health evaluation, with limited consensus regarding occupation and patient-specific criteria that may warrant additional enhanced screening for CVD. One of the most significant challenges facing CVD prevention is the "prevention paradox"; where patients at the highest relative risk for CHD can be identified based on risk factors, but most adverse cardiovascular events occur in patients considered to be low- or intermediate-risk by current clinical risk scores (Figs. 1 and 2).

2. Evidence review

The SCCT occupational working group reviewed published recommendations by cardiovascular societies and preventive task forces[4,5] and performed a comprehensive review of the literature[6–9] (PubMed, Scopus, EMBASE and Cochrane Library from their inception through March 2017) for all English-language evidence related to occupational health evaluations for CAD in pilots, astronauts, commercial drivers, military personnel, police officers and firefighters. (see Table 1)

To standardize the terminology throughout the document, the working group adopted the term "safety-sensitive" for occupations that have been assessed for elevated risk to the worker, society or work environment. This terminology was first used by the American College of Occupational and Environmental Medicine (ACOEM).[10] Before exploring the detail of the evidence identified in the literature search this manuscript outlines the basic concepts of occupational medicine, risk assessment and acceptable risk, which must be understood as a pre-requisite to

* Corresponding author. Associate Professor of Medicine, University of Washington, Associate Professor of Radiology, Tulane University School of Medicine, Pulse Heart Institute, 1901 S. Cedar Street, Suite 301, Tacoma, WA, 98405, USA.

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Abbreviations

CAC	coronary artery calcium
CAD	coronary artery disease
CHD	coronary heart disease
Cardiac CT	Cardiac computed tomography
Coronary CTA	Coronary computed tomographic angiography
ICA	invasive coronary angiography
GXT	graded exercise treadmill test
SPECT	Single Photon Emission Computerized Tomography
MACE	major adverse cardiac events

critically appraising the literature on cardiovascular disease in occupational risk assessment.

3. Occupational medicine: legal/ethical considerations

It is the impact of work on health, and health on work that forms the basis of occupational medicine.[11] Published literature defining occupational risk are sporadic and lack consensus, and agreement of the level of risk that mandates increased enhanced cardiovascular screening, for prevention of untoward outcomes (to both individuals and society), is variable and usually determined by the employer.

This document focuses on the diagnosis of CAD in working-aged adults and considers the evidence for commercial pilots and drivers, astronauts, military personnel, police officers and firefighters all of which are deemed "safety-sensitive" occupations. Among these professions, health screening aims to preserve personal and public safety, as occupational environments may expose these patients to an increased risk of major adverse cardiovascular events (MACE) or geographically limit the individual's access to timely healthcare.

Screening and investigation in occupational health is complex, and guidelines of the Faculty of Occupational Medicine advise that any screening procedures are both ethically and clinically justifiable. Additionally, the American College of Cardiology recommends that an appropriate test is one in which "the expected incremental information, combined with clinical judgment, exceeds the expected risks of the procedure and the downstream impact of poor test performance (such as a delay in diagnosis (false negatives), or inappropriate diagnosis (false positives)".[12]

Cardiovascular screening in safety sensitive occupations may be divided into initial screening and enhanced screening.[56] Initial screening often includes the use of risk assessment calculators, a standard 12-lead, or exercise, electrocardiogram, and screening bloods. Enhanced screening may include coronary artery calcium scoring and, increasingly coronary CT angiography (CTA). Enhanced screening is usually performed when either a positive first line screening test identifies a potential increased likelihood of occupationally significant cardiovascular disease or the level of risk acceptance is such that clear and unequivocal exclusion of occupationally relevant disease is required.

The decision to pursue screening or occupational investigation should first and foremost be made on clinical grounds, against defined risk parameters. The appropriate use of tests to detect CVD in occupational medicine and the concept of 'acceptable risk' are ill-defined in the literature, and there are a lack of studies that compare the impact of risk assessment tools on occupation health, public safety, resource utilization, and long-term outcomes.

In those who work in safety sensitive occupations, investigations must be requested, interpreted and acted upon with caution to avoid untoward career impact. There is understandable anxiety provoked by occupational health screening and investigation as test results may impact work eligibility, and any variability of interpretation of test results among experts may lead to regulatory and potentially legal challenges. Investigations may also lead to unexpected incidental findings, which in themselves may provoke anxiety or detect occupationally significant disease processes that were not previously of concern.

In occupational health, consideration is given to the duty to protect both the individual worker and society at large. The principle "first, do no harm" applies to both the worker and the potential population at risk. Screening policies must not be overly restrictive however, as this may have unintended secondary consequences. As an example, from an employer's perspective, among asymptomatic aging pilots with subclinical atherosclerosis and well controlled ASCVD risk factors, "it may be preferable to allow experienced pilots to continue to fly, possibly with

Fig. 1. Challenges of CAD prevention and risk assessment in safety sensitive occupations.

Journal of Cardiovascular Computed Tomography 15 (2021) 290–303

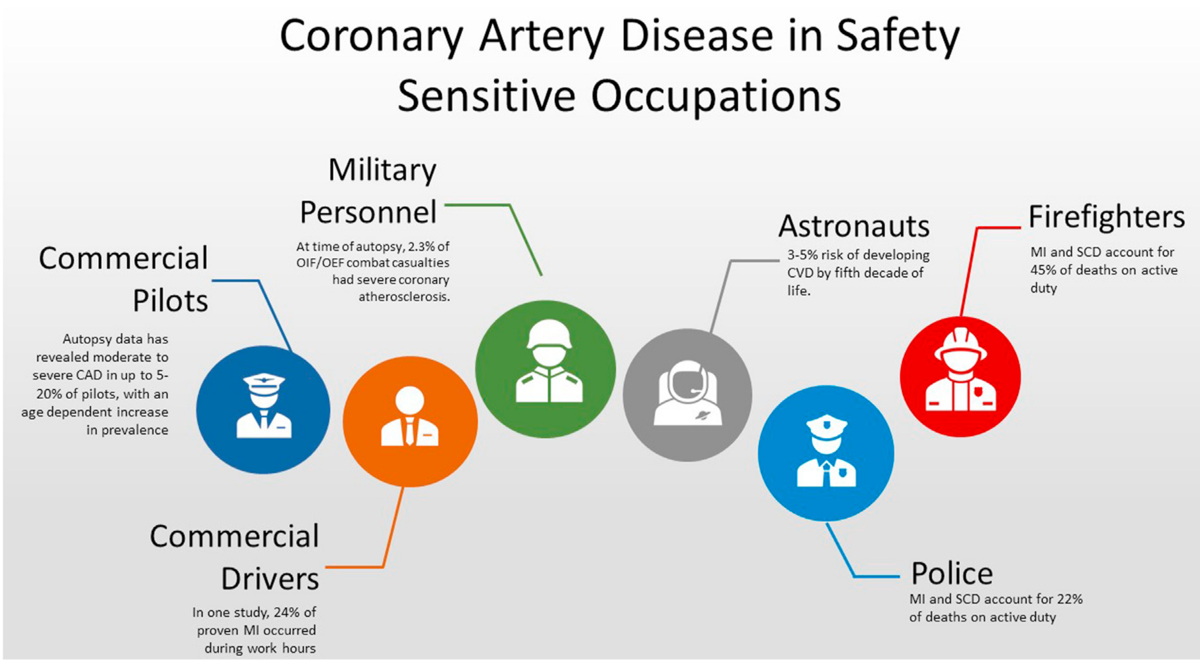

Fig. 2. Coronary artery disease in safety sensitive occupations.

restrictions on employment, rather than to replace their experience with novice pilots, as the use of overly strict medical criteria may paradoxically increase accident rates".[13,14] The use of radiation based investigations for enhanced screening must also be considered with the risk to the individual needing to be balanced against the requirement for employers to ensure safety in the high-hazard employment areas.

