Management of established coronary artery disease in aircrew with previous myocardial infarction or revascularisation

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ABSTRACT
This manuscript focuses on the broad aviation medicine considerations that are required to optimally manage aircrew with established coronary artery disease (CAD) without myocardial infarction (MI) or revascularisation (both pilots and non-pilot aviation professionals). It presents expert consensus opinion and associated recommendations and is part of a series of expert consensus documents covering all aspects of aviation cardiology.

Aircrew may present with MI (both ST elevation MI (STEMI) and non-ST elevation MI (NSTEMI)) as the initial presenting symptom of obstructive CAD requiring revascularisation. Management of these individuals should be conducted according to published guidelines, ideally with consultation between the cardiologist, surgeon and aviation medical examiner. Return to restricted flight duties is possible in the majority of aircrew; however, they must have normal cardiac function, acceptable residual disease burden and no residual ischaemia. They must also be treated with aggressive cardiac risk factor modification. Aircrew should be restricted to dual pilot operations in non-high-performance aircraft, with return to flying no sooner than 6 months after the event. At minimum, annual follow-up with routine non-invasive cardiac evaluation is recommended.

INTRODUCTION
When compared with the general population, aircrew are more likely to be found to have obstructive, flow-limiting, coronary artery disease (CAD) in the absence of significant symptoms. This is likely a result of the occupational periodic medical examinations (PME) that aircrew undergo that includes a thorough cardiovascular assessment. Revascularisation may be performed via percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), or a hybrid combination, to reduce angina, resolve ischaemia, abort myocardial infarction (MI), and/or decrease mortality and prolong life.

When considering returning aircrew to flight duties following revascularisation, three factors are usually paramount; the type of revascularisation (CABG vs PCI vs hybrid); expected reocurrence rates in the areas of revascularisation; and residual disease burden (including assessment of left ventricular (LV) ejection fraction and regional wall motion, scar burden, and viability). Decisions regarding revascularisation, including bystander disease, should be based on established clinical indications and not solely on aeromedical concerns. However, flight safety does require special consideration and in certain circumstances revascularisation may be considered outwith usual clinical indications, to mitigate specific occupational risk, after thorough discussion and consent with the aircrew.

The value of a multidisciplinary approach (between cardiologist, cardiovascular surgeon and aviation medical examiner (AME)/flight surgeon) cannot be over emphasised, nor can the importance of aggressive secondary modification of risk factors.

PERCUTANEOUS CORONARY INTERVENTION
In this paper, PCI refers to any catheter-based coronary artery revascularisation, including percutaneous transluminal coronary angioplasty (PTCA),
non-high-performance aircraft may be possible, depending on the risk threshold accepted by the individual aircrew’s respective regulatory authority.

Selection of grafts for aircrew during CABG is an area of ongoing research and should follow the latest guidelines. Competitive flow and lack of haemodynamically significant stenosis in the native vessel adversely effects graft patency and assessment of fractional flow reserve (FFR) should be done during angiography for any lesion with >50% stenosis to verify haemodynamic significance. Data support preferential use of arterial (internal mammary artery) grafts over venous grafts for all haemodynamically significant stenosis and strong consideration of bypass for moderate (51–70%) left sided lesions, while clinical guidelines suggest that moderate right sided lesions may be left untouched and treated medically.12–15

No surgical evidence supports revascularisation of stenoses ≤50% (non-obstructive lesion) or 51–70% (non-haemodynamically significant lesion). This is due to competitive flow that occurs when less than severe stenoses are grafted which negatively affects graft patency.16 High competitive flow induces a high oscillatory shear index (OSI); which is a quantification of the change in direction and magnitude of the wall shear stress. A high OSI is associated with endothelial dysfunction and atherogenesis, leading to graft failure and poor revascularisation outcome as well as repeat revascularisation.17 Saphenous vein grafts are less affected by competitive flow than arterial grafts, although arterial grafts are nowadays the preferred choice of conduit for the revascularisation of the left sided coronary artery lesions given the superior long-term patency rates. Radial artery grafts should not be used for stenoses that are less than critical (<90%), as this conduit is the most sensitive to competitive flow. FFR measurement during angiography is of great assistance to the surgeon in supporting the choice of targets and conduits for revascularisation and thus should be considered in all aircrew with borderline stenoses to verify their haemodynamic significance.

