CT Coronary Angiography vs. Coronary Artery Calcium Scoring for the Occupational Assessment of Military Aircrew

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INTRODUCTION: To ensure flight safety military aircrew undergo regular clinical and occupational assessment. Coronary artery calcium scoring (CACS) has been established as an imaging modality to noninvasively assess coronary artery disease (CAD). CT coronary angiography (CTCA) potentially offers a more accurate assessment of CAD, but has not been formally assessed in military aircrew. This retrospective cohort study is designed to compare the theoretical differences in downstream investigations and occupational outcomes in aircrew with suspected CAD comparing CTCA with existing CACS pathways.

METHOD: A 2-yr retrospective cohort study of consecutive UK military patients who underwent a CTCA and CACS was undertaken. Patient demographics, CTCA and CACS results, and initial and final occupational restrictions were analyzed comparing current UK, Canadian, and U.S. pathways.

RESULTS: There were 44 patients who underwent CACS and CTCA. The commonest indication for a CTCA was a positive exercise ECG. Increasing CACS, stenosis severity, and stenosis burden were associated with significantly greater likelihood of occupational restriction ($P = < 0.01$). Following CTCA, 26/44 (59%) patients were found to have evidence of CAD, with 13/44 (30%) having at least a single vessel stenosis ≥50%. All of these patients had subsequent occupational restrictions. Two patients with a calcium score ≤10 had at least 1 single vessel stenosis ≥50%.

DISCUSSION: A CTCA pathway is potentially a better discriminator of CAD burden in aircrew when compared with CACS and may reduce downstream testing, allowing a more efficacious approach to CAD assessment in military aircrew.

KEYWORDS: CT coronary angiography, coronary artery calcium scoring, occupational medicine, aviation medicine.

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In the UK military, coronary artery disease (CAD) remains the most common cause of cardiovascular medical discharge from service[5,20] and has been a common presentation during recent operational deployments.[6] Accurate occupational assessment of Armed Forces personnel is required to protect personnel from the demanding nature of the military environment. Specifically, military aircrew require a high degree of physical health to withstand the rigors of flying potentially high performance aircraft as well as undertaking their activities in hostile operational environments. Military aircrew includes all personnel with duties concerned with the flying or operation of an aircraft, or with the care of passengers or cargo in flight.[21] This comprises pilots, navigators and weapons systems operators, air traffic control officers, battle space managers, observers, remotely piloted aircraft system operators, and aeromedical evacuation personnel. CAD often serves as a bar to flying duties in aviation due to the myocardial oxygen demands in a hypobaric, hypoxic environment, and on suspicion of CAD aircrew are usually immediately grounded pending further investigation.[16,20] In exceptional circumstances aircrew may return to restricted flying duties if their disease is minor, or successful revascularization has occurred, and there is no significant residual cardiac dysfunction.

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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.[4,13] However, more recently CT coronary angiography (CTCA) has emerged as the imaging modality of choice to noninvasively assess coronary artery anatomy with high spatial and temporal resolution.[2,23] CTCA can be combined with CACS[23] to identify and quantify calcified coronary artery plaques, which, when combined with age and gender normalized CACS centiles, can provide both detailed coronary assessment and prognostic information about future cardiovascular events.[1,9] In the UK, CTCA has been used in the assessment of aircrew both for initial assessment of suspected CAD and to monitor disease progression when established CAD is identified. The aim of this paper was to review the occupational outcomes of military aircrew who underwent a CTCA and CACS in the United Kingdom, assess if a CTCA based approach more accurately predicts occupationally relevant CAD when compared with CACS, and compare downstream testing requirements required to reach an unequivocal CAD diagnosis using each approach.

METHODS

A retrospective review of all military aircrew who underwent a CTCA and CACS under the care of two Royal Air Force (RAF) consultant cardiologists over a 2-yr period was undertaken. Patient demographics, referral indication, Agatston unit calcium score, calcium score centile (corrected for age and gender), and stenosis burden were analyzed and extant CTCA and CACS pathways compared with regards to both downstream testing and the occupational disposition of those referred. Referral indications were classified as ≥2 risk factors for CAD, previous abnormal ECG, physiological or symptomatic presentation on exercise or cardiac stress imaging indicating possible CAD, chest pain, any dysrhythmia on Holter monitor, or any abnormality on resting ECG consistent with CAD. The initial and final occupational grade were expressed as no restriction, partial restriction (for instance unfit solo flying/controlling), and grounded.