Ethical and legal considerations also vary across occupation and between international regulatory agencies. In the US, for example, the Genetic Information Nondiscrimination Act of 2008 limits the use of family history and genetic tests in employment screening. This is notable in CVD risk assessment, as a family history of early CAD is associated with an increased risk of myocardial infarction and plaque burden in young patients. Age is a strong predictor of CVD risk, and yet judges have ruled that prior mandatory age retirements for pilots violate age discrimination legislation, both in the US and Europe.

Accurate reporting of medical conditions to licensing authorities can also be challenging, as occupation candidates are often required to self-report their medical history. While most candidates will provide full disclosures, the potential for recall bias and unreported (or undetected) illness remains.[15] In pilots, the International Civil Aviation Organization (ICAO) regulations require an independent aeromedical examiner (AME) to certify fitness, with full access to medical records. However, some countries (such as Germany) have laws that permit only a partial transfer of information, weighing patient privacy against public safety. Significant debate remains in this area and ongoing legal challenges continue to weigh up the interest of public safety versus individual's right to privacy.

4. Fundamentals of investigating CAD in safety sensitive occupations

Before looking at the specific investigations used to screen workers undertaking defined safety-sensitive occupations it is useful to explore the concepts of acceptable risk (to employers, or licensing authorities); the concept of a "healthy worker" effect; the age demographic of the workforce (as compared to the usual age-distribution from which much clinical evidence is gathered) and the inherent strengths and weakness of the investigations available to clinicians to investigate CAD, against the level of permitted risk.

4.1. *Acceptable risk*

All individuals who undertake any activity that requires a license may be subject to screening against an accepted risk standard. As an example, in the UK the acceptable annual risk for incapacitation to hold a standard driving license, for domestic purposes is 20% per annum (pa), whilst for a heavy goods vehicle (truck) driver it is 2% pa. In commercial aviation the acceptable risk basis used by the Federal Aviation Authority (FAA) in the United States, the European Aviation Safety Agency (EASA) in Europe and the Civil Aviation Authority (CAA) for dual-crew flying operations is 1% pa, with single seat commercial pilots (most often in the military) having far more rigid standards. Commercial rules are more stringent than those applied to those undertaking recreation flying.

It can immediately be realized that the level of evidence available against these very low risk acceptance levels is lacking in the usual clinical literature on cardiovascular medicine and therefore a different approach to cardiovascular risk assessment may be required to give assurance to the employer that the organizational risk threshold is not being exceeded.

4.2. *Healthy worker effect*

Many, but not all, individuals who undertake safety-sensitive activities are both screened for their level of fitness at recruitment and expected to meet certain fitness standards throughout their careers.

As an example, astronauts are generally regarded as a selected group of healthy workers. By the nature of their high levels of fitness and health, they are expected to show a lower risk of cardiac events compared with the general population ("healthy worker effect").[16,17] The healthy worker effect is determined by both the initial selection process (hiring more fit persons) and the continuing employment of healthy persons, who typically get annual physicals to assess levels of fitness and fitness for duty.[17] Evidence of a reduced mortality from CVD in safety sensitive professionals is often quoted, but evidence in aircrew, astronauts, the military and the emergency services all show similar prevalence rates of disease to the general population at the same age.

In aircrew, despite a consistent finding of lower risk of CVD mortality compared to the general population, the prevalence of CAD in pilots is the same as age-matched controls in the general population,[18,19] and

Table 1

Appropriate Use Guidelines for Cardiac CT in Safety-Sensitive Occupation Health Exams. Safety-sensitive defined as occupations where sudden incapacitation or sudden death may endanger the safety of others (ex. pilots).* By ACC/AHA Pooled Cohort Risk Calculator or equivalent. Note: GINA Act may limit use of family history for employment screening in the US.[206] CAC test may be appropriate if combined with functional testing to improve the sensitivity of a negative stress test when CAC = 0. CAD, coronary artery disease; DM, diabetes mellitus; HLD, hyperlipidemia.

Indication	Test	Rating
Symptomatic Patients Initial evaluation with no prior history of CAD. Evaluation after prior non diagnostic/equivocal stress test.	CCTA	Appropriate
Asymptomatic Patients Evaluation of asymptomatic left bundle branch block. Evaluation of prior non diagnostic/equivocal stress test. *Symptomatic Patients* prior non obstructive minimal CAD	CCTA	May Be Appropriate
Reassessment with no change in clinical status. Prior history of known significant CAD. Initial evaluation in asymptomatic patients without Left bundle branch block or prior non diagnostic/equivocal stress test.	CCTA	Rarely Appropriate

CAD, coronary artery disease defined as prior revascularization or known obstructive coronary atherosclerosis.

Indication	Test	Rating
Asymptomatic Patients for Estimation of ASCVD risk Initial Evaluation with an estimated >5% 10-year risk*, DM, familial hyperlipidemia, or family history of early CAD	CAC Score	Appropriate
Asymptomatic patients for ASCVD risk Interval (5-year) re-assessment when prior CAC = 0. *Symptomatic Patients*Ƥ	CAC Score	May Be Appropriate
Asymptomatic Patients for ASCVD risk Initial evaluation <5% 10-year risk*. Prior history of known Significant CAD. Interval (5-year) reassessment when prior CAC >0	CAC Score	Rarely Appropriate

*By ACC/AHA Pooled Cohort Risk Calculator or Equivalent
Ƥ If combined with functional testing to improve the sensitivity of a negative stress test when CAC = 0.
ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; DM, diabetes mellitus

whilst most experienced astronauts are middle aged, and at risk for developing major adverse cardiovascular events, recent contemporary data has revealed similar rates of developing CVD as the general population despite exposure to spaceflight.[20–23]

In the military, like the general population, the most frequent cause of death is CAD, with an increasing trend seen with increasing age.[24–26] Whilst recruiting at a younger age, a focus on physical fitness,[27,28] reduced obesity levels[29–31] and the early discharge of those with conditions known to predispose to CVD, such as diabetes,[29,31] chronic kidney disease or rheumatoid arthritis, may reduce the burden of CVD,[32,33] a higher proportion of males recruited from lower socioeconomic groups, increased rates of smoking[31,34–36] and a paradoxical increased rate of cardiovascular events due to vigorous exertion may not only negate any benefits, but worsen cardiovascular health in comparison to the comparative normal population.[37]

The "healthy worker effect" does not apply to either firefighters or commercial motor vehicle (CMV) drivers. The prevalence of cardiovascular risk factors is higher among CMV drivers relative to other occupations.[38] Commercial drivers have an especially high smoking prevalence,[39–41] frequent hyperlipidemia,[40–43] overweight or obesity range body mass indices,[39–43] diabetes,[41] and hypertension.[44–46] Multiple studies have demonstrated that firefighters have greater subclinical atherosclerosis than the general population, independent of coronary risk factors, and that traditional CVD risk assessment does not adequately identify at-risk firefighters.[47] Data suggests that police officers are less likely to die of CVD than firefighters while on duty[48] with mixed results when assessing whether they have increased atherosclerosis as compared to the general population.

