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D-2.1 - CARDIOVASCULAR DIAGNOSTIC METHODS AND TREATMENTS SUITABLE FOR USE IN AEROMEDICAL FITNESS ASSESSMENTS

CaVD-PACE

"Cardiovascular Diseases – Pilots and ATCOs Cardiovascular Evaluation"

New diagnostic measures and treatments for cardiovascular diseases

An Agency of the European Union

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Executive Summary

In report CaVD-PACE, D-1.1/D-1.2 "Review of diagnostic measures and treatment options" new diagnostic measures and treatments for cardiovascular diseases have been analysed. In continuation, the present report systematically discusses the suitability of the recommended methods and treatments for use in the aeromedical certification process as well as their impact and cost effectiveness. This Executive Summary presents summaries of the recommendations and findings concerning the diagnostic methods and treatments which are more systematically elaborated in the different chapters of this report.

Miscellaneous cardiovascular diseases and risk screening

General cardiological examination

Structured history taking and physical examination including blood pressure measurement form the mainstay of the cardiological examination. An 12-lead electrocardiogram (ECG) should be added at the first examination and renewal examinations according to time intervals defined for each class of pilots and for ATCOs. Special attention should be given to assessment of the cardiovascular (CV) risk factors. For Class 1 pilots and ATCOs - estimation of serum lipids, including cholesterol, shall be required at the examination for the initial issue of a medical certificate.

Peripheral artery disease and aortic disease

Peripheral artery disease or aortic disease are often markers of generalised atherosclerosis such as coronary artery disease. The severity of peripheral arterial and aortic diseases has significant influence on the assessment of the aeromedical fitness. Therefore, assessment of fitness of pilots and ATCOs with proven peripheral arterial and/or aortic disease (before and after a therapeutic intervention) should be performed by cardiologists with thorough knowledge of the medical requirements for pilots and air traffic controllers and their working conditions and environment.

Valvular Heart Disease

Echocardiography is the most important technique to establish the diagnosis of valvular heart disease (VHD) and for monitoring patients with VHD. For patients with VHD percutaneous therapeutic methods such as transcatheter aortic valve implantation (TAVI), edge-to-edge percutaneous repair of mitral regurgitation (Mitra-Clip) or trans-catheter treatment of tricuspid regurgitation are currently available (although not in all EU member states), besides the well-established operative treatments.

chapter 2	subchapter Valvular Heart Disease - Take away messages
➢	Echocardiography is the most important technique to establish the diagnosis of valvular heart disease (VHD) and for monitoring patients with VHD.
➢	Percutaneous therapeutic methods such as transcatheter aortic valve implantation (TAVI), edge-to-edge percutaneous repair of mitral regurgitation (Mitra-Clip) or trans-catheter treatment of tricuspid regurgitation are currently available (although not in all EU member states), besides the well-established operative treatments.

Thromboembolic Disorders

Venous thromboembolism and Pulmonary Embolism
In Pulmonary Embolism (PE) it is important to use echocardiography (leftwards septal shift?) and ECG (right axis deviation?, RBBB?, atrial fibrillation?) to investigate pressure overload of the right ventricle and pulmonary hypertension. In all pilots and ATCOs suffering from venous thromboembolism (VTE), a cardiovascular risk-assessment should be performed with use of an applicable risk estimation method such as SCORE2, SCORE2-OP, or SCORE2-Diabetes, irrespective of the occurrence of PE.

Arterial thromboembolism
Cardiological evaluation using Transthoracic Echocardiography (TTE) and ECG Holter monitoring is mandatory for pilots and ATCOs suffering from arterial thromboembolism. CT scan or MRI may be necessary to detect intracardiac thrombosis or tumour and aortic abnormalities. Coronary atherosclerosis should also be investigated with a coronary calcium score (CACS) and/or subsequently, with Coronary Computed Tomography Angiography (CCTA).

Chapter 2	subchapter Thromboembolic Disorders - Take away messages
	In all pilots and ATCOs suffering from venous thromboembolism (VTE), a cardio-vascular risk-assessment should be performed.
	Cardiological evaluation using transthoracic echography (TTE) and ECG Holter monitoring is mandatory for pilots and ATCOs with arterial thromboembolism.

Congenital, peri-, endo- and myocardial diseases

The risk of congenital heart diseases (CHD) and of peri-, endo- as well as myocardial diseases can vary from negligible to very high. Cardiomyopathies can lead to heart failure. Flying at high altitude without extra oxygen can be compromised by advanced CHD, which must be considered, especially in PPL, SPL, BPL and LAPL licence holders and student pilots for these licences.

Myocarditis
The use of cardiac MRI to ascertain the diagnosis of myocarditis is strongly recommended (check for oedema, or fibrosis).

Hypertrophic cardiomyopathy
Pilots or ATCOs with a first-degree relative diagnosed with Hypertrophic cardiomyopathy (HCM) should be screened with ECG and TTE initially and at 5-year intervals up to the age of 50 years. Screening should include genetic testing if a causal genetic mutation for HCM has been identified in a first-degree relative.

chapter 2	subchapter Congenital, peri-, endo- and myocardial diseases Take away messages
➢	Use of cardiac MRI to ascertain the diagnosis of myocarditis is strongly recommended. Myocarditis can cause dilated cardiomyopathy.
➢	Pilots/ATCOs with a first-degree relative diagnosed with hypertrophic cardiomyopathy (HCM) should be screened with ECG and TTE. Genetic testing in HCM-cases is indicated if a causal genetic mutation for HCM has been identified in a first-degree relative.

Heart Failure

Currently recommended diagnostic tests for heart failure should include BNP/NT-proBNP, 12-lead ECG, TTE, X-Thorax, and routine blood tests for comorbidities. Although pilots and ATCOs with symptomatic heart failure (NYHA II-IV) are considered unfit to fly, modern treatment with four drug classes, including SGLT-2 inhibitors, might improve the condition in some mild cases to a level of mild asymptomatic disease (NYHA I) and return to flying or ATC duties might be considered.

chapter 2	subchapter Heart Failure - Take away messages
➢	Diagnostic tests for heart failure should include BNP/NT-proBNP, 12-lead ECG, TTE, X-Thorax, and routine blood tests for comorbidities.
➢	SGLT-2 inhibitors in a combination with three classes medication, as recommended by the European Society of Cardiology, might improve the condition in some mild cases to a level of mild asymptomatic disease (NYHA I).

Syncope

A high-risk syncope is a syncope of cardiac origin. Diagnosis of the cause of syncope is of utmost importance for the aeromedical risk assessment. Modern diagnostic tools to diagnose the cardiac origin of syncope, such as MRI, implantable loop recorders, stress-echocardiography, and electrophysiological studies, should be considered to identify and manage high risk syncope of cardiac origin.

chapter 2	subchapter Syncope Take away message
➢	Modern diagnostic tools to diagnose the cardiac origin of syncope are MRI, implantable loop recorders, stress-echocardiography, and electrophysiological studies.

Cardiovascular risk level assessment

It is recommended to standardize the cardiovascular (CV) risk level assessment in the framework of the examinations for medical certification according to the 2021 guidelines of the European Society of Cardiology (ESC) in which new standards of CV risk calculation have been adopted: SCORE2 which estimates a 10-year risk of fatal and non-fatal CV disease (CVD) events in apparently healthy people aged 40-69 years, SCORE2-OP which is applicable for people aged >70 years, and the SCORE2-Diabetes algorithm for diabetic patients (the latter according to the 2023 guidelines of the ESC).

chapter 2	subchapter Cardiovascular risk level assessment Take away message
➢	It is recommended to use the SCORE2, SCORE2-OP, or SCORE2-Diabetes risk charts for cardiovascular risk level assessment in pilots and ATCOs.

Coronary Artery Disease, diagnostic tools, and treatments

Coronary Artery Disease

The primary goal of therapy in patients with Chronic Coronary Syndrome (CCS) is to relieve symptoms, delay or prevent progression of Coronary artery disease (CAD), and decrease the risk of major adverse CV events. The aeromedical fitness classification of pilots and ATCOs depends on the severity and the extent of the coronary lesions. When determining treatment options, or evaluating the fitness level after invasive treatments (PCI and CABG), a risk estimation has to be made in order to determine the individual's aeromedical fitness, including options of risk mitigation by operational limitations. The choice of the diagnostic cardiac imaging techniques to be used to identify and monitor the risk status of CAD cases is to be made by the consulting cardiologist. Non-invasive imaging techniques that currently allow consulting cardiologists to screen, diagnose, monitor, and manage coronary artery disease (CAD) and heart function are:

- CACS: anatomical method to detect the presence and the amount of calcium deposits in the coronary arteries;
- CCTA: anatomical method to assess coronary artery stenoses
- CCTA-FFR anatomical assessment of stenoses + functional assessment of flow (FFR=Fractional Flow Reserve)
- Echocardiography to assess structural abnormalities and heart function
- Stress echocardiography to assess presence of cardiac ischemia
- Exercise ECG-testing to check for cardiac ischemia: Method no longer recommended as a standard procedure due to low sensitivity and low predictive value.
- MRI to assess heart muscle function, areas of reduced blood flow, scars, and evaluate the impact of CAD on the heart function
- SPECT and PET functional methods to assess blood flow. SPECT also used during stress testing
- Carotid ultrasound to *qualitatively* assess atherosclerosis in the carotid arteries, used as *indicator* of systemic atherosclerotic disease including CAD.

CACS and CCTA are primarily anatomical methods. The other techniques mentioned above are functional tests. To adequately evaluate the severity and consequences of CAD for a pilot or ATCO a combination of an anatomical and functional method is indicated. Stress echocardiography, CMR, PET and CCTA (with FFR) have approximately the same sensitivity and specificity for the detection of myocardial ischemia. PET is more expensive and superior to SPECT because with PET measures myocardial blood flow quantitatively. These methods e.g. enable to differentiate in the level of risk, and consequent duration of unfitness and operational limitation(s), of pilots and ATCOs after they have had an invasive treatment of coronary artery obstructions (PCI, CABG).

chapter 4	subchapter Coronary Artery Disease - Take away messages
➢	To effectively evaluate the severity and consequences of coronary artery disease (CAD) for a pilot or ATCO, a combination of an anatomical and functional methods is indicated. Stress echocardiography, CMR, PET and CCTA (with FFR) have similar sensitivity and specificity for the detection of myocardial ischemia.
➢	Left Main disease is the CAD subset with the strongest evidence that revascularisation provides survival benefit over medical treatment.