All CTCA were performed using at least a 64-detector row scanner and reported by a Society of Cardiovascular Computed Tomography Level 3 accredited cardiac radiologist or cardiologist. The dose length product (DLP) for the CTCA and CACS were recorded. Clinically, flow-limiting CAD is commonly defined as luminal stenosis ≥50% in the left main stem or >70% in one or more major epicardial vessel.[19] However, due to the environmental and occupational demands of flying, potential flow limiting disease requiring immediate occupational restriction in this cohort is defined as ≥50% in any major coronary artery.[16] This is coherent with the UK Civil Aviation Authority medical standards that quote "there should be no stenosis more than 50% in any major untreated vessel, in any vein or artery graft or at the site of an angioplasty/stent, except in a vessel subtending a myocardial infarction."[3] In CTCA the degree of stenosis is often reported as a range. As CTCA overpredicts the degree of stenosis, the lower point of the reported range was used. To assess if a CTCA based approach more accurately predicted occupationally significant CAD than a CACS approach, the initial occupational outcome was compared using a binary correlation of single vessel stenosis of at least 50% on CTCA compared with an Agatston calcium score of >10 on CACS. Data on confirmatory invasive angiography was not collected in this study, but was performed where considered desirable at the discretion of the referring cardiologist.

Data was expressed as mean (standard deviation) if normally distributed, otherwise as median (interquartile range). The independent Student's *t*-test was used to compare the means of two independent, normally distributed data sets. The Chi-squared test, or Fisher's exact test where appropriate, were used to compare categorical variables. All statistical analysis was carried out using Stata Data Analysis and Statistical Software (StataCorp LP, College Station, TX). A two-tailed $P \leq 0.05$ was considered statistically significant. Due to the retrospective nature of the study, informed consent was not sought.

RESULTS

Over 2 yr, 44 aircrew referred to the two RAF cardiologists underwent a CACS and CTCA for suspected CAD. Full demographic details are shown in **Table I**. The cohort had a median age of 49 yr (range 24–69 yr), were predominantly men ($N = 43$ /44, 98%), and from the RAF ($N = 36$/44, 82%). The largest occupational group were pilots ($N = 23$/44, 53%) (Table I) and included multiengine, fast jet, rotary, and remotely piloted aircraft system operators. Air space managers were mainly air traffic controllers and battle space managers. Medical services personnel had aeromedical evacuation roles. The commonest primary indication was a positive exercise ECG [known as an exercise tolerance test in the UK] ($N = 15$/44, 34%); however, one-third of patients ($N = 15$/44, 34%) had more than one indication for referral.

Calcium scores were positively skewed with a median score of 1 (0 to 176) (Table I). Overall 21/44 (48%) patients had a calcium score of 0, indicating no evidence of calcified coronary artery disease. However, 3/21 (14%) of these patients subsequently had noncalcified disease of the left anterior descending (LAD) on CTCA. Patients with a positive (nonzero) score were significantly older than those with a CACS of 0 [54.0 (9.9) vs. 43.6 (8.9) years; $P < 0.001$].

Following CTCA 26/44 patients (59%) were found to have evidence of coronary artery plaques. Overall 13 patients (30%) had evidence of coronary artery disease warranting immediate occupational restriction (stenosis in a single vessel ≥50%), including all 4 patients whom had CACS scores >400 (Table I). One patient had disease affecting the left main stem, LAD, left circumflex artery, and right coronary artery (RCA), with 9/44 patients (35%) having evidence of triple vessel disease affecting the LAD, RCA, and left circumflex artery. One patient had evidence of positive remodelling in the RCA, a risk factor for

Table I. Flying Restriction Following CTCA.

VARIABLE & SUBVARIABLE	TOTAL (*N*)	FLYING RESTRICTION	NO FLYING RESTRICTION	*P*-VALUE
Occupation				
Pilot	23	11	12	0.03
Rear-Crew	7	7	0	
Air Space Manager	6	5	1	
Navigator	4	2	2	
Medical Services	2	0	2	
Air Engineer	2	2	0	
Indication				
Positive ETT*/stress test	15	8	7	0.89
Dysrhythmias/Abnormal resting ECG**	14	9	5	
Chest pain	8	4	4	
Previous abnormal imaging	4	3	1	
Risk Factors for CAD***	3	2	1	
Calcium score				
0	21	7	14	0.03
0–10	5	2	3	
10–100	6	3	3	
100–400	8	7	1	
>400	4	4	0	
Centile for age and Gender				
0	21	7	14	<0.01
0–25	0	0	0	
26–50	3	0	3	
51–75	6	3	3	
76–100	14	13	1	
CAD severity				
3 vessel disease	9	8	1	<0.01
1–49% in any one vessel	13	5	8	
≥50% in any one vessel	13	13	0	
Flow limiting disease	3	3	0	
Total Stenosis Burden				
0	18	5	13	<0.01
0–29	7	2	5	
30–75	11	8	3	
76–124	4	4	0	
>125	4	4	0	

* ETT (exercise tolerance test or exercise test); **ECG (electrocardiogram); ***CAD (coronary artery disease).

acute coronary syndrome. A further patient had complete RCA obstruction.