Most CVD studies of the police in the US were undertaken prior to 1990 and thus less relevant to current understandings of SCD among safety sensitive workers.[49,50] One study of 312 male and female police officers, compared to age-matched general population free of clinical CVD[51] demonstrated that police officers had elevated levels of age-adjusted CVD risk factors (blood pressure, total cholesterol, smoking prevalence) compared with the population sample.

4.3. The safety-sensitive occupational workforce

Military personnel, many emergency service personnel, and aircrew are usually significantly younger than the population normally associated with coronary or cardiovascular health concerns. This is an important factor when considering applying the published clinical literature on both diseases, and the effectiveness of investigations in detecting pathology, to this different cohort. The use of Bayesian theory is therefore important when considering the occupational population and when applying an evidence base that is based on older individuals who have a substantially higher disease prevalence. It would be expected that many individuals undertaking safety sensitive occupations would fall outside the usual "evidence-base" for decisions made in usual clinical practice.

4.4. Strengths and limitations of existing tests to screen for/investigate CAD

Given the low level of risk that many employers, or regulatory authorities, strive to, careful consideration must be given to whether screening investigations have enough sensitivity to exclude disease associated with a risk of just 1–2%. Additionally, the specificity of a test is also critical given the need to not exclude workers from employment unnecessarily whilst ensuring employers are not being falsely reassured or carrying undeclared risk in excess of that which is acceptable or mandated by the regulations.

4.4.1. Risk scores

Traditional risk scores are widely available and, by highlighting CVD risk factors, are usually first line tools. Unfortunately, risk scores have known limitations in their ability to risk-stratify patients. Evaluation often rely on history, physical exam, and resting electrocardiogram (ECG) alone. History may be unreliable considering potential reporting bias,[15,52,53] and rest ECG have poor accuracy in detecting ischemic heart disease (54).

In aircrew, current methods employed to screen for high-risk aviators suffer from reduced sensitivity and specificity, regardless of age group or pre-test risk of obstructive CAD[14,52,54] whilst the application of a Framingham risk model to pilots with a JAA Class 1 certificate in the U.K., demonstrated that 9% of pilots had an estimated 10-year CVD risk >20%.[54]

So, whilst many agree that the routine evaluation of pilots and other safety-sensitive workers is needed to screen for CVD, debate remains regarding the appropriate use of tests and the most appropriate test to detect CVD. The chosen test needs to accurately determine whether an individual has occupationally relevant disease and usually this requires the accurate identification of atheroma more than the identification of obstructive CAD (although the latter is clearly important also).

4.4.2. Exercise ECG

Many agencies that employ safety-sensitive workers utilize exercise stress electrocardiography (exercise ECG) as a first line test in individuals deemed to be at increased risk of cardiovascular disease. This is in a large part because exercise ECG is widely available, relatively inexpensive, and does provide useful prognostic information. The exercise ECG has limitations as a screening tool for obstructive CAD due to its limited sensitivity and specificity. However, it does provide useful risk stratification information, such as BP response to exercise, identification of exercise related arrhythmias, and aerobic fitness. In low-prevalence populations, a good level of aerobic fitness has significant negative predictive value for aeromedical disposition considerations. However, due to the limited sensitivity of the exercise ECG (60–70%),[55] an unacceptably high number of individuals with angiographically demonstrable obstructive CAD, will be deemed normal following a false negative test. Exercise ECG will also not identify widespread but non-obstructive CAD. Additionally, the exercise ECG has a very low positive predictive value for future coronary events. For this reason, the Exercise ECG should be discouraged as a stand-alone tool to determine significant CAD in those who undertake safety sensitive employment.[56]

4.4.3. Other non-invasive functional tests

All functional tests have a specificity and sensitivity, to determine obstructive CAD, of approximately 80% at best, and using Bayesian theory and understanding the prevalence of obstructive CAD in the safety sensitive workforce, a positive functional test will often more likely be a false positive than to reflect an obstructive coronary lesion. As with the exercise ECG, functional tests will also not identify widespread but non-obstructive CAD, that may well be occupationally important and confer a MACE event risk above the acceptable1–2% level required in many safety sensitive roles. False positive tests also potentially lead to further (unnecessary) investigations that may be associated with procedural risks from radiation exposure, intervention or the identification of additional incidental findings that require extensive further investigation. In safety sensitive workers, this may result in removal from work duty and delays in appropriate return with related impact on operational effectiveness and subsequent cost ramifications to both the worker and employee.

4.4.4. Coronary artery calcium (CAC) score

CAC Scoring is a proven independent CAD risk marker, providing improved patient-specific diagnostic and prognostic accuracy over traditional CAD risk factors alone.[57–59] Reporting of CAC has become standardized in clinical practice utilizing the Agatston method[60,61] with increasing CAC scores associated with a higher incidence of MACE.[10,53,57,62]

In the general population CACS provides valuable, patient-specific prognostic data and adds incrementally to a patient-centered discussion of initiation of primary prevention medical therapy.[5] A zero CACS is associated with very low CHD event rates (0.1%/year) and thus identifies a population of patients in which medical therapies may be deferred.[59,63–66] Conversely, a CACS >100 identifies a high-risk cohort which, regardless of calculated 10-year ASCVD risk, may benefit from the initiation of statin therapy.[59,66–68] In addition to identifying patients who are likely to benefit from primary prevention therapies, CACS may also identify asymptomatic patients with silent ischemia as it has been reported that in patients with extremely high CACS (≥400), ischemia is present in up to 50% of patients.[69,70]

As a risk marker, independent of traditional cardiovascular risk factors, CAC allows for the reclassification patients. However, in younger (<45 years of age), potentially fitter, individuals being screened or investigated for CAD a normal CACS may not identify occupational relevant non-calcified CAD, that may have an event risk that is in excess of the employer's regulatory limits.[119]

4.4.5. Coronary CT angiography (coronary CTA)

Coronary CTA is a non-invasive tool that provides high-resolution imaging of coronary artery anatomy, CAD distribution, and severity comparable to invasive coronary angiography (ICA).[71–73] Coronary CTA is well-validated in symptomatic patients with low to intermediate pretest risk for obstructive CAD.[74,75] Currently, coronary CTA is recommended as the initial test for diagnosing CAD in patients where obstructive CAD cannot be excluded by clinical assessment[60] and in stable symptomatic patients.[76] Coronary CTA also can assess plaque morphology and high-risk coronary CTA features should lead to an escalation of medical therapy.[11,77–79] This ability to thoroughly evaluate non-obstructive plaque for both high-risk characteristics and burden is vital to preventing future CV events.[4,5,77]

However, in an occupational health setting, most patients are asymptomatic at presentation and are referred for further assessment due to a raised cardiovascular risk or abnormal findings (such as on the ECG). The predominance of published data for coronary CTA in asymptomatic patients is in diabetics and high-global CHD risk patients[58,80,81] and this population is unlikely to be representative of the occupational cohort. A normal cardiac CT provides long term prognostication, as a normal coronary CTA (no plaque and zero CACS) confers a CV event rate of <1% over in 7 years of follow-up among symptomatic patients.[10,82,83] This level of diagnostic precision and accuracy may permit less frequent testing and cost savings given, in many instances, annual screening for raised CHD risk is undertaken.

