



## Short Communication

# Computer tomography coronary angiography as an alternative to invasive coronary angiography in the assessment of coronary artery disease in aircrew

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## ABSTRACT

Cardiac risk evaluation during the medical fitness of aircrew is stringent due to the strenuous nature of their employment. Cardiac risk assessment by various risk scoring tools, coronary artery calcium score, stress tests, and more recently computerized tomography coronary angiography (CTCA) have been employed to objectively assess, predict, and prevent catastrophic cardiac events. Here, we explore the potential use of CTCA in place of invasive coronary angiography for assessment of coronary artery disease in aircrew. With the advancement of hardware and software, the CTCA is able to not only define the luminal occlusion but also its functional significance and pathological state in the surrounding vessel wall. This could thereby avoid invasive procedures and the complications associated with them.

**Keywords:** Aircrew, Computer tomographic coronary angiography, Invasive coronary angiography

## INTRODUCTION

Medical fitness of aircrew is stringent not only due to the strenuous nature of their employment but also the acute incapacitation an illness can cause, leading to compromise of flight safety. Cardiac evaluation is of maximal concern given the acuteness and catastrophic implications of acute coronary syndromes in flight.

A cardiac risk assessment by various risk scoring tools, coronary artery calcium score (CACs), stress tests, and, more recently, computed tomography coronary angiography (CTCA) have been employed to assess, predict, and prevent catastrophic cardiac events objectively. Other tools to assess coronary artery disease (CAD) risk and monitoring include ankle-brachial index, B-mode ultrasound carotid intima-media thickness, B-type natriuretic peptide levels, and magnetic resonance imaging (MRI). However, the objectivity of these tests to effectively rule out significant CAD necessary for fitness to fly precludes their widespread use.

Here, we explore the potential use of CTCA in place of invasive coronary angiography (ICA) in the assessment of CAD in aircrew.

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## CTCA IN ASYMPTOMATIC AIRCREW WITH ECG FINDINGS SUGGESTIVE OF IHD DURING ROUTINE EXAMINATION

This category of aircrew will necessitate coronary imaging to exclude significant CAD. "Significant" CAD is defined in the Aeronautical Information Service of India<sup>[1]</sup> as 50% stenosis of epicardial vessels on ICA and shall also be utilized as the benchmark percentage stenosis with CTCA.

Cardiac risk-scoring tools have been developed, but they have been validated only on local populations where they were created. Hence, their use is speculative in our population.<sup>[2]</sup> It would also entail the crew being started on medication and restrictions in flying without credible evidence of significant obstructive heart disease.<sup>[3]</sup> Hence, more definitive and objective evidence of CAD is mandatory before laying restrictions on flying.

CACS is independent and significantly better for prediction of future cardiovascular events in comparison to traditional risk factors and risk predictive models. This quality can be used to estimate the risk of CAD and, if necessary, do an ICA. However, it is more useful in the "late ages" and has a higher sensitivity than specificity in those ages. The higher false negatives in younger ages and females could miss a few individuals warranting further investigation and treatment.<sup>[4]</sup> Thus, it too is inappropriate in the fitness estimation of aircrew.

CTCA has emerged as an acceptable modality for the purpose of assessment of coronary artery anatomy. This includes anomalous origin and course, atherosclerotic coronary occlusions, and graft anatomy after post-coronary artery bypass graft. CTCA offers the only non-invasive method of visualizing the coronary artery anatomy, unlike intravascular ultrasound, or optical coherence tomography which are the reference gold standards but require ICA.<sup>[5]</sup>

It is well known that lesions which are culprits in acute coronary syndromes are not always severely stenotic, thus requiring tools to assess the vessel wall along with the luminal stenosis. Plaque morphology, lipid and calcium content, necrotic core, and inflammatory states determine their propensity to rupture. Assessment of the coronary arteries thus requires not just the visual severity assessment of the stenosis but also determination of coronary plaque composition, as this contributes to plaque vulnerability.