### CORONARY ARTERY BYPASS SURGERY

To address the question of return to flight for commercial pilots, post-CABG, a dedicated sub-study of the CASS (Coronary Artery Surgery Study) Registry was used to select 2326 patients who had clinical and postoperative characteristics like those of commercial airline pilots. The probability of MACE over 5 years was 1.6% per year overall but decreased to 0.4% per year in those who had never smoked and had no history of hypertension.18 Historic data on CABG outcomes from within the civilian aeromedical community demonstrate death or MI rates of <2% per year, with repeat revascularisation rates of 3–4% per year.19 However, more recent data suggest the contemporaneous MACE rate is closer to 1% per year.20 Additionally, aircrew populations often have a lower cardiovascular risk compared with the general clinical population. Therefore, for aircrew following CABG, with aggressive risk factor modification and close follow-up, restricted return to flight duties in

Table 1  Recommendations for percutaneous coronary intervention

| Recommendations | Strongly recommended | Not recommended |
|-----------------|---------------------|-----------------|
| Bare metal stents and drug eluting stents are acceptable for aircrew. | | |
| Because of the high rate of early restenosis, non-stent (plain old balloon) angioplasty (POBA) is not recommended for aircrew. | | |
| Fully bioresorbable stents/scaffolds are not recommended for aircrew. | | |

Table 2  Recommendations for percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG)

| Recommendations | Strongly recommended | Recommended | Consider |
|-----------------|---------------------|-------------|---------|
| Published clinical guidelines rather than aeromedical considerations should be the primary consideration for determining revascularisation with PCI or CABG. | | | |
| A waiting period of at least 6 months after revascularisation is required before assessing aircrew for return to flight status. | | | |
| For aircrew being considered for proximal left anterior descending coronary artery (LAD) revascularisation, proactive consideration should be given to the left internal mammary artery (LIMA) graft over PCI, given long term benefit. | | | |
| Revascularisation may be considered for occupational risk modification outside clinical indications after thorough discussion and consent with the aircrew. | | | |
PCI VERSUS CABG

Over the past 30 years there have been many randomised controlled trials and meta-analyses regarding PCI versus CABG that have shown no difference in death or MI in most non-diabetic patients. However, MACE rates consistently favour CABG over PCI with 5 year event rates approximately 4% higher in those with PCI versus CABG. Revascularisation consistently drives the primary endpoints in all studies, and neither death nor MI have been demonstrated to be significantly different between PCI and CABG. One exception to this is the left internal mammary artery (LIMA) to left anterior descending coronary artery (LAD) revascularisation for any disease involving the left main and/or proximal LAD; given graft durability and likely a long-term mortality benefit over PCI in all patients, CABG is therefore recommended in the most recent guidelines. In all cases, calculation of a SYNTAX score and heart team approach with careful discussion between the general cardiologist, interventional cardiologist and cardiothoracic surgeon is paramount.

There are data to support favourable outcomes with hybrid revascularisation (combining PCI and CABG) and this approach can be utilised as indicated in aircrew. Overall, published clinical guidelines should be followed for aircrew, without regard to occupational flight status, which currently favours CABG for multivessel disease (three or more coronary arteries, or two if including proximal LAD or dominant left circumflex (LCx)) and left main stem disease. Repeat revascularisation following PCI or CABG can be as high as 5–9%, while MI and mortality rates are consistently <2% per year. Kaplan-Meier data consistently show an early spike in complication rates for both PCI and CABG, with a more linear curve after 6 months; therefore a waiting period of no less than 6 months following revascularisation is required before consideration of resuming aircrew duties (table 2).

Event rates after CABG or PCI in military aircrew may be lower than in the general population. In a retrospective review of United States Air Force (USAF) aircrew with no prior cardiac events that underwent coronary artery revascularisation with PCI or CABG, there were no cardiac deaths within 5 years and cumulative cardiac event rates (MACE) at 1 and 5 years were 1.0% and 3.6%, respectively. All aircrew requiring revascularisation were identified during annual re-evaluation (as described below), not by symptomatic re-presentation. These results may be at least partially attributed to the younger age of military pilots, as published data in young patients (<40 years of age) demonstrate 10 year event-free survival rates over 90%, even in the pre-statin era. These high success rates included patients revascularised with either PCI or CABG, regardless of presenting symptoms such as angina, ischaemia and/or MI.

FOLLOW-UP AFTER SIMPLE REvascularisation

Not uncommonly, aircrew will have a single high-grade stenosis in the setting of angina, MI and/or ischaemia, with no other angiographic evidence of CAD. The culprit stenosis is treated with revascularisation, such as DES, usually with excellent results. With no appreciable so-called ‘bystander’ disease, and a widely patent, stented artery, the important aeromedical question is that of risk for a future cardiovascular event. Aircrew will often have been informed—and feel as if—their CAD has been ‘cured’, despite revascularisation being a palliative procedure. However, in the aviation medicine setting, it is imperative to remember revascularisation has been used to mitigate potentially life-threatening CAD which is an end product of a complex metabolic, anatomic, immunologic and genetic disease process. Consequently, aircrew with revascularisation retain an increased lifetime risk of recurrent obstructive CAD. Aircrew who have undergone any form of revascularisation must undergo regular (at least annual) follow-up with non-invasive testing.