Bleeding risks of antithrombotic medications, especially after PCI and after CABG

After a coronary artery intervention (percutaneous coronary intervention = PCI or coronary artery bypass graft surgery = CABG) all patients need antithrombotic medication for the rest of their life. The bleeding risk under aspirin-therapy and under antiplatelet P2Y12 receptor blockers (i.e. clopidogrel) as monotherapy can be considered as low. The bleeding risk of patients using dual antiplatelet therapy (DAPT) is higher than with using a single antiplatelet drug and should be analysed on an individual basis. The result may lead to an operational limitation or to unfitness. Triple antithrombotic medication (anticoagulation included) has a very high bleeding risk and is considered not compatible with fitness for duty of pilots and ATCOs. The bleeding risk of anticoagulation with vitamin K antagonists (VKA) and with non-vitamin K oral anticoagulants (NOAC) is in generally considered equal or slightly increased compared the risk of aspirin. VKA or NOACs are considered compatible with a restricted aeromedical fitness, and, considering the recent literature, may be compatible with an unrestricted fitness in many cases. VKA treatment needs frequent monitoring of the INR (International Normalized Ratio).

chapter 4	subchapter Bleeding risks of antithrombotic medications, especially after PCI and after CABG Take away message
➢	After a coronary artery intervention (PCI or CABG) all patients need antithrombotic medication. Most patients have to use dual antiplatelet therapy (DAPT), at least for a certain defined time. Decisions about operational limitations or unfitness of pilots/ATCOs should be taken based on the individual bleeding risk of the patient using DAPT.

COVID-19

Pilots and ATCOs who have had a COVID-19 infection may be at risk for pericarditis and/or myocarditis (besides non-cardiac problems). Clinical screening and follow-up monitoring are therefore important. In case of suspicion of peri- and/or myocarditis, echocardiography or cardiovascular magnetic resonance imaging (CMR) might be required. After COVID-19 vaccinations reports of mild myocarditis mainly occurring in young adults have been published. Recovery was spontaneous in most described cases.

chapter 4	subchapter COVID-19 Take away message
➢	Pilots and ATCOs affected by a COVID-19 infection may be at risk for pericarditis and/or myocarditis which can be diagnosed and monitored by echocardiography or cardiovascular magnetic resonance imaging (CMR).

Arrhythmias

Atrial Fibrillation – Diagnosis and Treatment Many pilots and ATCOs with atrial fibrillation (AF) are asymptomatic or have non-specific symptoms. Methods for screening and monitoring of AF are resting ECG, Holter ECG, telemetry ECG or telemetry monitoring, and external or implantable event or loop recorders. Additionally, different wearables including watches and belts are available and are gaining importance along with their increasing reliability.

Atrial Fibrillation: Treatment

In most pilots and ATCOs, rhythm control will be the strategy of choice. This can be achieved by antiarrhythmic drug therapy and/or catheter ablation. Side effects of several antiarrhythmic drugs are often not compatible with flying or ATC. Therefore, catheter ablation will be the adequate treatment for many pilots and ATCOs with recurrent symptomatic AF. Long-term success has been shown to be better for catheter ablation than for antiarrhythmic drug treatment. Pulsed field ablation (PFA) for AF has higher myocardial tissue selectivity compared to conventional methods. PFA is effective for paroxysmal and persistent AF and is associated with low AF recurrence. DOACs are preferred for anticoagulation in most cases. Contraindications for DOAC are mechanical heart valves and moderate to severe mitral valve stenosis.

chapter 5	subchapter Atrial Fibrillation Take away messages
➢	Methods for screening and monitoring of atrial fibrillation (AF) in pilots/ATCOs are resting ECG, Holter ECG, telemetry ECG or telemetry monitoring, event or loop recorders (external or implantable).
➢	Catheter ablation is considered to be the effective treatment for many pilots and ATCOs with recurrent symptomatic AF. Long-term success rates are higher for catheter ablation than for antiarrhythmic drug treatment. Pulsed field ablation (PFA) for AF is currently a preferred method.
➢	DOACs are preferred for anticoagulation in most AF cases. Contraindications for DOAC are mechanical heart valves and moderate to severe mitral valve stenosis.

Ventricular and supraventricular ectopy

Premature ventricular complexes (PVCs) and premature atrial contractions (PACs) are common electrocardiographic findings during routine aeromedical examinations. In many cases PVCs or PACs are considered benign with no significant consequences for aeromedical fitness. However, frequent PVCs can lead to PVC-induced cardiomyopathy, and ventricular ectopy (VE) is associated with ventricular tachycardias with syncope or sudden cardiac death. In rare cases, atrial ectopy (AE) is associated with significant adverse outcomes and incident atrial fibrillation (AF). Assessment of the aeromedical fitness of pilots and ATCOs with advanced VE or AE disease should be performed by the medical assessor and, if necessary, in collaboration with the cardiologist expert consultant, appointed by the national aviation authority of EASA Member States. For advanced VE, there is a huge variety of treatment options, such as antiarrhythmic drugs and catheter ablation techniques.

chapter 5	subchapter Ventricular and supraventricular ectopy Take away message
➢	Frequent PVCs can lead to cardiomyopathy, and ventricular ectopy (VE) and might be associated with ventricular tachycardias with syncope or sudden cardiac death. However, most cases of PVCs and PACs are benign.

Bundle branch and fascicular blocks

Left bundle branch block (LBBB), right bundle branch block (RBBB), and fascicular blocks (FB) may be a sign of structural heart disease. Complete BBB requires cardiological evaluation to rule out structural heart disease, which is crucial for the fitness assessment of pilots and ATCOs. The most important screening and monitoring examination for BBB and FB is a 12-lead resting electrogram (ECG). ECG Holter monitoring may be helpful to identify intermittent BBB or FB, and exercise-induced BBB or FB can be identified by exercise-ECG. When complete LBBB or RBBB is detected for the first time, transthoracic echocardiography (TTE) is usually the first option for cardiological evaluation. To rule out cardiomyopathy (CM), coronary artery disease (CAD), or valvular heart disease (VHD) magnetic resonance imaging (MRI), coronary computed tomography angiography (CCTA), or invasive coronary angiography (ICA) are often required. A newly developed LBBB in combination with symptoms and/or abnormal laboratory findings could indicate acute myocardial infarction. Left anterior fascicular block (LAFB) may be associated with myocardial ischemia, and if newly acquired over age 40, underlying CAD should be excluded with CCTA. The combination of bi-fascicular block (BFB) plus first-degree atrioventricular block (AVB) can indicate a risk of progression to tri-fascicular block which might require pacemaker implantation.

chapter 5	subchapter Bundle branch and fascicular blocks Take away messages
➢	Complete BBBs require cardiological evaluation to rule out structural heart disease.
➢	For cardiological evaluation of complete LBBB or RBBB transthoracic echocardiography (TTE) is the first option. To rule out cardiomyopathy (CM), coronary artery disease (CAD), or valvular heart disease (VHD), magnetic resonance imaging (MRI), coronary computed tomography angiography (CCTA), or invasive coronary angiography (ICA) are required.
➢	A newly developed LBBB with symptoms and/or abnormal laboratory findings can indicate acute myocardial infarction. Left anterior fascicular block (LAFB) may be associated with myocardial ischemia, and if newly acquired underlying CAD should be excluded with CCTA.
➢	The combination of bi-fascicular block (BFB) plus first-degree atrioventricular block (AVB) can indicate a risk of progression to tri-fascicular block which might require pacemaker implantation.

Atrioventricular block

First-degree Atrioventricular Block (AVB) in asymptomatic pilots and ATCOs is considered a normal variant if the PR interval is ≤ 300 ms and needs no further evaluation which instead is necessary for a PR of >300ms. Asymptomatic second-degree AVB Mobitz type I (Wenckebach) as an incidental finding needs no further examination. Pilots and ATCOs with AVB Mobitz type II and complete AVB should be investigated for underlying structural heart disease and are unfit for performing their duties because of the risk of sudden cardiac death (SCD), syncope, bradycardia-related hemodynamic symptoms, and heart failure. In most of these cases pacemaker (PM) therapy is indicated. After detection of AVB in a resting ECG or in case of symptoms, ECG Holter monitoring can be carried out to determine the degree and consequences of AVB. An exercise ECG is important to evaluate if AVB normalizes or deteriorates under exercise. Further cardiological evaluation including echocardiography, CT, or MRI can be performed to identify possible underlying cardiac disease. Other methods used for screening and/or monitoring are telemetric ECG monitoring, external/ implantable event/loop recorders, and/or wearables including smart watches, belts or patches.

chapter 5	subchapter Atrioventricular block Take away messages
➢	Pilots and ATCOs with AVB Mobitz type II and complete AVB should be evaluated for structural heart disease and are to be declared unfit due to a risk of sudden cardiac death (SCD), syncope, bradycardia-related hemodynamic symptoms, and heart failure. In most of these cases pacemaker (PM) therapy is indicated.
➢	Evaluation of the degree and consequences of an AVB can be done with ECG Holter monitoring, exercise ECG, telemetric ECG monitoring, external/implantable event/loop recorders, and/or wearables. Echocardiography, CT, or MRI is recommended to identify possible underlying cardiac disease.