Thin-capped fibroatheromas are known to be "vulnerable" to rupture, and CTCA can detect these pathological changes. These include the phenomenon of positive remodeling (an increase in vessel diameter at the plaque site in comparison to the proximal segment which appears normal), low attenuation plaques (<30 Hounsfield units), spotty calcification (calcification <3 mm), and the "napkin-ring sign" thereby being predictive of future acute coronary

syndromes. Of these, the burden of low attenuation plaques (<30 Hounsfield units) is superior to both CACS and stenosis severity as this independently predicts future fatal and non-fatal myocardial infarction mostly effectively. Typically, these thin-capped fibroatheromas have little to minimal calcium and, thus, are missed by a pure calcium score screening study or a "coronary luminogram" by conventional ICA.

The presence of vulnerable plaques is a more important predictor of coronary events in the young and women; thus, the false negatives of CACS and ICA could be detected earlier and adequate primary preventive measures instituted.<sup>[6]</sup>

CTCA-enabled virtual histology analytical software has been validated with pathological studies and, thus, could further add to the predictability of CTCA in the detection and prognosis of CAD.<sup>[7-9]</sup>

A CACS is a non-contrast study and is done as a screening modality as a "stand-alone" investigation. On the contrary, CTCA is a procedurally separate investigation using contrast and hence in routine practice not clubbed with a CACS study. Thus, though a CACS is a good screening mode, a CTCA is far more informative and specific for coronary artery anatomy, especially in the subgroup of aircrew where luminal and vessel wall anatomy needs delineation. That is, a CACS adds little to a CTCA. Moreover, there are now artificial intelligence-based programs that produce virtual non-contrast scans, thus eliminating the need for additional radiation associated with the non-contrast computed tomography (CT) imaging for CACS and CTCA if both the procedures were to be combined.

CTCA has been accepted as a suitable non-invasive tool for detection and estimation of atherosclerotic CAD in patients who are symptomatic and have a low to intermediate pre-test probability or ambiguous stress imaging test results.<sup>[10]</sup>

The DISCHARGE trial revealed that when patients present with stable chest pain and have intermediate pre-test probability of CAD are referred for ICA, the risks of adverse cardiovascular events such as myocardial infarction, TIA, stroke, or death were similar when a CTCA was performed instead of ICA. Even the major procedure-related complications such as bleeding and iatrogenic coronary dissection were lower in the CTCA group compared to the ICA group.<sup>[11]</sup> Of note, however, is that the scans were done on 64-slice or higher technology CT scan machines with standardized protocols.

Another distinct advantage of use of CTCA in comparison to other non-invasive imaging modalities is the capability to derive a measure of atherosclerotic burden right throughout the coronary vascular tree. A variety of scores of semi-quantitative nature such as "Segment Involved Score" (SIS), and CT-adapted Leaman score have been developed to quantify the total coronary plaque burden into a single figure.<sup>[12]</sup> SIS has been robustly validated by meta-analysis and

can independently and reliably predict the extent of disease and cardiovascular mortality.<sup>[13]</sup> The recently published Coronary CT Angiography Evaluation for clinical Outcomes: An International Multicenter Registry showed that a SIS of more than 5 was a better prognostic marker for major adverse cardiac events than conventional cardiovascular risk factors such as hypertension and diabetes.<sup>[14,15]</sup>

CT scan can further complement coronary imaging by hemodynamically assessing the significance of a lesion by CT fractional flow reserve (CTFFR)<sup>[16]</sup> and CT perfusion (CTP). CTFFR applies computational fluid dynamics and physiological models of hyperemia and generates an estimate of the ICA fractional flow reserve (FFR), the diagnostic accuracy of which has been objectively validated.<sup>[17]</sup> The correlation between ICA FFR and CTFFR was good. CTFFR was significantly superior in comparison to CTCA alone in identifying hemodynamically significant lesions in CAD.