In many countries angiography is required in all military aircrew at 6–12 months, before return to flight status, and again at periodic (often 5 year) intervals while undertaking flying duties, regardless of non-invasive testing results. In a small USAF cohort of 76 asymptomatic aircrew with prior revascularisation and negative non-invasive studies, repeat angiography at 6 months, 3 years and 5 years demonstrated progression to severe disease in seven aircrew (9%) at 6 months with no additional cases of significant progression at 3 years. Unfortunately, there was progression to severe CAD in a further nine (12%) aircrew at 5 years; three of these underwent repeat revascularisation with the other six permanently disqualified from flying duties. We therefore recommend repeat angiography (coronary computed tomography angiography (CCTA) or invasive coronary angiography (ICA)) and functional ischaemia testing be done before return to flight status to ensure patency of the culprit vessel and grafts if present, as well as to evaluate residual disease burden (in non-revascularised vessels). Angiography should be done no earlier than 6 months after revascularisation then reconsidered at 5 year intervals if remaining on active flying duty (table 3). Secondary prevention with aggressive risk factor modification is mandated as discussed later in this article.

### Chronic total occlusions

Chronic total occlusion (CTO) refers to a coronary artery with either no flow, or flow that does not reach the end vessel when assessed with ICA. CTO has been reported in 15–30% of patients referred for ICA. Mortality rates for non-revascularised and revascularised CTO are consistently around 3% per year. Return to flight duties in the setting of non-revascularised CTO is not recommended (table 4). Return to flight may be permitted in revascularised CTO in exceptional circumstances, in asymptomatic non-pilot aircrew with good functional status, no evidence of infarct/scar or ischaemia, normal LV function, and optimal secondary risk factor modification.

### Table 3 Recommendations for follow-up after simple revascularisation

| Recommendations | Strongly recommended |
|-----------------|----------------------|
| Aircrew who have undergone a revascularisation procedure should undergo repeat angiography and/or functional ischaemia assessment no earlier than 6 months after the procedure as part of the assessment of return to aircrew duties. | Strongly recommended |
| Aircrew who have undergone revascularisation should have annual follow-up with non-invasive testing. | Strongly recommended |
| Aircrew who have been returned to flight duties after revascularisation or myocardial infarction should be considered for repeat angiography (invasive coronary angiography or coronary computed tomography angiography) every 5 years to remain on aircrew duties. | Consider |

### Table 4 Recommendations for chronic total occlusion (CTO)

| Recommendations | Consider |
|-----------------|----------|
| In exceptional circumstances, non-pilot aircrew that have undergone revascularisation of CTO may be considered for return to restricted flight duties. | Not recommended |
| Aircrew with CTO with or without revascularisation are not recommended to return to flight duties. | Not recommended |
Cardiology specialist consultation is strongly recommended for all aircrew with suspected MI before a return to flight/control duties.

Cardiac MRI is recommended in all aircrew where there is diagnostic uncertainty of the diagnosis of MI.

Aircrew with a history of MI may be considered for a return to operational duties. Pilots require restriction to non-high performance aircraft with another pilot qualified on type. Criteria include minimal scar burden with normal global left ventricular function, no evidence of ischaemia or arrhythmia, acceptably low residual coronary artery disease burden, and normal cardiopulmonary function off all antianginal medications.

Aircrew with a history of MI with any evidence of heart failure, ongoing tobacco use or diabetes should not be returned to flight duties.

Table 5  Recommendations for myocardial infarction (MI)

| Recommendations | Strongly recommended | Consider | Not recommended |
|-----------------|---------------------|----------|----------------|
| Cardiology specialist consultation | | | |
| Aircrew with MI | | | |
| Aircrew with MI and smoking | | | |
| Aircrew with MI and diabetes | | | |

Myocardial infarction in aircrew

Cardiology specialist consultation is strongly recommended to confirm any diagnosis of MI in aircrew given the occupational implications. In aircrew it is essential that the diagnosis of MI is properly confirmed, especially in cases where the luminal findings on angiography are equivocal. Acute myocarditis may cause clinical, biochemical and ECG findings similar to MI and needs to be actively excluded in these cases. In myocarditis the coronary arteries may be normal or demonstrate CAD that is unrelated to the event. It is essential for aircrew that these conditions are, as far as possible, delineated, as the occupational ramifications of each condition are significantly different. The gold standard for evaluation of myocarditis is cardiac MRI (CMR); the different pattern of cardiac scar in MI and myocarditis can be readily determined by late gadolinium enhancement uptake on CMR, and should be strongly considered in all aircrew with a history of chest pain where the diagnosis of MI/myocarditis is uncertain.