Comparing CACS of >10 and CTCA of ≥50% stenosis in at least a single vessel (**Fig. 1**), two patients (N = 2/44, 5%) who had no coronary calcification (and would have no flying restriction imposed if using a CACS-only approach) were found to have stenosis ≥50% on CTCA, including one patient with a critical LAD stenosis (Fig. 1 and **Fig. 2**). Both patients were immediately grounded with a final unfit solo flying limitation following revascularization and acceptable subsequent functional imaging. Conversely, seven patients with calcium scores >10 (range 15–217) had no demonstrable luminal stenosis ≥50% on CTCA (Fig. 2). Ultimately, 4/7 of these patients continued with no flying restrictions (including the patient with a calcium score of 217); one was made "unfit solo flying" and the remaining two were grounded. The three patients with a calcium score >10 on CACS but a stenosis <50% on CTCA who received a flying restriction received it for reasons unrelated to their CAD. We found four patients with a total stenosis burden or aggregate stenosis >125% (the sum of all stenosis), all of which had at least one coronary artery lesion ≥50%.

The median DLP for the CTCA was 108 mGy-cm (interquartile range 60–256 mGy-cm). The median DLP for the CACS was 41 mGy-cm (interquartile range: 31–50 mGy-cm). The median total DLP was 182 mGy-cm (interquartile: 120–301 mGy-cm). Using a standard thoracic conversion factor of 0.017, this equates to 1.8 mSv for the CTCA and 0.7 mSv for the CACS.

CTCA demonstrated no evidence of CAD (calcium score of 0 and no luminal narrowing) in 18 (N = 18/44, 41%) patients. Of these, 13 (72%) returned to full unrestricted flying duties, with the remainder (N = 5, 28%) being restricted due to structural heart disease, arrhythmia, or medical comorbidities unrelated to CAD. In 13 aircrew there was evidence of occupationally acceptable CAD (stenosis <50% on CTCA) and, of these, 8 (62%) returned to unrestricted duties, with the remaining 5 (38%) restricted for reasons other than CAD. All remaining aircrew (N = 13/44, 31%) with a stenosis ≥50% in any vessel were initially grounded, although 9 (71%) were able to return to work following further investigation or treatment.

There was no significant difference in age, gender, service, rank, or CTCA indication between those initially downgraded occupationally and those who returned to unrestricted duties. However, occupation (P = 0.03), calcium score (P = 0.03), CACS centile (P < 0.01), and the presence of flow-limiting disease on CTCA (P < 0.01) all affected likelihood of occupational restriction (Table I).

In 10 patients (N = 10/44, 23%), occupational restrictions resulted from noncoronary pathology; 5 presented with arrhythmias (2 atrial fibrillation, 1 ventricular tachycardia, 1 Mobitz type 2 heart block), 2 had underlying structural heart disease (1 cardiomyopathy, 1 LV aneurysm), and 3 had occupational restrictions for noncardiological conditions. One patient had nonflow limiting disease on his initial CTCA; however, a follow-up scan 1 yr later demonstrated significant progression of the disease, resulting in occupational restriction. While the intention of this review was to assess for CAD, other anomalies were seen in four patients (9%), including a nonsuspicious lung