Asymptomatic ventricular pre-excitation

A resting-ECG is the adequate screening examination for asymptomatic ventricular pre-excitation. Once detected, an exercise ECG is used to evaluate the presence of the delta wave during exercise. ECG Holter monitoring could detect intermittent delta waves, and short episodes of AF and/or AVRT. Echocardiography is used to identify associated cardiac disease. Important risks of asymptomatic pre-excitation are 1) the development of atrioventricular re-entrant tachycardia (AVRT) and 2) fast antegrade conduction over the accessory pathway (AP) in case of atrial fibrillation, potentially leading to ventricular fibrillation (VF) and sudden cardiac death (SCD). The most reliable diagnostic test for asymptomatic ventricular pre-excitation is an invasive electrophysiologic study (EPS) with testing for conduction properties of the AP, multiple APs, and the inducibility of AVRT. Invasive testing by EPS would usually only be required for the initial examination of pilots and ATCOs. In high-risk individuals, catheter ablation of accessory pathways is the only reliable treatment option.

chapter 5	subchapter Asymptomatic ventricular pre-excitation Take away messages
➢	Risks of asymptomatic pre-excitation are 1) the development of atrioventricular re-entrant tachycardia (AVRT) and 2) fast antegrade conduction over the accessory pathway (AP) in case of atrial fibrillation, leading to ventricular fibrillation (VF).
➢	Risk assessment of ventricular pre-excitation (WPW) is done by exercise ECG (delta waves during exercise?), ECG Holter monitoring (intermittent delta waves, short AF episodes, and/or AVRT?), echocardiography (cardiac disease?). Electrophysiologic study (EPS) to test conduction properties of the AP(s), and the inducibility of AVRT is only required for the initial examination of pilots and ATCOs.
➢	Catheter ablation of accessory pathways is the only reliable treatment option for high risk ventricular pre-excitation patients.

Channelopathies

Channelopathies are detected in the resting 12-lead ECG. AMEs should be vigilant during the initial aeromedical examination of pilots and ATCOs to detect suspicious ECG features of the different channelopathies because some of these are related to a high risk for fatal arrhythmias and sudden cardiac death. Therefore, suspicious ECGs always need thorough cardiological evaluation in order to take adequate therapeutic measures.

Evaluation methods can include genetic testing, invasive electrophysiologic study (EPS), and cardiac imaging techniques. Therapeutic measures can include implantation of an implantable cardioverter defibrillator (ICD).

chapter 5	subchapter Channelopathies - Take away messages
➢	AMEs should be alert to detect suspicious ECG features of channelopathies on ECGs of pilots and ATCOs because some channelopathies are related to a high risk for fatal arrhythmias.
➢	Cardiological expert evaluation of channelopathies includes genetic testing, electro-physiologic study (EPS), and cardiac imaging techniques. Therapeutic measures can include implantation of an implantable cardioverter defibrillator (ICD).

Cardiac Pacing, Implantable Cardioverter Defibrillator

Cardiac pacing may be considered as a treatment for pilots and ATCOs with sinus node disease (SND), atrioventricular block (AVB), or bradyarrhythmia with atrial fibrillation (AF). Conduction system pacing (CSP) is a new pacing method that can prevent pacing-induced cardiomyopathy. Under strict conditions pilots and ATCOs might be allowed to perform their duties with an implanted PM. While short-term complications of Cardiac Implantable Electronic Devices (CIEDs) placement, such as pneumothorax, can be excluded by an X-Thorax and postprocedural three months observation period, pilots and ATCOs with CIED can be affected by long-term complications, such as lead dislodgement/failure/destruction, erosion of the pocket, infection, hematoma, early battery depletion, or stroke or death. The risk of electromagnetic interference (EMI) with CIEDs is very low in commercial aircraft. Although not reported yet, cyber security risks are theoretically possible when using remote monitoring systems. Implantable Cardioverter Defibrillators (ICDs) are not compatible with flying or ATCO duties, because ventricular tachycardia or fibrillation can lead to a short incapacitation when the capacitor charges and the shock is delivered. After the shock is delivered, it can take a few seconds before the individual regains full orientation. Inappropriate ICD-shock delivery is also considered as an unacceptable risk for pilots and ATCOs. This applies also to subcutaneous ICDs (S-ICD) or extravascular ICDs (EV-ICD).

chapter 5/3	subchapter Cardiac Pacing, Implantable Cardioverter Defibrillator Take away messages
➢	Cardiac pacing may be considered as a treatment for pilots and ATCOs with sinus node disease (SND), atrioventricular block (AVB), or bradyarrhythmia with atrial fibrillation (AF). Conduction system pacing (CSP) is a new pacing method that can prevent pacing-induced cardiomyopathy.
➢	The risk of electromagnetic interference (EMI) with Cardiac Implantable Electronic Devices (CIEDs) is very low in commercial aircraft (chapter 3).
➢	Implantable Cardioverter Defibrillators (ICDs) are not compatible with flying or ATC duties, although for Class 2, Class 3, and LAPL exemptions may be possible when meeting strict conditions as mentioned in Chapter 5-subchapter Cardiac Pacing, Implantable Cardioverter Defibrillator. This applies also to subcutaneous ICDs (S-ICD) or extravascular ICDs (EV-ICD).

Cardiovascular incapacitation risk assessment

For cardiovascular risk assessment of pilots and ATCOs it is important to predict incapacitation levels ranging from subtle to complete with variable probabilities of occurrence while taking the operational impact of an incapacitation event and potential mitigation measures into account. This can best be done by using risk matrices, which plot the operational impact of an event (severity) against the probability of occurrence of the event and provide a semi-quantitative assessment of the flight safety impact of a broad spectrum of cardiological conditions with variable probabilities of occurrence. Severity levels have to be defined taking the operational circumstances into account (e.g. may be different for Class 1, 2, 3, or LAPL).

chapter 6	subchapter Cardiovascular incapacitation risk assessment Take away messages
➢	For cardiovascular risk assessment of pilots and ATCOs it is important to predict incapacitation levels ranging from subtle to complete with variable probabilities of occurrence while taking the operational impact of an incapacitation event and potential mitigation measures into account.
➢	Risk assessment and the tolerability of the risk can be done by using a risk matrix, which plot the operational impact of an event (severity) against the probability of occurrence of the event.

Contents

1. Introduction

Report CaVD-PACE D-1.1/D-1.2 "Review of state-of-the-art diagnostic measures and treatments in cardiology" provided the results of the review and interpretation of the main findings concerning current state-of-the-art diagnostic tools to identify cardiovascular risks as well as benefits and risks of currently recommended treatments of the different cardiovascular conditions.

The present report is based on the results described in report CaVD-PACE D-1.1/D-1.2 and reports the analysis of currently state-of-the-art diagnostic tools and treatments in terms of suitability to identify and/or treat cardiovascular pathologies in the context of assessing the risk of pilot/ATCO incapacitation. In addition, impact, cost-effectiveness, risks, and availability of the tools and treatments at EU Member State level are discussed. The recommendable recently developed diagnostic tools and treatments as identified in report CaVD-PACE D-1.1/D-1.2 are systematically discussed and recommendations concerning suitability of methods and treatments for aeromedical risk assessment will be presented using a standardized format. Details on application of the recommended methods and treatments in the aeromedical fitness requirements will be elaborated in the context of task 4, 5, and 6 in which the risk of pilot/ATCO incapacitation for each class of aeromedical certification will be taken into account.

For detailed scientific background, considerations, and literature of the methods or treatments discussed in the present report the reader is referred to Report CaVD-PACE D-1.1/D-1.2 (https://www.easa.europa.eu/en/research-projects/new-treatments-and-diagnostic-measures-cardiovascular-diseases-pilots-and-atcos).

2. Miscellaneous cardiovascular diseases and risk screening

Cardiological examination

The issue and comments in this document are related to Report CaVD-PACE D-1.1/D-1.2 subchapter 2.1.

Importance of this issue, especially for use in aeromedical fitness assessment:

Cardiological examination is important, because it is part of a general clinical examination as first milestone in the aeromedical evaluation of a pilot or an ATCO. As outlined in the corresponding subchapter in the report CaVD D-1.1/D-1.2, the clinical (cardiological examination) should always consist of a structured history taking and of a physical examination also including blood pressure measurement. An electrocardiogram (ECG) should be added at the first examination and at certain follow-up examinations according to a defined time plan which varies in the different pilot classes and ATCOs. Many pilots/ATCOs check spontaneously and regularly themselves certain health parameters using devices such as blood pressure monitor systems or wearables in order to check pulse or the number of daily steps etc. The information of such data can be included into the medical history. Special attention should be given to an assessment of the cardiovascular (CV) risk factors. At least for class 1-pilots, determination of the lipids should be made at the first examination and at certain follow-up examinations, also according to a defined time plan. If there are striking findings in the medical history, in the clinical examination or in the ECG, further examinations might be required. Detailed recommendations about time periods for ECG and blood sampling (mainly for checking lipids) with respect to the different pilot classes and ATCOs will be provided in task 4 and task 5,

Which methods can be used for screening and which for monitoring purposes and frequency of the assessment

The criteria which should be followed when performing a clinical (including cardiological) examination - as well for an initial screening examination as for a routine follow-up examination - have been described above. The frequency of the clinical examination in healthy pilots and ATCOs is defined which varies in the different pilot classes and ATCOs (this will be recommended in detail in task 4 and 5). In presence of striking findings, such as suspicion of a CV disease or a proven CV disease, additional diagnostic methods are necessary, and the frequency of the follow-up assessments might differ from those which are valid in pilots and ATCOs without striking findings. And in such cases, the frequency of the follow-up examinations must be defined on an individual basis.

Costs and cost-effectiveness

The costs for routine clinical (cardiological) examinations are low, and the cost-effectiveness in the long-term perspective is good in the context of managing CV risk factors. In case of additional diagnostic methods and/or specific therapeutic measures, the costs rise, and the cost-effectiveness has to be evaluated on an individual basis.

Availability of the method: by AME, by specialist (cardiologist), smaller or middle-sized hospitals, only center hospitals?

The clinical examination of pilots and ATCOs as described above is performed by the aero-medical examiner (AME). Specialists, hospitals or specialized centres are only involved if the presence of striking findings demand additional diagnostic and/or therapeutic measures.

Availability of the methods and of special expertise at EU member state level

Clinical (including cardiological) examinations can be performed in all European countries.

Classification of the risk of the diagnostic methods

There are no risks related to the interview about medical history, to the clinical examination and to the performance of an ECG. And the risk of side effects if blood sampling is undertaken in general is minimal.

Aeromedical fitness assessment of pilots/ATCOs in routine AME-examinations
Of course, the aeromedical fitness assessment of pilots/ATCOs is related to the results of the examinations. Conditions with enhanced CV risk and conditions with proven CV diseases are discussed in other subchapters where the specific issues such as coronary artery disease, valvular heart disease, arrhythmias etc. are described. And in task 4 and 5, more detailed information concerning the aeromedical fitness assessment in respect to the different pilot classes and ATCOs will be recommended.