Despite the clinical utility of both CACS and coronary CTA in asymptomatic patients, there remains a lack of guidance on the utilization of these modalities in the screening of certain high-risk occupational health populations. The use of either CACS or coronary CTA should not be applied indiscriminately to all individuals who may be employed in safety sensitive fields, but used if initial screening identifies a potential increased likelihood of occupationally significant cardiovascular disease, or if the level of risk acceptance is such that clear and unequivocal exclusion of occupationally relevant CVD is required.

4.4.6. *Invasive coronary angiography*

The routine use of invasive coronary angiography (ICA) is problematic in asymptomatic safety sensitive workers for several reasons. This is because ICA is associated with a risk of stroke, MI, coronary dissection and vascular access damage in as many as 1 in 30 cases.[84] The overall risk of death with ICA is approximately 1 in 1000. ICA is preferably undertaken based on clinical indications for individuals likely to require intervention. Its use for an occupational indication requires detailed discussion and appropriate consent from the patient concerning risks and benefits, given the possible career implications of a procedure-related event.

5. Specific safety sensitive occupations

This section reviews the evidence for cardiovascular investigation as well as investigations to screen for occupationally relevant CAD for specific safety sensitive occupations and the current occupational standpoints with regards the effect of CVD on these professions.

5.1. *Commercial pilots*

With an estimated rate of nearly 0.1 fatalities per million flights, aircraft loss attributed to cardiovascular disease (CVD) in pilots is rare.[82] Similarly, pilot incapacitation in-flight is uncommon, with a reported incidence of 0.1–0.8 per million flight hours.[15,85] However, exceptions do exist where pilot incapacitation results in aircraft accidents and fatalities.[82,86,87] As a result of these rare events, screening for CVD and its risk factors remain essential components of licensing requirements to ensure air safety.[88–90]

The International Civil Aviation Organization (ICAO) sets the minimum standards for pilot licensure[91–93] but additionally, individual agencies guide commercial pilot licensure, including the Federal Aviation Authority (FAA) in the United States, the European Aviation Safety Agency (EASA) in Europe and the Civil Aviation Authority (CAA) in the UK. Despite efforts to unify standards, diverse approaches exist to evaluate a pilot's risk for CVD events with variable requirements to report medical conditions to authorities, although efforts have recently been undertaken to improve consensus in cardiovascular risk assessment by a group of aviation cardiologists working as part of a NATO initiative to develop international consensus in this field.[94]

When considering occupational limitations in aircrew, the usual acceptable risk of incapacitation for multi-pilot commercial flying is based on the so-called "1% rule." This rule states the maximum acceptable risk of pilot incapacitation should be less than 1% per year from any medical condition. This concept was developed at the first UK Workshop in Aviation Cardiology[95] at which time, the all-cause accident rate for commercial airlines was approximately 0.2 per million flying hours. For assessing medical risk, the Workshop decided upon a target of 0.1 fatal accidents per one million flying hours (one in 10^7 flying hours). Further, it was argued that aircrew, as part of the overall aircraft system, should not contribute more than 10% to the total risk. Based on these assumptions, it was argued that medical incapacitation should result in a fatal accident no more often than one in 1000 million flying hours (1 in 10^9) (for details see text box). While this approach has been used for decades, the 1% rule has some limitations[96–98] and the concept of acceptable risk in commercial aviation remains debatable, with proposed risk limits ranging from 0.5 to 2% per year.[97,99,100] Additional requirements for older pilots have attracted additional controversy[89] since studies demonstrate an age-dependent risk of pilot incapacitation, although the value of experience is a significant factor in reducing accident risk.[99,101] In 2006, ICAO mandated the requirement for a co-pilot under age 60 to minimize the risk of single-pilot incapacitation in commercial flying.[101]

Using a set of assumptions pertaining primarily to commercial civil aviation operations including average duration of flights (1 hour), critical phases of flight (limited to landing and take-off, representing 10% of flight time i.e. 6 minutes), and the presence of a co-pilot able to take over in the case of sudden incapacitation (which reduces risk by a factor of 100), it was calculated that only one pilot incapacitation in 1000 would be likely to lead to a fatal accident. For a target accident rate of 1 in 10^9 hours, if only 1 in 1000 incapacitations is likely to lead to an accident, the acceptable medical incapacitation rate is 1 in 10^6 hours. Since there are 8760 hours in a year, ($\sim 10^4$), the acceptable annual medical event rate to meet this target is 1% per year. ($10^4 \times 10^2 = 10^6$). Reproduced with permission from Grey G, Rienks R, Davenport ED, Guettler N, Manen O, Syburra T, D'Arcy JL, Bron D, Nicol E D. Assessing Aeromedical Risk: A three-dimensional risk matrix approach. Heart 2019. Jan; 105 (Suppl 1): s9-16.

It is estimated that 6 pilots from 1965 to 1981 of regularly scheduled commercial airliners died suddenly from coronary disease while in the air and the copilot was able to land the plane safely, and the passengers were not harmed.[102] The FAA reports that from 1994 to 2007 only 5 pilots (under the age of 60 years) died whilst in control of commercial aircraft (103). This is mirrored globally with similar safety records among older commercial pilots in Japan, with no accidents over a decade, in pilots aged 60–63 years, compared to 323 total accidents and 27 air-transport accidents in younger pilots (age< 60).[90] Most CVD-related accidents occur in general/private aviators where the acceptable medical risk is significantly greater than for commercial pilots.[88,89]

5.1.1. *Cardiac investigation for CAD in commercial pilots and aircrew*

Most pilots with subclinical CAD will never manifest during their careers, and yet latent CAD remains a prevalent finding in aircrew. Autopsy data has revealed that moderate-to-severe coronary artery stenosis is seen in up to 5–20% of pilots, with an age-dependent increase in prevalence.[104–107] Consequently, ICAO does not require routine exercise ECG, whilst multiple guidelines have provided variable recommendations for screening with an exercise ECG in pilots.