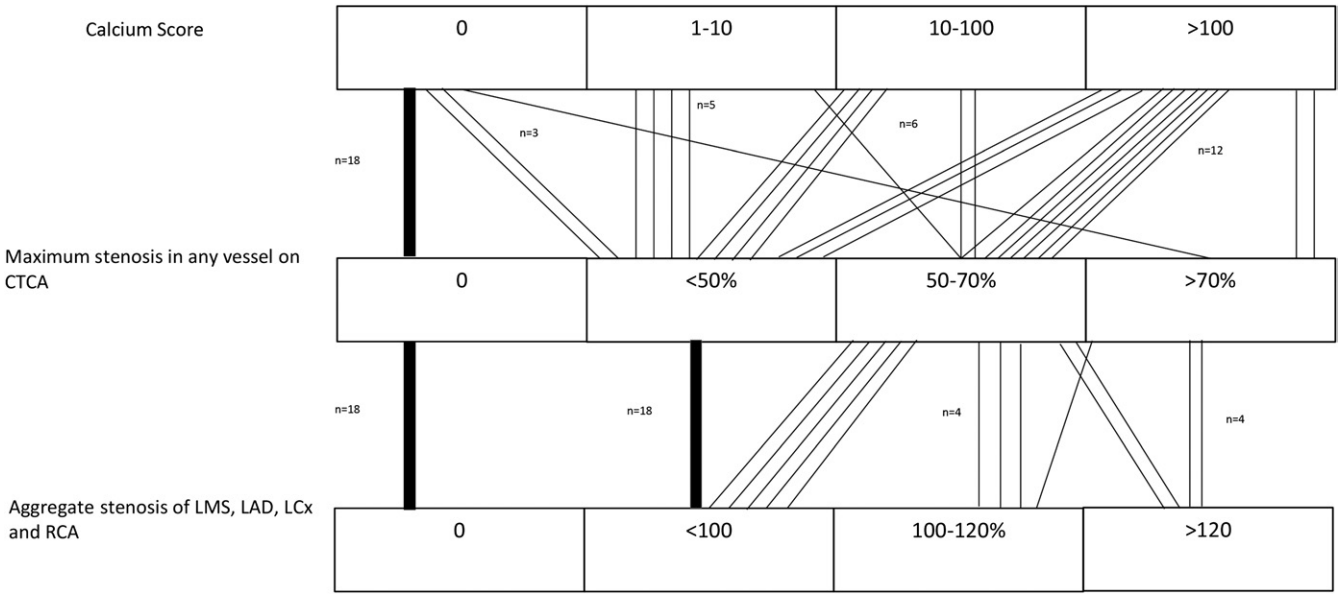

Fig. 1. Figure comparing CT calcium score, CT coronary angiography maximal stenosis, and aggregate stenosis.

nodule, a basal LV aneurysm, an insignificant distal LAD muscle bridge, and an anomalous RCA origin.

DISCUSSION

CTCA is known to reliably rule out significant CAD in patients with a low or intermediate risk of CAD[14] and has a consistently high negative predictive value.[15,17] Additionally, CTCA can ascertain the presence of anomalous coronary arteries, a known common cause of nontraumatic mortality in military service.[4,20] CTCA, with or without a separate calcium scan, has the potential to be used as a single noninvasive test to assess aircrew with suspected CAD.

Although the overall cohort investigated in this study is small, there is potentially a large economic benefit in reliably excluding coronary disease in these patients. Military aircrew costs millions of dollars to train[18] and rapid assessment to appropriately ground, restrict, or return to operational flying duties is cost effective.[21] In this cohort, of the 23 pilots assessed, over half (12/23, 52%) returned to unrestricted flying duties following a single CTCA.

In addition to crude stenosis assessment, several studies have demonstrated the potential role of CTCA in characterizing atherosclerotic coronary plaque composition and identifying high-risk, vulnerable plaques that are more prone to rupture and adverse future events.[25] Previous studies have reported no significant differences between CTCA and invasive intravascular ultrasound in detecting plaque types.[7] Vulnerable plaque types on CTCA include those associated with outward "Glagov" remodeling, those with spotty calcification, and noncalcified (low attenuation) plaques, including those with 'napkin ring' like features.[25] These plaque types are associated with an increased risk of acute coronary syndrome and cannot be identified using calcium scoring. Even in this small study population, we identified eight patients (18%) with adverse plaque morphology, of which only four had ≥50% stenoses. Recent evidence would also suggest that calculating accurate calcium scores from a CTCA dataset is both technically feasible and reproducible.[22]

We found that absolute CACS, CACS centile corrected for age and gender, stenosis severity, and total stenosis burden were all significantly correlated with occupational outcome, with, however, significant differences in those who were identified as having "true" significant disease from an aviation standpoint. The U.S. Airforce currently screen their aircrew based upon age and risk factors. If the calculated 10-yr event risk is >7.5%, they proceed to CACS. If the CACS is <10 the patient can be returned to full duties.[4] With a CACS of 11–399, the patient is referred for functional imaging, while those >400 are referred for anatomical imaging (which can be either invasive coronary angiography or CTCA).