Peripheral artery disease and aortic disease

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 2.3.

Importance of this issue, especially for use in aeromedical fitness assessment

This issue considers “peripheral arterial disease” and “aortic disease”, as they are both diseases of the arteries, but the manifestation of these two diseases is different. This issue is important, because the prevalence of these two diseases is not negligible, especially in the age group older than 65 years for both types of diseases; and concerning the aortic diseases (aortic aneurysm), those, which are caused by connective tissue disorders like Marfan syndrome, Ehlers-Danlos syndrome etc. and by congenital disorders such as bicuspid aortic valve, often occur at a younger age. And both types of diseases are often also a marker of generalized atherosclerosis like coronary artery disease (CAD). The severity of peripheral arterial and aortic diseases has significant influence on the assessment of the aeromedical fitness.

Which methods can be used for screening and which for monitoring purposes and frequency of the assessment

The methods, which shall be used for establishing the diagnosis of relevant peripheral arterial and/or aortic disease or for performing follow-up examinations before and after interventions (percutaneous intervention or operation) are described in the corresponding subchapter in report CaVD D-1.1/D-1.2. Detailed recommendations about time periods of the follow-up examinations in respect to the different degrees of disease severity and in respect to pilot classes and ATCOs will be given in task 4 and task 5.

Costs and cost-effectiveness

The extent of the costs is related to the choice of the diagnostic methods and to the choice of the therapeutic actions. If the international guidelines concerning diagnostic and therapeutic measures are followed, then cost-effectiveness should be guaranteed, even if the costs for the one or other diagnostic step or for the chosen intervention might be high. As preventive actions, it is important to evaluate and manage the cardiovascular (CV) risk factors, as it is highlighted in the corresponding subchapter in report CaVD D-1.1/D-1.2. As result of such measures, the occurrence of peripheral arterial and aortic diseases might be avoided, or - in presence of such diseases - their progression might be delayed. All this has positive consequences to the costs and to the cost-effectiveness.

Availability of the method: by AME, by specialist (cardiologist), smaller or middle-sized hospitals, only center hospitals?

Initial examination (performing medical history taking, medical examination, checking of CV risk factors, etc.) can be undertaken by general practitioners or aero-medical examiners (AME). Advanced methods must be performed by angiologists or cardiologists. Percutaneous interventions and operations are conducted in specialized centres. Follow-up examinations can be performed either by general practitioner/ AME or specialists according to the demanded methods of examination. The assessment of the aeromedical fitness of pilots and ATCOs with proven peripheral arterial and/or aortic disease (before and after a therapeutic intervention) should be performed by the medical assessor and, if necessary, in collaboration with the cardiologist expert consultant, appointed by the national aviation authority of EASA Member States.

Availability of the methods and of special expertise at EU member state level

The clinical examination for the assessment of peripheral arterial and aortic disease and the additional diagnostic methods, mentioned in the corresponding subchapter in report CaVD D-1.1/D-1.2, can be performed in all European countries. But differences might be found in the choice of invasive treatments. There are especially differences in the choice of treatment of aortic aneurysms. More and more percutaneous therapeutic methods are used, but for these procedures, a great expertise is required. And there exists differences in the amount of such specialized experts and specialized centres in the different European countries.

Classification of the risk of the diagnostic and therapeutic methods, when suspected or proven peripheral arterial and/or aortic diseases are present, and aeromedical fitness assessment of pilots/ATCOs

There are no relevant risks for all methods which are used for diagnosing and monitoring patients with suspected or proven peripheral arterial and/or aortic diseases. But the invasive therapies of peripheral arterial and aortic diseases (operation, percutaneous interventions) are associated with certain method-related risk, which varies according to the chosen method (risk being between low until high). Furthermore, the applied medication might have side effects which must also be considered, especially the bleeding risk if antithrombotic drugs are used. And the risks should be considered which are related to the peripheral arterial and aortic diseases per se such as thromboembolic events, dissection of aortic aneurysm etc., and also to other arteriosclerotic diseases like CAD, because there is a higher probability, that other forms of arteriosclerotic diseases exist, if peripheral arterial and/or aortic diseases are present. The aeromedical assessments must consider the different risk situations. In presence of advanced cases of peripheral arterial and aortic diseases before or after therapeutic percutaneous or surgical intervention, an aeromedical fitness without restriction is only possible in selected cases and in lower categories of pilot classes. In difficult cases, an interdisciplinary medical approach is demanded, also considering the individual situation. But the definitive assessment of the aeromedical fitness of pilots and ATCOs with proven peripheral arterial and/or aortic disease (before and after a therapeutic intervention) should be performed by the medical assessor and, if necessary, in collaboration with the cardiologist expert consultant, appointed by the national aviation authority of EASA Member States. Detailed recommendations of aeromedical assessments, also considering the different pilot classes and ATCOs, will be undertaken in task 4 and task 5.

Valvular Heart Disease

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 2.4.

Importance of this issue, especially for use in aeromedical fitness assessment

This issue "Valvular heart disease" is of great importance, first because the prevalence of valvular heart diseases is not negligible, especially in the age group older than 60 years. Second, in general, it is a challenge to choose the right moment and the appropriate interventional procedure in cases with advanced valvular heart disease, and this is even more challenging in pilots and ATCOs in whom the compatibility of the chosen therapeutic procedure with the aeromedical fitness (with or without restrictions) should also be considered. There is a huge variety of heart valve situations concerning the severity of the diseased heart valves per se, and concerning specific cardiovascular (CV) conditions resulting of the valve diseases like heart failure, arrhythmias etc. And heart failure can also lead to pulmonary hypertension (PH). If this is the case, this form of PH would belong to the PH group 2 in the classification of PH according to the current PH-guidelines (Humbert et al., 2022).

Which methods can be used for screening and which for monitoring purposes and frequency of the assessment

The methods, which shall be used for establishing the diagnosis of relevant valvular heart disease, and which shall also be used for monitoring patients with proven relevant valvular heart disease or for performing follow-up examinations after interventions (operation or percutaneous intervention) are well described in the corresponding subchapter in Report CaVD D-1.1/D-1.2. The frequency of the follow-up assessments must be defined on an individual basis.

Costs and cost-effectiveness

Of course, the extent of the costs is related to the chosen diagnostic method and therapeutic procedure. Because the indications as well for the choice of diagnostic methods as for therapeutic procedures are clearly defined in international guidelines, cost-effectiveness should be guaranteed, even if the costs for the one or other diagnostic step or chosen intervention might be high.

Availability of the method: by AME, by specialist (cardiologist), smaller or middle-sized hospitals, only center hospitals?

Patients with suspicion of valvular heart disease and with proven relevant valvular heart disease with or without intervention must be checked and followed by a cardiologist. Some of the diagnostic techniques as well as operations and percutaneous interventions can be performed only in specialized centres. The assessment of the aeromedical fitness of pilots and ATCOs with valvular heart disease should be performed by the medical assessor and, if necessary, in collaboration with the cardiologist expert consultant, appointed by the national aviation authority of EASA Member States. This should be the case in the initial stage when the diagnosis of valvular heart disease is established as well in all stages of follow-up examinations before and after interventional therapy.

Availability of the methods and of special expertise at EU member state level

The methods needed for establishing the diagnosis of relevant valvular heart disease and for monitoring patients with proven relevant valvular heart disease with or without intervention are available in all European countries, as echocardiography is the most important technique in this respect, and echocardiography is widely used in all countries. But differences can be found in the choice of invasive treatments. More and more percutaneous therapeutic methods such as transcatheter aortic valve implantation (TAVI), edge-to-edge percutaneous repair of mitral regurgitation (MitraClip) or transcatheter treatment of tricuspid regurgitation etc. are used. Because these techniques can be performed only by specialized experts in specialized centres, there exist differences in the choice of therapeutic techniques in European countries.

Classification of the risk of the diagnostic and therapeutic methods which are used in patients including pilots and ATCOs with relevant valvular heart disease

There is no real risk for all methods which are used for diagnosing and monitoring patients with valvular heart disease. It is the valvular heart disease per se which consists a specific risk, which is in relationship with the severity of the disease. And the invasive therapies (operation, percutaneous interventions) are associated with certain method-related risk, which vary according to the chosen method (risk being between low until high). The bleeding risk has also to be taken into account in those cases with mechanical heart valves, who all are under anticoagulation; the anticoagulation in this situation is performed by the use of vitamin K antagonists (VKA). The bleeding risk is low, if the anticoagulation is well controlled. In the current EASA requirements, there are clearly defined recommendations concerning the international normalized ratio (INR) values. Such or similar requirements should remain part of the requirements in the context of valvular heart disease.

Aeromedical fitness assessment of pilots/ATCOs with valvular heart disease

Mild forms of valvular heart disease do not compromise the aeromedical fitness of pilots of all classes and of ATCOs. If an affected heart valve reaches a higher degree of disease, the aeromedical fitness might or should be restricted. As described in the corresponding document in task 1, there exist clear data/guidelines which define the severity of an affected heart valve, and which also determine the indications for invasive treatment options (operation or percutaneous intervention). And for pilots and ATCOs, also clear criteria in respect to aeromedical fitness must be defined for the different kinds of valvular heart disease when a higher degree of disease is reached and an unrestricted aeromedical fitness cannot be declared any more. The definition of aeromedical fitness in the postinterventional situation is another task. If the postinterventional result is good, and if there are no other relevant CV or other significant diseases, the aeromedical fitness can be defined with restriction and probably in certain pilot categories and maybe as well in ATCOs without restriction. As mentioned above, the assessment of the aeromedical fitness of pilots and ATCOs with valvular heart disease should be performed by the medical assessor and, if necessary, in collaboration with the cardiologist expert consultant, appointed by the national aviation authority of EASA Member States.