In addition to scar assessment, contrast-enhanced CMR can also characterise myocardial and microvascular injury and can provide additional detail on myocardial function and cardiac remodelling, and provide predictive value and prognosis for medium to long-term LV function. CMR may also be useful for risk stratification in individuals who have had an MI, allowing assessment of the presence/absence of scar tissue, although no data exist that reliably quantifies scar burden with arrhythmia risk.

Prior MI increases the event rate for all significant CAD groups, with or without revascularisation. Short term (30 day) mortality for ST elevation MI (STEMI) and non-ST elevation MI (NSTEMI) is 2–5% irrespective of type of reperfusion (fibrinolysis or urgent revascularisation). Long-term mortality rates after MI are also consistently 2–5% per year, with the highest mortality rates in NSTEMI patients (up to 8%) and lowest in STEMI patients (as low as 2%). Over 15 years mortality rates following MI have improved to approximately 2% per year; however, this increases dramatically to over 45% in those with heart failure symptoms or tobacco use, up to 65% in those with diabetes, and >80% in

Figure 1  Aeromedical disposition recommendations based on coronary angiographic findings. 1 Luminal diameter stenosis based on angiography. 2 Return to non-pilot aircrew duties may be considered after careful risk assessment and risk mitigation if aggregate stenosis otherwise <120%. 3 Restrictions include non-single seat and non-high performance aircraft. 4 Aircrew with 30–50% stenosis may be restricted to non-high performance flight depending on local civilian and/or military regulations. Note: The recommended dispositions are an agency decision and may be modulated by associated coronary risk factor modification. FFR, fractional flow reserve; MI, myocardial infarction.
those with an ejection fraction <30%. Aircrew with any signs of heart failure, tobacco use or diabetes, in addition to CAD, are not recommended to return to flight duties (table 5).

While the overall mortality rates following MI would breach the usual ‘1% rule’ in aircrew (referring to over 1% risk of sudden incapacitation), the short and long-term mortality data are much improved in younger patients. Mortality rates in patients <50 years old are approximately 1% at 6 months, 3% at 4 years, and 6% at 5 years. A small study of USAF aircrew followed over 5 years post-MI demonstrated no cardiac deaths and no recurrent MI. Annual rates of revascularisation were 4% in the first year, 2.3% at 2 years and 2.4% at 5 years; no aircrew presented with a recurrence of symptoms, and all revascularisations were because of abnormalities detected on scheduled annual testing. With newer generation stents, newer surgical techniques and more aggressive risk factor modification, the risk of sudden incapacitation likely falls below 1% per year, allowing consideration for return to limited flight duties for most aircrew.

Based on the above data, aircrew with a history of MI may be considered for return to operational duties. Pilots require restriction to non-high performance aircraft with another qualified pilot. Other aircrew require a detailed risk assessment related to their particular operational duties. Criteria for return to duties include minimal scar burden with normal global LV function, no evidence of ischaemia or arrhythmia, acceptably low residual CAD burden, and normal cardiopulmonary function off all antiangiial medications. The final determination with regards to return to flying duties will also depend on the risk threshold accepted by the individual aircrew’s respective regulatory authority.

**Residual disease after revascularisation**

In otherwise healthy aircrew, MI is not uncommonly the result of atherosclerotic plaque rupture of a single ‘culprit’ coronary artery lesion. Culprit vessel revascularisation in the acute setting decreases recurrent MACE, including mortality. However, controversy remains with regards to revascularisation of other, non-culprit artery, obstructive CAD. Current European Society of Cardiology (ESC) and American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend only infract artery revascularisation unless there is cardiogenic shock in the presence of multiple critical stenoses, although there is evidence that those with multivessel CAD do have higher 30 day mortality rates. More recently, two large studies have shown significant decreases in MACE with complete revascularisation, including non-culprit lesions, as early as 30 days after revascularisation, with no difference in stroke, bleeding or nephropathy.