The Prospective Longitudinal Trial of FFRct: Outcome and Resource IMpacts study<sup>[17]</sup> showed a 61% reduction in the diagnosis of non-obstructive CAD, thereby leading to fewer ICA and associated reduction in costs.

CTFFR has a major advantage over other non-invasive tests in that it provides accurate assessment both anatomical and functional without the need for additional stress imaging or radiation exposure. However, it is dependent on the image quality, which may give unreliable results.

### RECOMMENDATIONS FOR CTCA FOR THE EVALUATION OF NATIVE CORONARY ARTERIES FOR THE EVALUATION OF CORONARY LESIONS IN ASYMPTOMATIC OR SYMPTOMATIC AIRCREW

1. CCTA is an appropriate first-line investigation in asymptomatic aircrew with no previously known CAD or high risk of CAD to assess the presence of significant disease.
2. CCTA is an appropriate first-line investigation in symptomatic aircrew with atypical/typical angina or angina equivalents.
3. CCTA is an appropriate evaluation tool for CAD after inconclusive functional testing.
4. The CTCA has to be performed on a contemporary CT machine not less than 64-slice accusation with an adequate software.
5. Evaluation of the entire coronary circulation for atherosclerotic burden and semi-quantify the risk of CAD events in the future.
6. The radiologist must strive to do CTFFR for assessing the functional assessment of the lesions seen on CTCA.

### CTCA IN AIRCREW AFTER PERCUTANEOUS

## CORONARY INTERVENTION

In symptomatic or asymptomatic aircrew after coronary revascularization, functional non-invasive tests such as the treadmill test, stress echocardiography, or perfusion MRI are recommended to ascertain any residual or new ischemic burden, the sensitivity and specificity of which vary around 45–94% and 61–95%, respectively.<sup>[2,3,10]</sup>

Objective assessment for coronary stenosis is still done by ICA.

CTCA so far has not been advocated in clinical practice for aircrew with coronary stents because stents can decrease the diagnostic efficacy of CTCA. The factors known to do so include motion and beam hardening artifacts, calcific plaques that limit lumen visualization, and volume averaging related to stent struts. Stent sizes <3 mm, and strut thickness >100 µ, bifurcation stents, heart rates >65/min, and presence of calcific coronary plaques in the adjacent non-stented segments were associated with reduced diagnostic accuracy.<sup>[18]</sup>

The diagnostic accuracy of coronary CTA for stent imaging has significantly improved with advances in CT technology. Specifically, these include improvements in scanner and detector coverage and temporal resolution, the evolution of model-based iterative reconstruction algorithms, improved imaging protocols, and very thin slice reconstruction.<sup>[18]</sup> Thus, the reliability of contemporary CTCA in assessing proximal coronary arteries (especially more than 3 mm diameter), with a well-controlled heart rate, has significantly improved. Further, the current generation drug-eluting stents have struts <100 µm, thereby decreasing the volume rendering and distortion of luminal visualization.

Over the past decade, there has been a remarkable improvement in the temporal and spatial resolution of CTCA due to the advances in software and the utilization of CT scanners with 64-slice to 2x128-slice capability. Third-generation state-of-the-art dual source multi-detector scanners using mono-energetic reconstructions >130 keV are increasingly being used. The addition of reliable functional assessment with CTFFR and CTP study protocols further adds to the physiological significance of the lesions.<sup>[19]</sup>

This has not only increased the sensitivity and specificity for detecting high-grade in-stent stenosis from 90% to over 95% but also raised the negative predictive value to near 100%. This diagnostic accuracy was significantly higher in stents with diameters ≥ 3.0 mm, despite a high coronary calcium score (Agatston score >2000), and independent of the heart rate or body habitus.<sup>[20]</sup>

In a recent feasibility study for detecting in-stent restenosis (ISR) in symptomatic patients using third-generation dual-source CTCA, ISR (>50% narrowing) could be ruled out in two-thirds of patients, signifying its excellent negative

predictive value and a false-negative rate of <1%. The inconclusive findings or false-positive rate or was 25%, necessitating an ICA to objectively assess the stenosis objectively. This was especially seen in patients with higher body mass index (BMI), multiple stents, or stent sizes of <2.5 mm.<sup>[21]</sup> ISR >50%, or cases with any ambiguity were also referred for ICA.