Reference

Humbert, M., Kovacs, G., Hoeper, M. M., Badagliacca, R., Berger, R. M. F., Brida, M., . . . Group, E. E. S. D. (2022). 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J, 43*(38), 3618-3731. doi:10.1093/eurheartj/ehac237

Thromboembolic disorders

For the scientific background and literature references the reader is referred to the corresponding subchapter 2.5 of report CaVD-Pace D-1.1/D-1.2.

Importance and suitability of recommended methods for use in aeromedical certification examinations

In *venous thromboembolism (VTE), pulmonary embolism (PE)* is the most important clinical manifestation. Because PE may lead to pressure overload of the right ventricle and in persistent cases to pulmonary hypertension, it is important to investigate these risks using echocardiography (leftwards septal shift?) and ECG (right axis deviation?, RBBB?, atrial fibrillation?) in all VTE cases, irrespective of the occurrence of PE. In pilots and ATCOs suffering from VTE a cardiovascular risk-assessment should be performed with use of an applicable risk estimation method such as SCORE2. Based on the cardiovascular risk-profile a stratified cardiological assessment can be indicated.

Arterial thromboembolism can cause cerebrovascular stroke and peripheral arterial embolization and it is very important to investigate its cardiac and non-cardiac causes, such as atrial fibrillation, atrial septal defect, left-sided endocarditis, acute anterior myocardial infarction, atherosclerotic disease, and aortic aneurysm. Therefore, cardiological evaluation is mandatory for pilots and ATCOs suffering from arterial thromboembolism and should consist of (transthoracic) echocardiography and ECG Holter monitoring (atrial fibrillation?). CT scan or MRI may be necessary to detect intracardiac thrombosis or tumour and aortic abnormalities. The likelihood of coronary atherosclerosis should be investigated with a coronary artery calcium score (CACS) and/or subsequently, with coronary CT angiography (CCTA).

Comparison with other diagnostic methods

There are no other screening methods (for VTE) or diagnostic methods (for sequela of PE and for arterial hypertension) than those that are currently recommended.

Use of recommended method for screening and for monitoring purposes and frequency of the assessment

For screening of cardiovascular risk in VTE the SCORE2, SCORE2-OP, or SCORE2-Diabetes are recommended. When pulmonary hypertension is suspected, it is recommended to perform a cardiological assessment at 3 to 6 months after the acute phase of PE. When this evaluation does not show evidence for persistent arrhythmias and/or signs of pulmonary hypertension there is no indication for further follow up. The frequency of monitoring/assessment in cases of arterial thromboembolism depends on the consequences of the findings of the full cardiological evaluation which was performed after the occurrence of the arterial thromboembolism.

Costs and cost-effectiveness

The indicated methods are considered cost-effective in that they provide accurate essential information at reasonable costs. It should, however, be considered that the costs of medical services, including imaging, may vary considerably between countries, regions, and healthcare systems.

Availability of the method

The charts of the different SCORE2 risk estimators are freely available. ECG is available for AMEs. Echocardiography and Holter monitoring are available in most -also smaller- hospitals. CACS and CCTA are generally available in medium-sized hospitals, while MRI might not be available in each European region. Where the different imaging methods are available there is almost always the necessary cardiological and radiological expertise available.

Risk of the method

The CACS is a non-contrast, cardiac-gated CT that can be done in 10-15 minutes, with about 0.5 to 1 mSv of radiation. Radiation dose and use of i.v. contrast is sometimes mentioned as a potential risk. In CACS the low radiation dose is considered as no risk for the individual examined. CCTA requires an intravenous contrast injection, and often i.v. β -blocker administration to slow the heart rate to around 60 bpm to optimize image acquisition. With modern scanners, the dose from a CCTA is between 0.2 mSv and 5 mSv depending on the technique and exposure time. Radiologists who do not want to use an i.v. β-blocker, need to scan more phases of the heart cycle with consequent longer radiation exposure time and dose. Using the correct techniques and new iterative reconstruction algorithms, it is possible to keep the radiation dose considerably lower than 1 mSv which is considered safe.

Advantages and disadvantages of the methods

The described methods enable an adequate evaluation of the cardiac risks of pilots and ATCOs suffering from VTE and arterial thrombo-embolism.

Congenital, peri-, endo- and myocardial diseases

The issue and comments in this document are related to the following corresponding subchapters in Report CaVD D-1.1/D-1.2:

2.6 Congenital heart disease
2.7 Pericardial and endocardial disease
2.8 Myocardial disease

Importance of this issue, especially for use in aeromedical fitness assessment

In this issue, some heart diseases are taken together, which are not so common. Therefore, they do not have the same priority in the chapter of cardiovascular (CV) aeromedical requirements like for example coronary artery disease (CAD), valvular heart diseases or arrhythmias. On the other hand, it is important that in a single case, who is affected by one of these diseases, adequate decisions concerning aeromedical fitness are made based on a well evaluated risk estimation. The risk of congenital heart diseases (CHD) and of peri-, endo- as well as myocardial diseases can vary from negligible until very high. The clinical presentations and the risk classification are well described in the corresponding subchapters in report CaVD D-1.1/D-1.2. For example, CHD can be categorized in cyanotic and acyanotic forms, and the risks of thrombo-embolic events and of arrhythmias are emphasized. Flying in high altitude can be compromised by advanced CHD, which also has to be considered, especially in private pilots (PPL, SPL, BPL) and LAPL-pilots and student pilots for these licences. Per definition, CHD is diagnosed mostly in the younger age group. Thus, in most cases, the AME is confronted with this disease at the first aeromedical examination; therefore, this first aeromedical examination is essential for the aeromedical fitness assessment; this is the fundament for the later career of the pilot or ATCO affected by such a disease. Pericarditis and endocarditis are the prominent manifestations of endo- and pericardial diseases. Their clinical course is often transient; therefore, a declared aeromedical unfitness or restricted fitness can often abolish after a certain time period. Concerning myocardial diseases, a differentiation must be made between transient myocarditis and different forms of cardiomyopathies. There have been new classifications of the various forms of cardiomyopathies within the last years, which resulted in more differentiated diagnostic methods and newer specific treatment options. Myocarditis can cause dilated cardiomyopathy. Details are described in the corresponding subchapters in report CaVD D-1.1/D-1.2, where hypertrophic cardiomyopathy (HCM) and restrictive cardiomyopathy (RCM) are especially highlighted. One - among others - important remark concerns the significance of genetic testing in HCM-cases. Many of the described diseases, especially the cardiomyopathies, can lead to heart failure. In this subchapter “Congenital, peri-, endo- and myocardial diseases” heart failure is not especially mentioned. But there is a specific subchapter which is dedicated to the issue heart failure, it is subchapter 2.9.

Which methods can be used for screening and which for monitoring purposes and frequency of the assessment

The methods, which shall be used for establishing the diagnosis of congenital, peri-, endo- and myocardial diseases or for performing follow-up examinations are well described in the corresponding subchapter in report CaVD D-1.1/D-1.2. The frequency of follow-up checking must be determined on an individual basis. Detailed

recommendations about time periods of the follow-up examinations in respect to the different degrees of disease severity and in respect to pilot classes and ATCOs will be given in task 4 and task 5.

Costs and cost-effectiveness

The costs vary according to the extent of the disease in question. It is often not easy to make a precise diagnosis in the big spectrum of the congenital, peri-, endo- and myocardial diseases. Accordingly, it is also a challenge to make good choices of the diagnostic and therapeutic methods. Those choices have a big influence on cost-effectiveness. Whenever possible, international guidelines should be respected.

Availability of the method: by AME, by specialist (cardiologist), smaller or middle-sized hospitals, only center hospitals?

Even if a general practitioner or an aero-medical examiner (AME) might have the suspicion of the presence of one of the diseases which are described in this subchapter, a clear diagnosis can be made only by a cardiologist. A special situation is given in persons with CHD. Cases with relevant CHD are diagnosed in general at or early after birth or in childhood; here the medical history is important and of help when such a person presents for a first aeromedical examination. As well for diagnostic as for therapeutic measures, pilots and ATCOs with the diagnosis of a congenital, peri-, endo- or myocardial disease have often to be analysed and/or treated in specialized centres. The assessment of the aeromedical fitness of pilots and ATCOs with proven diagnosis of one of the diseases mentioned here should be performed by the medical assessor and, if necessary, in collaboration with the cardiologist expert consultant, appointed by the national aviation authority of EASA Member States.

Availability of the methods and of special expertise at EU member state level

The diagnostic examinations for the assessment of congenital, peri-, endo- and myocardial diseases and the therapeutic procedures can probably be performed in many European countries. But because for some advanced and complicated cases a great expertise is required, there might exist differences in the number of specialized experts and specialized centres in some of the European countries.

Classification of the risks of the diseases and of the corresponding diagnostic and therapeutic methods, also considering the aeromedical fitness assessment of pilots/ATCOs

As mentioned above and as described in the corresponding subchapters in report CaVD D-1.1/D-1.2, congenital, peri-, endo- and myocardial diseases represent a wide spectrum of clinical situations and therapeutic procedures, and the risks of the diseases vary enormously. The risks are between irrelevant until very high. The risk of the applied diagnostic methods is surveyable. Therapeutic measures are associated with certain method-related risk, which varies according to the chosen method. Furthermore, the applied medication might have side effects which must also be considered, especially the bleeding risk if antithrombotic drugs are used. The aeromedical assessments must consider the different risk situations. In difficult cases, an interdisciplinary medical approach is demanded, also considering the individual situation. But the definitive assessment of the aeromedical fitness of pilots and ATCOs affected by one of the congenital, peri-, endo- and myocardial diseases should be performed by the medical assessor and, if necessary, in collaboration with the cardiologist expert consultant, appointed by the national aviation authority of EASA Member States. Detailed recommendations of aeromedical assessments, also considering the different pilot classes and ATCOs, will be undertaken in task 4 and task 5.

Heart Failure

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 2.9

Importance of this issue, especially for use in aeromedical fitness assessment

This issue "Heart failure" is per se of great practical importance in cardiology, but it is only of moderate importance in the aeromedical fitness assessment, because pilots and ATCOs with established heart failure are in general unfit to perform their duties. It is a challenge to define exemptions of this, this means to define in which situations a certain fitness - fitness with limitations (OML or OSL) - can still be declared. The different forms of heart failure and their clinical manifestations are well described in the corresponding subchapter in task 1. Advanced forms of heart failure can also lead to pulmonary hypertension (PH). This form of PH would belong to the PH group 2 in the classification of PH according to the current PH-guidelines (Humbert et al., 2022).