5.2. *Military pilots and aircrew*

Military air operations often are performed by pilots and aircrew operating high performance aircraft that require their full engagement throughout the mission. While acute incapacitation among military pilots is rare, in the United States Airforce (USAF) cardiac events are a leading cause of in-flight incapacitation.[108–110] Autopsy studies among military pilots and aircrew reveal that atherosclerotic cardiovascular disease is a common finding, and in some cases, there is evidence of severe disease.[18,111] Furthermore, there is evidence of systemic underreporting of cardiac symptoms among the military pilot and aircrew population[112]

likely stemming from aircrew being cognizant that CV disease is the most common reason for flight disqualification.[56,112–114]

5.2.1. Cardiac investigation for CAD in military pilots and aircrew

Prior to the utilization of CACS, the absence of coronary artery calcifications by fluoroscopy demonstrated a high negative predictable value for significant coronary artery disease among asymptomatic military aircrew.[115]

Historically, functional assessment, both with and without myocardial perfusion scintigraphy (MPS), among USAF pilots and aircrew has been a poor predictor of future cardiovascular events, with MPS demonstrating a poor sensitivity and specificity. Over 20 years similar cardiac event rates occurred in those with normal or abnormal functional assessment tests.[56] Among USAF pilots with an abnormal functional assessment, 62% had no evidence of coronary artery disease while 12% had evidence of obstructive CAD.[56]

Pilots and aircrew with CACS of 10–99 have a predicted annual cardiac event risk of 0.5%, while those with CACS of >100 had a >1% annual risk of major adverse cardiac events (MACE).[52,116,117] This correlated to ICA data on USAF pilots, where luminal irregularity had an annual event rate of 0.5%, an aggregate stenosis of up to 50%, a 1% event rate and the presence of a stenosis of >50% was associated with annual MACE event rate of 2.2%.[118] In comparison the presence of more than one 50% stenosis, a single stenosis >70%, or a >50% stenosis in the left mainstem were all associated with a >3% annual MACE event rate.[119]

While there is currently no outcome data for coronary CTA in aircrew, a recent publication on UK military aircrew demonstrated that coronary CTA was able to detect clinically and aeromedically significant CAD, even in those with a CACS of zero, and argued that coronary CTA could be the investigation of choice in those deemed high risk of occupationally relevant CAD.[120]

5.3. Astronauts

Maintenance of cardiovascular health among astronauts is important given the recognized cardiovascular adaptations associated with spaceflight.[94–99,115,121–125] To date, there is contradictory evidence associating these physiological effects to an increased lifetime risk for cardiovascular disease (CVD).[126–128] In the past researchers have suggested that astronauts have a 3–5% risk of developing CVD by their fifth decade of life[128] but the absolute risk of all-cause mortality during space flight is unknown. All deaths during space flight have been related to catastrophic failure of critical life support systems or the transport vehicle.

5.3.1. Cardiac investigation for CAD in astronauts

Current National Aeronautics and Space Administration (NASA) guidelines, established with the assistance of a committee of national experts, use a criterion of coronary artery calcium score (CAC) to exclude astronauts from the corps.[127–129] High performance aircraft personnel must be examined by a certified NASA Flight Surgeon or Aviation Medical Examiner and screened for anomalies and conditions that could pose a health or safety threat to the individual or mission.[129] Cardiovascular status is assessed using standardized cardiovascular risk assessment tools, including the Framingham Risk Score and the Reynolds Score. If the calculated 10-year risk for an adverse cardiovascular event is $\geq$ 10%, evaluation by a cardiologist is required and any confirmed cardiovascular disease is disqualifying.[129] Recently the Astronaut Cardiovascular Health and Risk Modification (Astro-CHARM) tool was developed and validated to enhance cardiovascular risk prediction among astronauts and the general population.[130] A patients' 10-year risk of ACVD is determined through an integration of risk factors (including family history of early MI and high sensitivity C-Reactive Protein (Hs-CRP) in combination with CACS and was developed across 3 large population cohorts. In a large population cohort, it was validated and found to improve CV risk prediction when compared to traditional risk factors.[130]

5.4. Military personnel

Military personnel are recruited from their parent nation and allies but are not often reflective of the wider population. Many aspects of military service, such as the primacy of mission success and training for that purpose, are generalizable. However, recruitment policies and differing health economies coupled with cultural and racial[131–133] variances may impact on background levels of cardiovascular disease (CVD).[134,135]

As in the general population, age is an important determinant for CVD in the military,[124–126] with the incidence of death in the US military secondary to CAD for those <35 years of age being 0.65 per 100 000 service years, 13.69 in those >35 years of age, and 83.5 in those >50 years.[136] Overall annual rates of ischemic heart disease (IHD) having decreased from 0.80 per 1000 person years to 0.68 per 1000 person years) over the past decade[136] but may now be again on the increase.[118] In the UK Armed Forces over a 16-year period from 1995 to 2011, the overall mortality rate from CVD, was 7.81 per 100 000 service years, with CAD being the most common cause of sudden cardiac death (SCD)[26] and the most frequent cause of cardiovascular medical discharge from service.[26] A retrospective review of 126 atraumatic deaths of 6.3 million military recruits aged 18–35 years of age demonstrated that coronary artery abnormalities, including anomalous coronary origins, were the predominant structural cardiac abnormality (61%).[137]

5.4.1 cardiac investigation for CAD in asymptomatic military personnel

Notably, 2.3% of US military service personnel who died of combat, or unintentional injury, during recent operational deployments, to Iraq and Afghanistan, had severe coronary atherosclerosis.[138] As previously described exercise ECG is still often used as a first line test in individuals deemed to be at increased risk of cardiovascular disease, although this is increasingly recognized as being suboptimal for the detection of occupationally relevant CAD.[139] The US military often uses CACS to risk modify individuals with a 10-year atherosclerotic CVD risk of 5–20% as directed by the ACC/AHA guidelines[140,141] Coronary artery calcium scoring (CACS) has been established in both the U.S. and Canadian military as a validated screening tool for the assessment of CAD in aircrew.[120]

The use of cardiac CT for the screening of asymptomatic service personnel is not used for either the US or UK Armed Forces given the limited evidence for its use in asymptomatic individuals in the general population.[142] In the UK Armed Forces, safety sensitive groups such as divers and aircrew are 'screened' with periodic ECG, with a low threshold for further evaluation if abnormalities suggestive of CAD are found.[143,144] This may include cardiac imaging following comprehensive clinical assessment.[142–145] In the UK and Germany coronary CTA is preferred to CACS due to the ability to assess for non-calcified and vulnerable plaques, anomalous coronary origins and the higher negative predictive value of CCTA that additionally reduces subsequent downstream testing.[120,142]

5.4.2. Cardiac investigation for CAD in symptomatic military personnel

Military personnel presenting with symptoms of IHD require expeditious evaluation. The US military have forward deployed cardiologists in recent conflicts[146,147] due to cardiovascular complaints being a common reason for aeromedical evacuation with chest pain being a common complaint.[148] Over 80% of military personnel presenting with cardiovascular symptoms during recent conflicts are returned to the front-line, with operational presentations of ACS being relatively uncommon,[24,149] albeit resource intensive.[146,148] Death from CVD on operational deployment is declining (4.1 per 100,000 person-years in the US military) although more prevalent in the reserve component.[150]

Societal guidelines, which favor a probability-based approach to the investigation of stable CAD, arguably do not provide acceptable levels of diagnostic certainty to allow for adequate risk assessment for military patients due to the low prevalence of CAD.[142,151,152] The principle test

requirements for military personnel are a high sensitivity and negative predictive value. Coronary CTA has been studied in the military population, demonstrating its accuracy in ruling out occupationally significant CAD,[153] identifying anomalous coronary artery origins,[154] and informing cardiovascular prognosis.[155] Coronary CTA also demonstrated lower rates of subsequent evaluations for chest pain and repeat testing,[156] and an increase in the use of preventive cardiovascular medications,[157] whilst reducing the radiation exposure to service personnel.[158] A recent meta-analysis demonstrated a CCTA can exclude anatomically defined coronary artery disease in nearly all patients regardless of their pre-test probability.[159] Service personnel without evidence of coronary atherosclerosis have an excellent prognosis over mean follow of 24 months[155] aligning with 10-year event free survivals against cardiac death and non-fatal myocardial infarction.[78] This assurance reduces scheduled and unscheduled re-evaluations for in those with a history of chest pain79 and is now the cornerstone of the UK Armed Forces approach, that also reflects existing reflecting NICE guidance for those with stable chest pain60.