Thus, CTCA is a valuable tool for safely excluding ISR and helping avoid invasive diagnostic procedures.

CTCA not only assists in the detection of “stent failure” but also in diagnosing its cause. Stent failure is predominantly due to ISR and thrombosis, with in-stent neo-atherosclerosis (NA), neointimal hyperplasia, stent fracture, and under-expansion being the common causes of these. All these pathophysiological mechanisms, especially NA, can be accurately diagnosed on high-resolution CT scans, thus helping in tailoring the treatment strategy.

There is a close association between the development of NA inside stents causing ISR and the progression of atherosclerotic CAD in native coronary arteries, indicating a common pathophysiological mechanism.<sup>[22]</sup> CCTA can be a useful tool for detecting this progression of disease and changes in medical management strategies and restrictions on flying.

The other advantages of CTCA (as discussed in the section dealing with asymptomatic ECG abnormality in flight crew) are also applicable to flight crew being evaluated after a stenting procedure to the coronary arteries. These include assessment of overall plaque morphology, lipid and calcium content, necrotic core, and estimate of total burden of atherosclerosis throughout the coronary tree and hemodynamic significance of a lesion by CTFFR and CTP.

#### **RECOMMENDATIONS FOR CTCA FOR THE EVALUATION OF NATIVE CORONARY ARTERIES FOR THE EVALUATION OF CORONARY LESIONS AFTER PERCUTANEOUS CORONARY INTERVENTIONS (POST-STENTING) IN ASYMPTOMATIC OR SYMPTOMATIC AIRCREW**

1. CTCA is appropriate for evaluation of the stent patency and coronary anatomy in asymptomatic or symptomatic aircrew 9 months after the revascularization.
2. The CTCA has to be performed on a contemporary CT machine not <64-slice accusation with an adequate software.
3. Any ambiguity on CTCA assessment must be confirmed by an ICA. This lies at the discretion of the assessing cardiologist.
4. Evaluation of the entire coronary circulation for any additional lesions, pathology of the lesion, and atherosclerotic burden.

5. The radiologist must strive to do CTFFR for assessing the functional assessment of the stent.

#### **CTCA IN AIR CREW POST-CABG**

ICA is mandatory in assessing the graft and native coronary artery status before being re-flighted. ICA involves increased catheter manipulation, higher contrast use, and radiation exposure, increasing peri-procedural morbidity. CTCA is highly accurate for detection of stenosis in bypass grafts without necessitating an arterial puncture, potential graft injury, stroke and lesser contrast and radiation exposure. It has sensitivity, specificity, positive, and negative predictive values of 97%, 97%, 99%, and 93%, respectively, thus ascertaining its usefulness in these patients. Moreover, the lesser motion of the grafts enables adequate imaging even in patients with higher BMI, or higher or irregular heart rates with low-dose contrast techniques.<sup>[23]</sup> Simultaneous to the graft vessel assessment, the distal run-off in the native vessels and their patency can also be defined reliably. Furthermore, post-surgical complications such as sternal dehiscence, osteomyelitis, and abscess can be accurately detected by CTCA, thereby enabling precise diagnosis and management of these cases.<sup>[24]</sup>

If the primary goal of the study is graft patency, then coronary CTA is an appropriate and well-validated investigation. When assessment of the condition of native coronary arteries is the clinical question, then it is crucial that careful attention is paid to image acquisition and optimal image quality using CTA is ensured. Although the CT image distortion by coronary stents is absent, the presence of coronary artery calcium and the placement of surgical clips can cause artifacts and ambiguity in vascular patency assessment. Functional testing by CTFFR and CTP should be considered in such situations to aid in the overall estimation of significance of the lesion hemodynamically. Furthermore, CT imaging is very helpful in planning for CABG, especially during repeat procedures where retrosternal adhesions and the location of the LIMA is crucial for safe outcomes.<sup>[23,24]</sup>