Which methods can be used for screening and which for monitoring purposes and frequency of the assessment

The methods, which shall be used for establishing the diagnosis of heart failure and which shall also be used for monitoring patients who are under treatment of established heart failure, are also well outlined in the corresponding subchapter in task 1. The frequency of the follow-up assessments must be defined on an individual basis.

Costs and cost-effectiveness

Costs are related to the chosen treatment. If device-related therapies such as cardiac resynchronization therapy (CRT) and implantable cardioverter-defibrillator (ICD) are used, the costs become much higher compared with the sole use of medical treatment and of lifestyle measures. And the costs rise even more if heart transplantation is performed, or if the patient is put on a left ventricular assist device (LVAD). It is clear that those treatment options with higher costs (CRT, ICD or combined CRT/ICD, heart transplantation, LVAD) must rely on clear indications based on the corresponding guidelines; then the cost-effectiveness is guaranteed.

Availability of the method: by AME, by specialist (cardiologist), smaller or middle-sized hospitals, only center hospitals?

Patients with suspicion of heart failure and with proven and treated heart failure must be checked and followed by a cardiologist. This does not exclude that a general practitioner may still have a role, especially for adapting and controlling medical treatment according to the clinical situation and also for checking the compliance of the patient. The insertion of devices or heart transplantation including follow-up controls are bound to specialized centres.

Availability of the methods and of special expertise at EU member state level

The different therapeutic options mentioned above should be available in many European countries. But there might be a lot of differences, especially for the application of LVAD and heart transplantation, because the number of specialized experts and of specific facilities needed for these methods is probably not sufficient in all countries, and the high costs also constitute an additional limiting factor.

Classification of the risk of the diagnostic and therapeutic methods which are used for patients including pilots and ATCOs with suspicion or with proven and treated heart failure

There is no need to give clear answers to these risks, because - as mentioned above - pilots and ATCOs with heart failure are in most cases unfit to perform their duties.

Aeromedical fitness assessment of pilots/ATCOs with heart failure

Despite the fact, that in most cases, pilots and ATCOs with heart failure are unfit to fulfil their duties, the question remains, in which exceptional situations, a pilot or an ATCO with proven and treated heart failure can be declared fit with restriction (like OML- or OSL-restriction) to fulfil their duties; such cases would implicate an exemption. Such an exemption is not possible in the acute phase and/or in the symptomatic situation of heart failure. It can be discussed in mild asymptomatic cases of heart failure or in those cases, which have been treated with medical therapy - maybe also including a CRT-treatment - for a certain time, and in which the initial cardiac situation has shown a significant improvement. The declaration of an exemption for fitness should be restricted to cardiologist expert consultants, appointed by the national aviation authority of EASA Member States. In general, pilots/ATCO's with ICD and those after heart transplantation should be considered as unfit; exemptions for class 2-pilots and for LAPL-pilots and maybe also for ATCOs might be made in very specific situations; for class 1-pilots there should be no such exemptions. All pilots/ATCOs having a LVAD are unfit to fly.

Reference:

Humbert, M., Kovacs, G., Hoeper, M. M., Badagliacca, R., Berger, R. M. F., Brida, M., . . . Group, E. E. S. D. (2022). 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J, 43*(38), 3618-3731. doi:10.1093/eurheartj/ehac237

Syncope

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 2.10.

Importance of this issue, especially for use in aeromedical fitness assessment

This issue "Syncope" is of great importance, first because the incidence of syncope in pilots and ATCOs is not low (see the incidence data in the corresponding task 1-document). Second, the determination of the etiology (classification) of a syncope under investigation is sometimes quite difficult, and in such a situation, it is also a challenge to assess the aeromedical fitness and to define the time period for a declared aeromedical unfitness or restriction.

Which methods can be used for screening and which for monitoring purposes and frequency of the assessment

The diagnostic methods, which shall be used for establishing the diagnosis of syncope and for classifying the kind of syncope, and which shall also be used for monitoring patients who have had a syncope, are well described in the corresponding chapter in task 1. The frequency of the follow-up assessments must be defined on an individual basis.

Costs and cost-effectiveness

See the list of risk categories and the list of investigations in the corresponding task 1-document. The costs for investigations of category 1-syncopes are low. The costs for investigations of categories 2- and especially of category 3-syncopes are higher as soon as an implantable loop recorder and/or methods like cardiac magnetic resonance imaging (MRI) are used and/or a neurologist is involved.

Availability of the method: by AME, by specialist (cardiologist), smaller or middle-sized hospitals, only center hospitals?

Pilots and ATCOs who have had a syncope can be checked by the general practitioner and/or the AME in a first step. But in most cases, there is a need to involve a cardiologist in a second step. In situations of risk categories 2 and 3 (see the corresponding task 1-document), it is recommended that the involved cardiologist corresponds to a cardiologist consultant, appointed by the national aviation authority of EASA Member States. Specific methods like cardiac MRI etc. (see above), are performed in hospitals or specialized centres.

Availability of the methods and of special expertise at EU member state level

The methods needed for establishing the diagnosis of syncope and for monitoring patients who have had a syncope are available in all European countries. Special expertise is only required for the aeromedical assessment of pilots and ATCOs who have had a syncope, but such expertise should be available in all European countries, as all National aviation authorities have nominated cardiologists who are involved in aeromedical assessments.

Classification of the risk of the diagnostic and therapeutic methods which are used in patients including pilots and ATCOs who have had one or several syncopes

There is no real risk for all methods which are used for diagnosing and monitoring patients, who have had a syncope, with exception of the electrophysiological study and of the tilt table test. These two tests have a certain, but not very high risk for side effects, however the probability that one of those two methods are used in the evaluation of syncope is very low. Risks are mainly related to the underlying disease, this means, if a relevant cardiovascular disease like for example significant arrhythmias is the cause of a syncope, then this cardiac disease might be related with an important risk.

Aeromedical fitness assessment of pilots/ATCOs who have had one or several syncopes

As stated in the corresponding task 1-document, it is important to differentiate the kind of syncope. The most common cause of syncope are reflex syncopes (vasovagal and situational syncope). Other forms of syncope (for examples those which are related to a relevant cardiac disease) represent a higher risk, those forms should be excluded in a first step of investigation. Alone a profound discussion with the patient, in which the situation including the accompanying symptoms related to the syncope is interrogated, can lead to a classification of the syncope in many cases (reflex syncope or other form of syncope). The classification of syncope in reflex syncope or other forms of syncope should be the first step of investigation. Then, it is important to know if the syncope is a single (first) episode, or if the syncope is part of recurrent syncopes. Reflex syncopes being a first episode can be categorized as low risk episode. In this situation, a fit assessment of the pilots and ATCOs to fulfil their duties without restriction can be considered either shortly after the event or after a certain time period after the event; the decision concerning the time after which the applicant is again fit without restriction must be made on an individual basis. If the pilot or ATCO has had recurrent reflex syncopes, then this person has to be advised by specialists in which way he can avoid situations which might lead to a syncope; and a longer time period of unfitness has to be declared until a new aeromedical assessment can be undertaken. If the syncope

(single episode or recurrent episodes) does not correspond to the category of reflex syncopes and as such representing a higher risk category, the aeromedical assessment must be stricter, and it must be performed on an individual basis. If for example the cause are significant arrhythmias, then the treatment of those arrhythmias has priority, and the aeromedical assessment is primarily related to this arrhythmia.

Cardiovascular risk level assessment

The issue and comments in this document are related to the corresponding subchapter 2.11 of report CaVD-Pace D-1.1/D-1.2.

Importance and suitability of recommended screening methods for use in aeromedical fitness

It is recommended to standardize the cardiovascular (CV) risk level assessment in the framework of the examinations for medical certification according to the recent (2021 and 2023) guidelines of the European Society of Cardiology (ESC) in which new standards of CV risk calculation have been adopted: SCORE2 which estimates a 10-year risk of fatal and non-fatal CV disease (CVD) events in apparently healthy people aged 40-69 years, SCORE2-OP which is applicable for people aged >70 years (both introduced in 2021), and the SCORE2-Diabetes algorithm for diabetic patients (introduced in 2023). - The variables used in SCORE2 are age, gender, systolic blood pressure, smoking behaviour and non-HDL cholesterol levels which represent all cholesterol levels except the HDL-cholesterol. Country-specific baseline CV risk levels of a population should be determined before entering the clinical variables in the matching SCORE risk chart. The interpretation of the SCORE2 and SCORE2-OP and the recommended approach to risk factor treatment is shown in the following table:

CVD risk	<50 years	50-69 years	≥ 70 years	recommendation
Low-to-moderate	<2,5%	<5%	<7,5%	Risk factor treatment generally not recommended
High	2,5 to <7,5%	5 to <10%	7,5 to <15%	Risk factor treatment should be considered
Very high	≥7,5%	≥10%	≥15%	Risk factor treatment generally recommended

Table 1: Interpretation of SCORE2 and SCORE2-OP and recommended approach to risk factor treatment

It is recommended to start systematic CV risk assessment in male pilots and ATCOs at the age of 40 years (females at 50 years) because 1) there is strong evidence that elevated non-HDL cholesterol in adolescence is associated with coronary atherosclerosis in mid-adulthood and 2) because from this age on the CVD risk starts to increase significantly (Simons et al., 2021). Individuals with a high or very high CVD risk should be referred to a cardiologist who should further evaluate the CVD risk using a stratified approach (e.g. Simons et al., 2021) and consider treatment of risk factors. Detailed ESC 2021 Guidelines for systematic CVD risk assessment can be found in subchapter 2.11 of Report CaVD-Pace D-1.1/D-1.2.