In the US military, single photon emission tomography (SPECT) remains the most frequently performed imaging modality for risk stratification although with a demonstrated false positive rate of nearly 15% and nearly 93% those referred for ICA having no evidence of obstructive CAD.[160] In contrast, CCTA effectively rules out obstructive CAD in 98% of patients with 16.5% having non-obstructive coronary atherosclerosis, with an incident of referral to invasive coronary angiography required in just 2.4%.[153]

In the military, a deployed CT scanning capability has proven invaluable for the management of trauma in recent conflicts.[161] One interesting example was a non-gated cardiopulmonary CT performed for acute chest pain and shock in the operational environment that confirmed both situs inversus totalis and an acute mid-LAD thrombus in an Indian military contractor, who was immediately treated with thrombolysis and transferred for secondary coronary intervention.[162]

5.5. *Firefighters*

The risks of both burns and smoke inhalation are well understood in firefighters.[163] However, less appreciated is that the most frequent cause of death among firefighters is heart disease. Cardiovascular events, specifically MI and SCD account for 45% of deaths among firefighters on active duty.[163,164] In contrast, such events account for 22% of deaths among police officers on duty, and 11% of deaths among emergency medical services workers.[16,48,164]

Firefighters are generally regarded as a selected group of healthy workers. By the nature of their high levels of fitness and health, they are expected to show a lower risk of cardiac events compared with the general population ("healthy worker effect").[16,17] The healthy worker effect is determined by both the initial selection process (hiring more fit persons) and the continuing employment of healthy persons, who typically get annual physicals to assess levels of fitness and fitness for duty.[17]

The US Fire Administration (USFA) collects data on all on duty firefighter fatalities occurring in the United States, and reliable measures of the number of US career firefighters are available from the Current Population Survey (CPS).[165,166] In addition, the National Institute for Occupational Safety and Health (NIOSH) performs independent investigations of firefighter line-of-duty deaths.[167] In a 14-year study of >300 000 US full-time male career firefighters, aged between 18 and 64 years, the rates of SCD were similar to the US male general population and military personnel similar among younger persons, but diverged after the age of 45 years. After 45 years, the rates were 30–56% lower among firefighters than age-matched groups in the military and this was felt to be because less fit persons would retire from firefighting, thereby reducing the population at-risk. The pattern of SCD observed in firefighters is similar to sports related SCD in the general population, although firefighters experience higher rates of SCD compared with athletes.[168] The incidence rates (IR) of SCD was lower for low-risk duties (IR 11.0 per 100 000 person-years, 95% CI 8.9 to 13.7) compared with high-risk duties (IR 38.3 per 100 000 person-years, 95% CI 31.5 to 46.6).[37]

5.5.1. *Cardiac investigation for CAD in asymptomatic firefighters*

Much work has been done exploring sub-clinical atherosclerosis among active duty firefighters in the US. CACS and carotid intimal thickness (CIMT) have both been extensively investigated and shown to be useful for identifying increased risk and in subsequently implementing primary prevention.[169] In one study of 495 firefighters, 131 (26.9%) had positive CACS and underwent CT coronary angiography; 40 (8.1%) had >50% stenosis on coronary CTA and underwent subsequent ICA.[169] In a further study of 296 professional firefighters, assessing CVD risk with CACS and CIMT, linear regression demonstrated homeostasis model assessment (HOMA) as the strongest predictor of increased CIMT, raised fasting glucose was the strongest predictor of total coronary lesion number and score, and insulin resistance was shown to be directly correlated to CVD.[170] In a study of 399 asymptomatic firefighters increased CACS was found only in men >34 years of age. Of the 53% who had an Agatston score >0, 87% had higher CACS compared with age matched subjects in a national database,[171] a finding mirrored in a study of 647 asymptomatic firefighters, where employment as an active duty firefighter was independently associated with a 41-point increase in the age-matched CACS.[172]

5.6. *Police officers*

Police officers are known to have higher mortality rates than the general population secondary to suicide, increased rates of cancer and cardiovascular disease (CVD).[49,50,173–176]

As compared to firefighters, relatively little research has been performed into understanding the increase in ASCVD among police, with only two small longitudinal studies having been reported. In one study, 220 male police officers demonstrated no statistically significant difference in the IR of coronary heart disease at 10-year follow-up when compared to a general population cohort.[174] A second study of 232 male retirees from the Iowa Department of Public Safety reported a statistically significant increase in the incidence of self-reported cardiovascular disease when compared with controls.[173]

5.6.1. *Cardiac investigation for CAD in asymptomatic police officers*

In one study police officers exhibit increased CIMT and increased levels of atherosclerosis compared with a general population sample, not completely explained by elevated CVD risk factors whilst a second study of 2064 New York City police demonstrated a positive CACS in 74% of men and 80% of women but no increase in the prevalence of CAD compared with the general population.[51]

5.7. *Commercial drivers*

Of the estimated 3.5 million US drivers that have a commercial driver's license, nearly all Commercial Motor Vehicle (CMV) license holders are required to meet federal medical standards as a condition of employment.[177,178] Evaluation and treatment of coronary heart disease (CHD) is intended to reduce the probability of sudden death during commercial driving that can result in harm to the general public and the drivers themselves.

The National Health and Nutrition Examination Survey (NHANES 2001–2012) reported that 8–10% of those over 40 years of age have CHD (defined as having prior heart attack, angina, or diagnosis of congestive heart failure) that can predispose to sudden death events.[179] Among those who died from sudden death, the most likely etiology was ischemic coronary heart disease. Prolonged sedentary habits, infrequent structured physical activity and erratic shift-work hours and sleep schedules can lead to additional CHD risk. In addition to traditional CHD risk factors, prolonged performance of vigilant tasks to avoid adverse

consequences, such as long-haul driving, has been associated with hypertension and CHD in humans.[180,181] Although commercial driving involves variable degrees of physical activity, it mostly comprises sedentary driving where the likelihood of activity-related sudden death event is lowest.[182] However, drivers may have to exert themselves such as when changing a tire on the vehicle, securing the load, or loading or unloading cargo which will place them at higher risk of SCD during or soon after exertion.[183–185]

Commercial drivers face also additional stressors, including the need to adhere to tight schedules, long hours in a seated position, traffic congestion, poor social support, and the need to maintain courtesy despite belligerent passengers.[40,42,186,187] Increased stress has been shown to lead to catecholamine and cortisol release that increases arterial tone, myocardial excitability and contractility, and stimulates thrombus formation.[186] Environmental exposures such as excessive noise, temperature extremes, air pollution, whole body vibration, and oncoming glare routinely encountered by commercial drivers may also have detrimental effects on cardiovascular health.[38,181,188,189]