#### **RECOMMENDATIONS FOR CTCA FOR THE EVALUATION OF GRAFTS/NATIVE CORONARY ARTERIES FOR THE EVALUATION OF CORONARY LESIONS AFTER CABG IN ASYMPTOMATIC OR SYMPTOMATIC AIRCREW**

1. CTCA is accurate in the evaluation of graft patency and coronary anatomy in asymptomatic or symptomatic aircrew 12 months after the revascularization.
2. The CTCA has to be performed on a contemporary CT machine not <64-slice accusation with an adequate software.

3. Any ambiguity on CTCA assessment must be confirmed by an ICA. This lies at the discretion of the assessing cardiologist.
4. Screening for post-CABG complications involving the mediastinum, sternum, and lungs must be commented on by the radiologist.
5. Evaluation of the entire coronary circulation for any additional lesions, pathology of the lesion, and atherosclerotic burden.
6. The radiologist must strive to do CTFRR for assessing the functional assessment of the stent.

## LIMITATIONS

The limiting factors for CTCA are diagnostic inaccuracies due to:

1. Irregular or fast heart rates.
2. Very high BMI
3. Presence of coronary arteries with extensive calcium
4. Radiation.

The Society of Cardiovascular Computer Tomography (SCCT) recommends that a minimum 64-slice CT scanner with dual-head power injectors be used for CTCA, and the images be stored in the DICOM format for universal access.<sup>[4]</sup> This assists in the temporal and spatial resolution of the coronary anatomy, with easy comparison and analysis, especially in aircrew with fast or irregular heart rates, high BMI, and presence of coronary artery calcium. Various new tools like “subtraction CCTA” and the use of sharp or medium-sharp convolution kernels are being developed to make scanners more accurate for visualizing the stent lumen.<sup>[4,25]</sup>

In patients post-CABG, the radiation dose in CTCA is double as the scanning area is twice the length for visualizing native coronary arteries alone, that is, from the subclavian arteries to below the diaphragm. Prospectively gated acquisition in CTCA has significantly reduced the radiation dose to 2–3 mSv for CTCA of the graft and native coronary arteries, in post-CABG scans. This is because acquisition is limited to 10% of cardiac cycle at the end of diastole. However, as prospective gating necessitates a regular rhythm <60 bpm, newer retrospectively gated CTCA protocols with electrocardiographically controlled tube current modulation have been developed which keep the radiation dose low and below 10 mSv.

With the technical advancement of CT scan equipment, both dose of radiation and the amount of contrast media have decreased, making these studies safe in patients with risk of contrast nephropathy.<sup>[25]</sup>

Besides anaphylaxis to iodinated contrast, there is no absolute contraindication to CTCA. However, relative contraindications, including pregnancy, hemodynamic instability, acute

decompensated heart failure, inability to hold breath for >5 s, and renal insufficiency (CrCl <30 mL/min/1.73 m<sup>2</sup>), need consideration before doing a CTCA.<sup>[4]</sup>

## CONCLUSION

CTCA is an accurate and objective non-invasive alternative to ICA to visualize the graft and coronary anatomy. In addition to estimating vessel stenosis, it enables assessment of the coronary vessel wall for vulnerable plaques, total atherosclerotic burden, and hemodynamic significance (by CTFRR and CTP) of the lesion.

The use of higher than 64-slice CT scan machines with modern software has markedly increased the diagnostic accuracy in post-stenting and CABG patients while reducing the complication of routine diagnostic ICA.

We propose that CTCA is an objective, non-invasive, accurate and cost-effective means of assessment for CAD in aircrew. It offers an anatomical, pathological, and hemodynamic evaluation of coronary arteries akin to ICA and should be the investigation of choice for the same. In cases of ambiguity, an ICA can be done.

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