Whether done at time of event, or staged (PCI of culprit vessel, followed by repeat PCI or CABG non- culprit lesions later), it is imperative that all aircrew have no residual haemodynamically significant disease. Non-revascularized CAD burden, including aggregate stenosis, can then be calculated on non-obstructive disease to determine risk. All aircrew with a prior MI and/or revascularisation should be risk assessed, and if within acceptable risk limits, can be considered for limited aircrew roles (ie, non-high-performance airframes), and for pilots, limited to dual pilot operations, with another suitably qualified pilot on that aircraft type, even when residual disease is minimal. All aircrew must also meet secondary risk factor recommendation goals for return to flight duties (table 6). Figure 1 summarises the occupational disposition of pilot aircrew based on angiographic findings.

**Secondary prevention and follow-up**

Secondary prevention guidelines have been published by the ACC, AHA and ESC, and are summarised in table 7. Consensus between these guidelines for those with documented CAD include the use of aspirin and statins, aggressive blood pressure control, smoking cessation, regular exercise and weight control through dietary modification.

| Table 6 Recommendations for residual disease after revascularisation |
|-----------------------------------------------|
| **Recommendations** | Highly recommended |
| For return to flight duties, aircrew with revascularisation should have no residual haemodynamically significant disease. | |
| Non-revascularised coronary artery disease burden, to include aggregate stenosis, should be calculated in non-obstructive disease to determine risk. | |
| All aircrew with myocardial infarction and/or revascularisation should be limited to non-high performance airframes and for pilots, limited to dual pilot operations. | |
| All aircrew must meet secondary risk factor recommendation goals for return to flight duties. | |

Statin therapy (or equivalent if statin not tolerated) should be prescribed for all aircrew with confirmed coronary artery disease regardless of baseline low-density lipoprotein cholesterol to decrease myocardial infarction and stroke risk. Abstinence of tobacco use is mandatory for return to flight/ control duties.

**Follow-up**

While most major society guidelines argue against routine non-invasive cardiac evaluations in asymptomatic patients even with known CAD, these guidelines do not take into account high
risk occupations such as those performed by aircrew where flight safety is paramount. Initial follow-up of aircrew for return to flight status should occur no sooner than 6 months after MI and/or revascularisation to ensure acceptable flight safety risk. After return to operational duties, aircrew should, at minimum, have an annual follow-up with their primary care provider, AME and cardiologist.

Although there are few data regarding the evaluation of asymptomatic patients post revascularisation, functional and physiologic testing has been shown to be highly predictive of future events. Even at 12 years of follow-up, those with normal stress testing demonstrate an annual mortality rate of approximately 0.9%. Determination of ischaemia is significantly higher with non-invasive imaging (85% sensitivity) compared with exercise stress testing (ExECG) alone (45% sensitivity) and non-invasive functional imaging assesses the extent of ischaemia and vascular territory.

All functional imaging modalities are acceptable in aircrew; both single photon emission CT (SPECT) nuclear imaging and stress echocardiography are acceptable forms of imaging with a negative predictive value of over 98% over 36 months, while positron emission tomography (PET) has been shown to have increased sensitivity and specificity, with improved spatial resolution, when compared with SPECT and stress echo imaging. Stress CMR affords the highest spatial resolution, less soft tissue artefact, and provides anatomic and functional data without ionising radiation.

ExECG alone is not recommended as a sole investigation of ischaemia in aircrew (Table 9); however, it is still of value when assessing cardiopulmonary functional status as a good functional capacity has consistently been shown to predict a lower long-term mortality rate. Exercise stress is preferred over chemical stress if possible. However, if imaging modalities do not allow exercise, then annual ExECG should also be considered for assessment of cardiopulmonary functional status. Other tests that should be considered annually, given the risk of adverse cardiac remodelling, include an ECG, resting echocardiogram, and 24-h Holter monitor.

CONCLUSION/SUMMARY

All aircrew with coronary artery revascularisation and/or MI have an increased risk of death, myocardial infarction, revascularisation and possibly stroke. However, modern revascularisation techniques, advanced medical therapy and adherence to lifestyle changes can significantly decrease event rates. Depending on the underlying pathology, intervention and acceptable post-revascularisation investigations (ie, preserved LV function, no or minimal scar burden, no evidence of ischaemia, acceptable residual CAD burden), return to operational aircrew duties may be considered based on a detailed risk assessment. The predicted event rates require that pilots be restricted to dual pilot operations in non-high performance aircraft. As with all clinical decision-making in aircrew, the choice of revascularisation should be based on published guidelines. Outside the acute setting, consideration should be given to total plaque burden (aggregate stenosis) and the most appropriate strategy for treating multivessel or multi-lesion CAD (online supplementary table 10).

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