In several studies of sudden incapacity for drivers in any vehicle, arrhythmia was the most common cause although the prevalence ranged widely from 21% to 100% of cases.[117,190,191] Interestingly, early studies reported drivers who suffered arrhythmias or died suddenly on the job did not cause serious harm to the general public.[192–194] Most of the drivers were able to stop their vehicles without injury.[195] One of the potential reasons for relatively low incidence of crashes from arrhythmia or SCD is due to the length of time between the onset of the cardiovascular event and incapacitation. A typical motor vehicle crash can occur in 5 s or less. However, prior to an accident, the time required for a driver to recognize illness and slow down or stop the vehicle may take up to five to 10 seconds.[196] The arrhythmic abnormalities leading to incapacity requires a time of onset, during which blood flow to the brain is partially maintained allowing the driver to become aware that something is wrong and have time to react. In many instances, drivers can quickly identify that they are ill and have time to pull to the side of the road.[182,196] An early study of commercial drivers, 50 proven myocardial infarctions, 12 (24%) occurred during scheduled work hours but no vehicle crashes resulted.[197] More recent reports show that 20–50% of drivers experiencing a SCD stopped their vehicles with minimal injury to themselves or others.[192–195,198] One of the studies found 1/3 of drivers were able to stop the vehicle before becoming unconscious with only 6% of other people at risk in the car accident suffering minor injuries.[193] Subsequent investigations suggest that accidents in commercial vehicles can be as high as 80%[198] although mortality of either occupants of the vehicles or other drivers is rare.

5.7.1. Cardiac investigation for CAD in asymptomatic commercial drivers

CHD risk screening of commercial drivers is recommended using validated risk scores, such as the Framingham risk score[199] or the atherosclerotic cardiovascular disease (ASCVD) score (63) to initiate aggressive risk factor management or additional cardiac testing However, additional cardiac stress testing is more controversial and other testing, such as CACS, has not been reported in this population.[200,201] The United States Preventive Services Task Force (USPSTF) concluded that screening asymptomatic individuals in certain high-risk occupations, such as commercial drivers, could be recommended based on the possible benefit to public safety.[178,202] However, the USPSTF cited insufficient evidence to recommend for or against routine cardiac stress testing of asymptomatic commercial drivers with CHD risk factors.[202] The American College of Cardiology and American Heart Association Guidelines for Exercise Testing[203] similarly noted that there are insufficient data to justify routine treadmill stress testing although "evaluations are done for statutory reasons"[5] in some cases.

5.7.2. Evaluation of drivers with known CHD or prior aborted SCD

Advances in the treatment and management of CHD allow commercial drivers with known disease to return to the workforce. While the commercial driver's license does not restrict work activity, drivers need to be able to display the ability to perform reasonable exertion in order to be certified.[203] Treadmill or other cardiac stress testing evaluated the driver's ability to work at a specified level of exertion prior to returning to work without cardiac symptoms or evidence of ischemia or arrhythmia. The ability to increase exercise capacity [measured by metabolic equivalent term (MET) on the exercise test] in both employees with a history of MI and healthy individuals correlated with decreased cardiovascular disease and all-cause mortality compared to those with less robust exercise tolerance.[204] Completion of Stage II (>6 METS) of the standard Bruce treadmill protocol, equivalent to lifting heavy objects of 50 lbs or more, is considered sufficient for a commercial driver to perform job-related tasks.[205] There are little data on patients returning after an aborted SCD although in one study, of thirty-five (70%) individuals that returned to commercial driving after a SCD event, 5 probably had a second SCD, with 2 of 5 found dead at the side of the road in their trucks, 2 at service stations, and 1 while working a non-driving job.[197]

6. Summary

A review of the current occupational guidelines suggests that many organizations still rely on traditional CHD risk evaluation with or without the use of cardiac stress testing (whether exercise ECG or functional imaging). This approach runs the risk of missing important occupational CAD. The literature review performed has identified that a cardiac CT based approach to determining occupational cardiovascular risk can be valuable mainly due to the unparalleled negative predictive value a of coronary CTA. For risk assessment in individuals undertaking safety sensitive work, both CACS and coronary CTA can evaluate an employee's risk for CVD events with a high degree of accuracy. Whether CACS or coronary CTA is performed is most likely determined by the level of risk accepted by an employer and the importance of determining non-calcified CAD as part of any occupational assessment. In most cases, the presence of mild CAD alone should not trigger untoward restrictions, even in pilots with no symptoms. Instead, the identification of subclinical CAD should serve as an opportunity to control modifiable ASCVD risk factors.

In summary, the decision to pursue a test for occupational screening must weigh individual considerations against the duty to protect society at large, considering various occupational hazards and access to medical care. 'First do no harm' applies both to the patient and the population at-risk. All studies identified in the literature review demonstrated an increase in identified atherosclerosis burden correlated closely with an increased risk of SCD, therefore screening of a safety sensitive workforce seems prudent, given the increased risk of CVD and SCD, and the ample treatments (lifestyle and pharmacologic) available to mitigate the effect of disease in those at risk (Figs. 3 and 4).

7. Limitations

We recognize several limitations in our consensus document and available evidence. While we aimed to provide a comprehensive review of the literature, potential exists for missing data and publication bias. To minimize this, we reviewed multiple databases including grey literature and a recursive search of references. Our consensus document provides a review of risk assessment in various safety-sensitive occupations but is not all-inclusive of occupations that may warrant evaluation for CVD and its risk factors. We recognize that different risk applies to different professions and impact on safety to the general public, an example will be the presence of co-pilot in commercial flights and the absence of one in military flights, or the duration of the mission and distance for astronauts that does not apply to other professions. However, the authors attempted to provide a comprehensive "enhanced screening" for all these professions with as little variance possible as long as they remain active in their profession. It is not the intention of the authors, to advocate