Arterial Hypertension

Arterial Hypertension should be thoroughly screened and considered by AMEs as a risk factor for CVD and stroke. A higher than normal blood pressure as defined by the European Society of Hypertension (ESH: 130-139 / 85-89 mmHg), should alert the AME, who may subsequently indicate (ambulatory) monitoring and further

specialist examinations depending on the results of monitoring. The objective of therapy of primary arterial hypertension is to lower blood pressure to <140/80mmHg, and if possible to <130/80mmHg, because this has been shown to further reduce the risk of stroke. Detailed ESH 2023 Guidelines for the necessary medical evaluation and treatment of arterial hypertension can be found in subchapter 2.2 of Report CaVD-Pace D-1.1/D-1.2.

Comparison with other CV risk estimation methods

The frequently used Framingham CVD risk score is based on US data of 1968-1987 and is considered to overestimate CVD risk in a 21-century-society (EASA, 2019). QRISK3 risk prediction algorithms are based on data of the UK population and use many more additional risk factors than other risk calculators (chronic kidney disease, systolic blood pressure variability, migraine, systemic lupus erythematosus (SLE), severe mental illness, erectile dysfunction, use of corticosteroids or antipsychotics), which may add to the predictive value, but also makes QRISK3 more complicated to complete. The PROCAM risk estimator is based on data of German health employees (baseline 1978–1995) and includes traditional risk factors such as LDL-cholesterol and HDL-cholesterol (EASA, 2019). The Pooled Cohort Equations replaces the obsolete Framingham risk calculator and is based on data of a US population including Afro-Americans (EASA, 2019). The Reynolds Risk Score is based on a limited non-random sample of US health employees and physicians (volunteers) and includes hs-CRP in addition to traditional risk factors (EASA, 2019).

The initial SCORE risk estimations only predicted fatal CVD events, whereas for in-flight incapacitation risks prediction of non-fatal CVD events is considered at least equally important (EASA, 2019). The updated SCORE2, SCORE2-OP, and SCORE2-Diabetes risk charts predict both non-fatal and fatal CVD events and are easy to use as tools adapted to country-specific baseline CV risk levels of a population and therefore suit different European populations. Moreover, these SCORE2 concepts use non-HDL cholesterol values which represent the cholesterol levels VLDL, VLDL-remnants, and LDL, and are considered a better predictor of CV risk than LDL alone which is used in most other risk estimators.

Use of recommended method for screening and for monitoring purposes and frequency of the assessment

The SCORE2, SCORE2-OP, and SCORE2-Diabetes are recommended for screening of aviation personnel. In those individuals who have undergone CVD risk assessment in the context of opportunistic screening, a repetition of screening after 5 years (or sooner if risk was close to treatment thresholds) may be considered.

Costs and cost-effectiveness

Costs associated with the screening method are mainly related to the measurement of non-HDL cholesterol levels which represent the cholesterol levels VLDL, VLDL-remnants, and LDL. The cost-effectiveness is considered to be favourable.

Availability of the method

The SCORE2, SCORE2-OP, and SCORE2-diabetes risk charts are freely available for AMEs and cardiologists in each member state and are easy to interpret. Most medical analytical laboratories will have the skills and equipment to measure and interpretate non-HDL-cholesterol levels.

Risk

There is no other risk associated with the method than a hematoma caused by a venipuncture.

Advantages and disadvantages

Screening with SCORE2, SCORE2-OP, and SCORE2-Diabetes risk charts is recommended to predict non-fatal and fatal CVD events in European pilots and ATCOs. Advantage: The method is based on firm data of EU country-specific baseline CV risk levels and therefore suit different European populations. Disadvantage: Risk estimation is based on European populations, and this should be taken into account when examining pilots or ATCOs with non-EU roots (e.g. Indian, Asian, Chinese applicants).

Therapeutic options

Appropriate management of the classic modifiable risk factors in combination with medication such as statins, ezetimibe, PCSK9 inhibitors, bempedoic acid, and antiplatelet agents may significantly lower LDL-C and risk levels in high risk patients. In patients with established atherosclerotic CV disease (ASCVD), lipid-lowering treatment with an ultimate LDL-C goal of <1.4 mmol/L and a >50% reduction of LDL-C versus baseline is recommended.

In patients with type 2 DM, the use of an SGLT2 inhibitor or GLP-1 receptor agonist is considered to reduce future CVD and total mortality. The treatment options of risk factors, including anti-hypertensive treatment, are in the realm of the cardiologist. All commonly used statins, ezetimibe, bempedoic acid, and PCSK9 Inhibitors require an initial ground trial and exclusion of side effects that may interfere with safe functioning. Considerations of anti-hypertensive treatment in pilots and ATCOs should be taken into account.

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3. Effects of in-flight conditions on Cardiac Implantable Electronic Devices

For the scientific background and literature references the reader is referred to the corresponding subchapter 3 of report CaVD-Pace D-1.1/D-1.2.

Importance and suitability of the considerations for use in aeromedical certification examinations

Environmental and working conditions as well as electromagnetic radiation exposure of pilots and ATCOs are considered unchanged in the last decade. The overall risk of clinically significant adverse events during flight in recipients of Cardiac Implantable Electronic Devices (CIEDs) including among others Implantable Cardioverter Defibrillators (ICDs) is very low, although theoretically possible. In contrast to pilots, ATCOs are not exposed to changes in pressure, temperature, humidity or vibrations, however ATCOs may be exposed to electromagnetic

influences. Although there are no specific studies of ATCOs wearing medical devices, it may be accepted that the risk of exposure for pilots and ATCOs in terms of electromagnetic fields is approximately the same. Because considerations on the use of CIEDs or ICDs and the environmental conditions have not changed in the last decade(s), there are no recommendations to change EASA's policy on this matter. The potential effects of electromagnetic radiation on CIEDs are mentioned in subchapters 5.8 and 5.9 of report CaVD-Pace D-1.1/D-1.2.

4. Coronary Artery Disease and COVID-19

Coronary artery disease (CAD), definitions and therapeutic procedures

The issue and comments in this document are related to the following corresponding subchapters in Report CaVD D-1.1/D-1.2:

4.1 Chest pain, myocardial ischemia and indications for coronary artery revascularization
4.2 Management of stenoses of the left main (LM) coronary artery
4.3 Indications for revascularization in coronary artery disease and follow-up data after revascularization
4.5 Procedure in asymptomatic coronary artery disease (chronic coronary syndrome)
4.10 Role of artificial intelligence in CAD
4.11 Significance of genetic evaluation of coronary artery disease

Importance of this issue, especially for use in aeromedical fitness assessment:

This issue is of extreme importance as well for the general population as well for the fitness assessment of pilots and ATCOs. It represents a wide spectrum of clinical presentations and diagnostic as well as therapeutic procedures. These procedures have revealed an enormous progress within the last years, which is also partly due to the inclusion of artificial intelligence-methods, especially in cardiac imaging techniques. The different cardiac functional and anatomical imaging techniques which are used for the evaluation of myocardial ischemia and for the assessment of the severity of coronary lesions are described in another summarized task 2-subchapter, therefore they are not mentioned in detail in this document.

Different manifestation forms of coronary artery disease (CAD), especially in relation to aeromedical fitness assessment

- Acute myocardial infarction (MI): The situation of acute MI with ST-segment elevation or non ST-segment elevation MI (STEMI or NSTEMI respectively) is not relevant for pilots and ATCOs, because in those acute situations, they are clearly unfit to fulfil their duties. But the middle- or long-term follow-up after an acute MI is of importance (see below).

- Chronic coronary syndrome (CCS): The burden of it is great in the general population, and its prevalence increases with age. The presence of coronary lesions outside of an acute MI, leads to the diagnosis of CCS. Complications of CCS are not rare, manifestations may be angina (chest pain), MI, heart failure and arrhythmias. In order to prove the presence of CCS, specific functional and anatomical imaging techniques can be used. As first step, non-invasive specific methods shall be used for the evaluation of myocardial ischemia and for the assessment of the severity of coronary lesions. Coronary computed tomography angiography (CCTA) has currently to be considered as one of the most important techniques in this context.

- Chest pain: If chest pain can be put into relationship with coronary artery stenoses then it is the expression of cardiac ischemia in most such cases. Chest pain per se does not mean that this must be of coronary

artery origin. The spectrum of diseases which lead to chest pain is wide, and it is a challenge to correctly classify chest pain. Among others, a psychosomatic disorder as origin for chest pain can often be found. There are specific lists for the investigation of chest pain. General practitioners and AMEs shall follow those lists.

- Coronary lesions: In order to classify coronary lesions, the following questions are important: How many coronary lesions are present, and where are they located in the coronary artery tree? Does the one or other coronary lesion lead to a stenosis, and if yes, how severe is this stenosis? Is an obstructive coronary lesion producing ischemia? How big is the ischemia in relationship to the whole myocardium? Are the lesions complex, like for example lesions involving coronary-artery branch points (bifurcations)? Are the lesions calcified or noncalcified, or are they mixed forms? Is there any further information about the character of the lesion (stable or unstable etc.), for example if in vivo imaging techniques of the vessel wall of the coronary arteries have been applied such as intravascular ultrasound (IVUS) or optical coherence tomography" (OCT)? Intravascular coronary imaging either with IVUS or with OCT should be or should become standard in cases with "complex" coronary lesions. Is the left main (LM) coronary artery involved (see below)?

- Left main (LM) coronary artery: The presence of a significant coronary artery stenosis within the LM coronary artery represents a very high risk. Therefore, LM disease is a CAD subset with the strongest evidence that revascularization provides survival benefit over medical treatment, also in stable patients.

- Treatment options: They consist of short- and long-term medical treatment as well as invasive treatments either by percutaneous coronary intervention (PCI) including stenting or not or by coronary artery bypass graft surgery (CABG). For the choice of treatment, a very differentiated approach is mandatory, and this approach is very much demanding. The primary goal of therapy in patients with CCS is to relieve symptoms, delay or prevent progression of CAD, and decrease the risk of major adverse CV events. It is preferential, if the decision about the treatment option is made within a multidisciplinary heart team.

- Importance for pilots and ATCOs: For pilots and ATCOs, it is very important to know, if CAD is really present, and if yes, which its severity is. If the coronary situation is clear, a risk estimation can be made which results in treatment options (see above), and which is the basis for the aeromedical classification (pilots or ATCOs fit or unfit or fit with limitations to fulfil their duties).