We believe there to be several potential pitfalls with this approach. Firstly, while a low calcium score has been shown to have good prognostic outcome in population-based studies,[11,12] several multicenter CTCA studies have demonstrated between 7–20% of patients with a CACS = 0 had at least one stenosis of ≥50% at invasive angiography.[8,24] To highlight this further, in a study assessing the prevalence and severity of CAD among 10,037 symptomatic patients with a CACS = 0 who underwent CTCA, 84% had no CAD and 13% had nonobstructive lesions, with 3.5% having ≥50% stenosis and 1.4% having ≥70% stenosis. Of the 50% stenosis group, 3.9% experienced a cardiac event compared with 0.8% of patients with a CAC score of 0 and no obstructive CAD over a median follow-up of 2.1 yr. Furthermore CACS did not add incremental prognostic information to CTCA.[26] This has clear flight safety ramifications in aircrew and even in our small cohort we identified two patients with calcium scores of 0 and 1, respectively, who had occupationally important disease, one of whom had a subtotal occlusion of his LAD (Fig. 2).

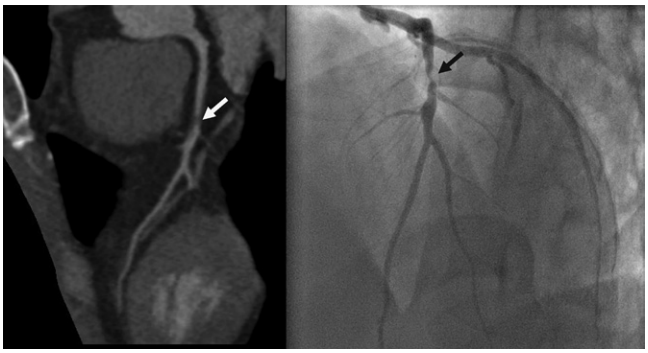

Fig. 2. CT coronary angiography of a pilot with significant LAD stenosis, but a calcium score of 0, confirmed by invasive angiography (see arrows).

Secondly, we believe a high calcium score (used at the prescribed U.S. and Canadian Air Force cut-offs) may not be the best discriminator for significant disease in aircrew. We identified seven patients who had a calcium score of 11–399 who had no single vessel stenosis ≥50% on CTCA and in whom no further investigation was required to exclude occupationally important CAD. Under U.S. and Canadian Air Force guidelines, these patients would have had downstream tests required for a further waiver that would not be necessary using a CTCA pathway.

Thirdly, we would challenge the use of CTCA in patients with a CACS >300. It is well known that increasing levels of calcification reduce the diagnostic accuracy of CTCA. This is due to the 'blooming' artifact of the calcified plaque, leading to overestimating the perceived luminal obstruction on CTCA.[10,15] In our cohort all four aircrew who had a calcium score >400 had at least a single vessel stenosis ≥50% on CTCA and were consequently all initially excluded from flying duties. Subsequently all underwent a functional test and invasive angiography. Of these, three patients had no evidence of ischemia and the stenotic burden was overestimated on CTCA.

Undoubtedly, the radiation dose for a CTCA is greater than a CACS. In this study, our median dose length products were 108 mGy-cm to 41 mGy-cm, respectively. In performing both the median dose was 182 mGy-cm. Recent studies have proposed and validated algorithms to calculate the calcium score from the CTCA,[23] thus giving a vastly greater amount of anatomical information for a still modest dose length product.

This is a small, single-country study of a highly selected group of aircrew undergoing investigation of suspected CAD. It is subject to the usual bias associated with small studies and, as a result, bold statements cannot be made based on this data. However, it does offer some insight into the potential role of this technique in the investigation of CAD in aircrew.

The undeniable benefit of CTCA is its negative predictive value. The spatial resolution of CTCA is limited when compared to invasive angiography (0.3 mm^2 vs. 0.1 mm^2), so the same apparent stenosis may in fact not be equal. This is important when applying predetermined cut-offs for occupation restriction. However, a 50% cut-off using CTCA does appear to have a sensitivity that is appropriate in a population using the 1% rule.[24] Further, large-scale studies are required to confirm or refute the findings of this small pilot cohort study.

This small aircrew cohort study would suggest that a CTCA pathway may be superior to a CACS pathway in efficiently ruling in/out occupationally significant CAD and CTCA may reduce the requirement for downstream testing when compared to a CACS pathway. CTCA allows a single anatomical risk assessment and even with its limited spatial resolution appears to support appropriate restriction or return to full duties for aircrew. We would argue that functional imaging should be used to identify ischemia in patients who could be candidates for revascularization while aircrew at high risk should proceed directly to coronary angiography, as with other patients. CTCA is a rapidly evolving noninvasive modality to assess calcium burden, absolute stenosis, atheroma burden, and high-risk plaque characteristics, all of which could be used to accurately risk-stratify aircrew.

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