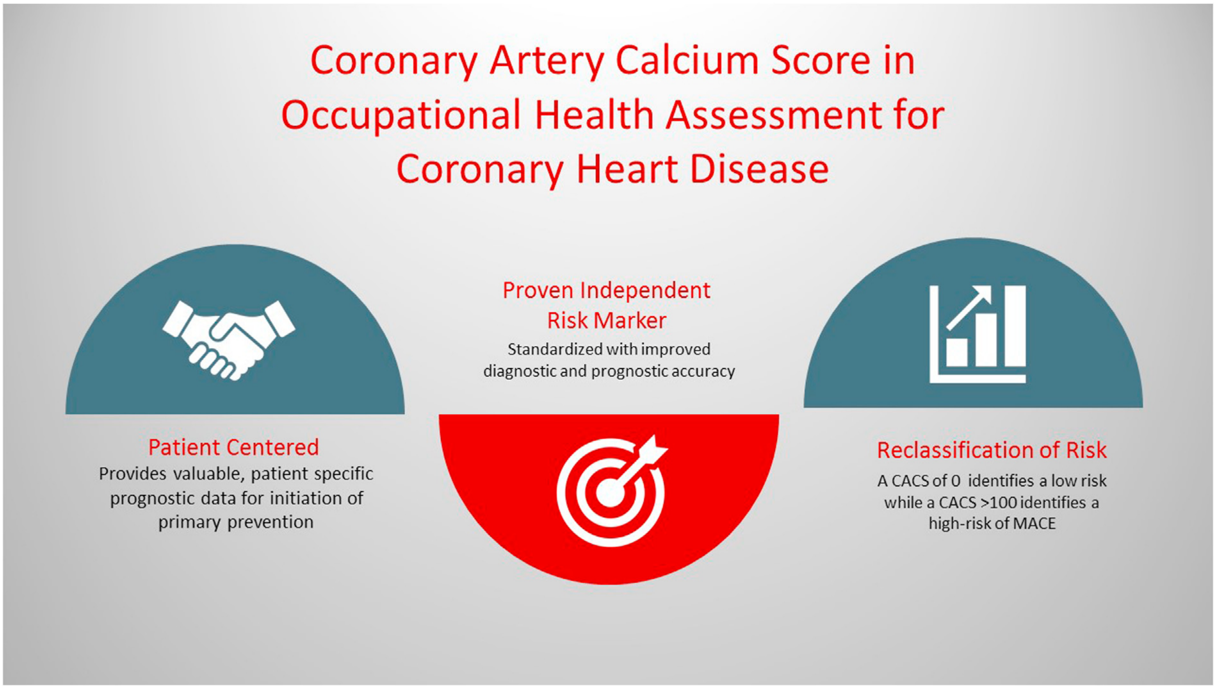

Fig. 3. Role of calcium score in occupational health assessment.

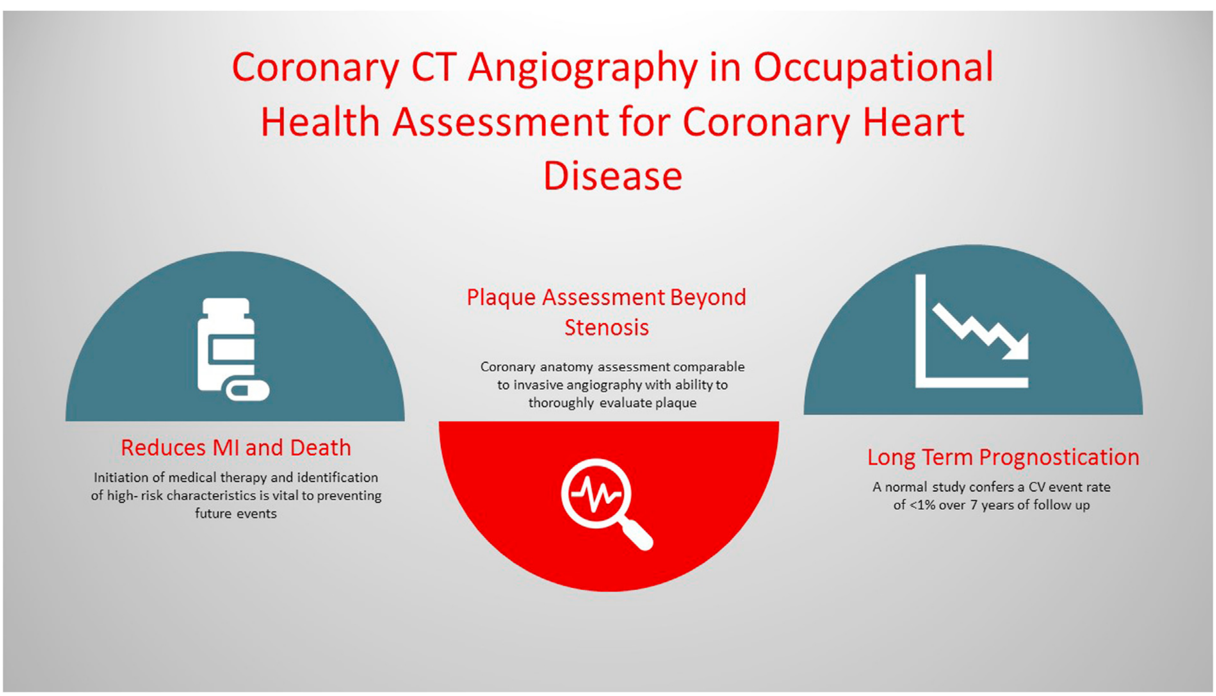

Fig. 4. Role of coronary CT in occupational health assessment.

enhanced screening to be applicable to the general population in contradiction to current national or international guidelines but rather to address the need for enhanced screening in those with high-risk occupations. Attention was given to primary ASCVD risk assessment in patients without known cardiovascular disease. Secondary risk assessment in occupation candidates with a history of known obstructive CAD, prior myocardial infarction or revascularization was not considered, as the role of CAC and CTA is more limited in these patients. Beyond the scope of this consensus document, adverse cardiac events may result from structural heart disease, physiologic responses to occupation environments, conduction disorders, arrhythmias, and adverse effects of medications.

As with existing guidelines, our consensus document is subject to author and responder bias. To minimize this, we incorporated a broad review of evidence with feedback from multiple specialties. While our consensus document provides guidance for the use of CAC testing and coronary CTA, the need for any cardiac testing remains at the discretion of occupation health providers and their regulation agencies. Variations in individual presentations are expected, and deviations from this consensus document may occur. Consequently, open communication is encouraged among providers, employers and patients to clarify any

testing requirements. Lastly, the precise role for health screening in occupation exams remains an ongoing debate, and collaboration is needed among interest groups to provide transparent criteria for occupational exams that balance individual health, patient rights and public safety.

Disclosures

The Society of Cardiovascular Computed Tomography ensures compliance with all existing standards for the declaration of conflict of interest by all authors and reviewers for the purpose of clarity and transparency. The opinions and assertions herein are those of the authors' alone, and do not represent the views of the Office of the Surgeon General, Department of Defense, or the United States Government. All authors declare no competing interests.

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Ahmad M. Slim[a,*], Emilio Fentanes[b], Michael K. Cheezum[c], Iain T. Parsons[d], Christopher Maroules[e], Billy Chen[f], Suhny Abbara[g], Kelley Branch[h], Prashant Nagpal[i], Nishant R. Shah[j], Dustin M. Thomas[c], Todd C. Villines[k], Ron Blankstein[l], Leslee J. Shaw[m], Matthew Budoff[n], Ed Nicol[o], Writing Group

[a] *Pulse Heart Institute, Tacoma, WA, USA*
[b] *Tripler Army Medical Center, Honolulu, HI, USA*
[c] *Parkview Health, Parkview Research Center, Fort Wayne, IN, USA*
[d] *King's College London, London, UK*
[e] *Naval Medical Center Portsmouth, Portsmouth, VA, USA*
[f] *Cedars-Sinai Medical Center, Baldwin Park, CA, USA*
[g] *University of Texas Southwestern Medical Center, Dallas, TX, USA*
[h] *University of Washington, Seattle, WA, USA*
[i] *University of Iowa Hospitals and Clinics, Iowa City, IA, USA*
[j] *Brown University Warren Alpert Medical School, Providence, RI, USA*
[k] *University of Virginia Health System, Charlottesville, VA, USA*
[l] *Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*
[m] *Weill Cornell School of Medicine, New York, NY, USA*
[n] *Lundquist Institute, Torrance, CA, USA*
[o] *Royal Brompton Hospital, London, UK*

* Corresponding author. Associate Professor of Medicine, University of Washington, Associate Professor of Radiology, Tulane University School of Medicine, Pulse Heart Institute, 1901 S. Cedar Street, Suite 301, Tacoma, WA, 98405, USA.

E-mail addresses: amslim@multicare.org, ahmadmslim@gmail.com (A.M. Slim).