- PCI and CABG: Both PCI as CABG are established methods. After such an invasive procedure, pilots and ATCOs are unfit to fulfil their duties for a certain time. In the current EASA aeromedical requirements this time consists of six months in most cases (cases where the cardiac situation remains stable after the invasive intervention). And after six months, class 1 pilots can fly only with an OML-limitation. It is not correct to put all pilots/ATCOs, who have had an invasive treatment, into the same pot; there are big differences: On one side a PCI of just one single coronary artery lesion, the location of which is not in a proximal part of one of the big coronary arteries; on the other side several PCIs in presence of multiple coronary lesions. The first example can be classified as a low risk situation, the second example as a high or very high-risk situation. It is justified to make exemptions as well for the duration of unfitness as well for the limitation with OML for class 1-pilots in the long-term follow-up. Thus, in pilots/ATCOs with a low risk situation a shorter unfit period could be considered, and for class 1-pilots an OML-limitation in the long term follow up might be eliminated. The conditions for such exemptions should be clearly defined like for example age $\leq$ 65 years, no 3-vessel disease, not more than 2 stents or 2 bypasses in case of CABC, no signs of ischemia, left ventricular function normal or only mildly reduced, most cardiovascular (CV) risk factors under control.

- Middle- and long-term follow up: In presence of CAD, especially after an acute MI, with or without a history of invasive treatment, preventive measures are essential to decrease the risk for a relevant second CV event. Secondary prevention includes issues such as cardiac rehabilitation, lifestyle management, pharmacological treatment, considerations of comorbid conditions (mainly chronic kidney disease and diabetes) etc.

- Primary prevention: Those pilots/ATCOs who have no proven CAD, should also be checked for the presence of CV risk factors, and if CV risk factors exist, they should be approached. In this respect, it is important that an optimal communication is accomplished between the AME and the pilot/ATCO at the routine aeromedical examination.

- Genetic testing: Currently, genetic testing for CAD is not a tool to be applied when checking pilots and ATCOs for their CV risk situation.

Which methods can be used for screening and which for monitoring purposes and frequency of the assessment?

As mentioned above, the different cardiac functional and anatomical imaging techniques which are used for the evaluation of myocardial ischemia and for the assessment of the severity of coronary lesions are described in another summarized task 2-subchapter. The frequency of repeated checking of the CAD-situation of pilots and ATCOs must be determined on an individual basis in those cases who have not had an invasive intervention. In those who have had PCI with or without stenting or CABG, there shall be clear requirements in time periods and in cardiac and overall conditions similar as they can be found in the current EASA-medical requirements. But we recommend that time limits and decisions for aeromedical fitness should be based on a more differentiated level, like it is described in the section above (see under PCI and CABG). Thus, an update of the current EASA-medical requirements is necessary. Furthermore, exercise ECG-testing shall not anymore be a standard procedure when checking for ischemia, for example for the long term follow up of pilots/ATCOs after PCI and CABG. It can still be used in selected cases, but this should be an exemption.

Costs and cost-effectiveness

The costs of the diagnostic cardiac imaging techniques vary according to the chosen method. For example, coronary artery calcium score (CACS)-determination is much cheaper than CCTA, but its prognostic value is below the one of CCTA; the choice of the method must be based on a cost-benefit evaluation. The same is true, if a selection must be made between single-photon emission tomography (SPECT) and positron emission tomography (PET), knowing that PET costs much more than SPECT, just to give another example. Because CAD is covering a not negligible part of the total healthcare expenditure, it is routine that the different diagnostic and therapeutic methods have been and still are analysed in many cost-effectiveness studies. Of course, all invasive interventions are expensive, but if there is a clear indication to perform such a treatment, then the costs must be accepted.

Availability of the method

Diagnostic and invasive treatments are performed in hospitals, mainly in specialized centres. Medical treatment and the control of CV risk factors can be performed by a general practitioner/AME; but in case of pilots and ATCOs, the overall treatment should be based on recommendations given by a cardiologist, whenever possible by the cardiologist consultant appointed by the national aviation authority of EASA Member States.

Availability of the methods and of special expertise at EU member state level

Most diagnostic and therapeutic requirements in respect to the issue given in this document can principally be fulfilled in all EU member states. But there might be differences in the selection of cardiac imaging techniques. The choice, which method should be used for the detection of myocardial ischemia, is influenced by site expertise and availability of the methods. Some centres have more experience with CMR than with nuclear medicine methods, and in other centres it is vice versa. And the costs also play a role. And the decision in a specific situation, if an invasive intervention or only a medical treatment shall be performed, might also differ, even if quite clear guidelines exist in this respect.

Risk classification of the different manifestations of CAD

As CAD represents a wide spectrum of clinical situations and therapeutic procedures, the risks vary enormously. The risks are between very low until very high. Under the section "Different manifestation forms of coronary artery disease (CAD), especially in relation to aeromedical fitness assessment" (see above), the consequences of these different risk categories for the aeromedical assessment are described.

Advantages and disadvantages of diagnostic and therapeutic options in CAD

Advantages: There are clear international guidelines concerning the application of diagnostic and therapeutic methods in the different CAD-situations or in the situation in which CAD is suspected. The great variety of diagnostic and therapeutic options (as well medical as by intervention) allows a targeted approach to each patient. It is also positive, that CV risk factors can be positively influenced by very effective drugs; a good example are the lipid-lowering drugs, first of all the statins. And patients with proven CAD are judged also for adjacent diseases like diabetes or chronic kidney disease, what allows a better estimation of the overall risk situation.

Disadvantages: The long-term follow-up in patients with proven CAD with or without a history of invasive intervention remains a challenge. How often should pilots/ATCOs been checked by cardiac imaging methods? And how much do comorbidities, such as diabetes, chronic kidney disease or cerebral ischemic events, influence the overall aeromedical assessment?

Non-invasive imaging techniques in coronary artery disease (CAD)

The issue and comments in this document are related to the following corresponding subchapters in Report CaVD D-1.1/D-1.2:

4.6 Echocardiography
4.7 The actual role of CT coronary artery calcium score CACS) and Coronary computed tomographic angiography (CCTA) in the detection of Coronary artery disease (CAD)
4.8 Cardiac MRI in coronary artery disease (CAD)
4.9 Nuclear medicine methods: SPECT and PET

Importance of this issue, especially for use in aeromedical fitness assessment

Non-invasive imaging techniques are important in the diagnosis and management of coronary artery disease (CAD), as they allow the evaluation of coronary arteries and heart function without the need for invasive procedures like catheterization. They are classified in anatomical and functional imaging methods. Here is a summary of the most used non-invasive imaging techniques: Echocardiography: Echocardiography allows to asses structural abnormalities as well heart function. - Computed tomographic (CT) coronary artery calcium

score (CACS): It allows to detect the presence and the amount of calcium deposits in the coronary arteries. - Coronary computed tomography angiography (CCTA): CCTA visualizes coronary artery anatomy including for example the presence of coronary stenoses. - Cardiac magnetic resonance imaging (MRI): It is used to assess heart muscle function to detect areas of reduced blood flow and of scars as well as to evaluate the impact of CAD on the heart. - Single-photon emission tomography (SPECT) and Positron emission tomography (PET): These nuclear medicine methods, in conjunction with radioactive tracers, allow to assess blood flow. SPECT is often used during stress testing. PET is superior to SPECT, it has a better diagnostic and prognostic accuracy. - Exercise stress test: During an exercise stress test (treadmill or bicycle), the patient's heart is monitored by electrocardiogram (ECG) and/or echocardiography (stress ECG and stress echocardiography respectively); they are mainly used for checking the presence of cardiac ischemia. If a patient is unable to exercise, pharmacological stress testing is an alternative. Whereas stress echocardiography is an established method, stress ECG has a lower predictive value, and its use should be an exemption. - Carotid ultrasound: Carotid ultrasound, even if it is not specific for coronary arteries, can be used to assess atherosclerosis in the carotid arteries, which can be an indicator of systemic atherosclerotic disease including CAD. Carotid ultrasound should be performed in a qualitative way; the measurement of the intima media thickness of carotid arteries has no significance anymore and should be avoided. - Summary: CACS and CCTA are primarily anatomical methods. The other techniques mentioned above are functional tests. When using fractional flow reserve (FFR), then also CCTA has a functional significance. In special situations, a combination of some of the techniques mentioned above is used.

Methods which can be used for screening and for monitoring purposes and frequency of the assessments

All methods described above can be used for screening and monitoring purposes. They are used in pilots and ATCOs, especially if a suspicion of relevant CAD is present and in cases with proven CAD. The method which should be chosen must be decided on an individual basis. The same is true concerning the frequency (time intervals) of the monitoring in the middle- or long-term setting. Regular monitoring helps to check if the cardiovascular (CV) condition remains stable which is of importance for the aeromedical assessment.

Cost and cost effectiveness

The costs and cost-effectiveness of non-invasive imaging methods used in medical assessments, including those for CAD and aeromedical fitness evaluation, can vary significantly depending on several factors. For example, a simple exercise stress test or an echocardiography are generally less expensive than more advanced methods like cardiac MRI or CCTA. State-of-the-art equipment and specialized centres may be more expensive. The costs of medical services, including imaging, can vary greatly depending on the country, region, and healthcare system. Different healthcare providers may charge different fees for the same imaging services. For aeromedical fitness assessments, the frequency of required imaging may vary based on regulations and on the pilot's medical history and clinical situation. For high-risk patients and/or those with specific symptoms, the costs of imaging may be justified by the diagnostic and prognostic information the imaging method provides. If the information obtained from imaging tests leads to more accurate diagnoses, better treatment choices, and improved outcomes, the tests may be considered as cost-effective. On the other hand, missing a diagnosis of a significant medical condition (e.g., undetected CAD in a pilot) can have serious consequences, including in-flight emergencies or accidents. In this context, the costs of a missed diagnosis can be far higher than the costs of the imaging test.

Availability of the method: by AME, by specialist (cardiologist), smaller or middle-sized hospitals, only center hospitals?

Most of the imaging techniques can be performed only in hospitals or specialized centres. The assessment of the aeromedical fitness of pilots and ATCOs with proven CAD should be performed by the medical assessor and, if necessary, in collaboration with the cardiologist expert consultant, appointed by the national aviation authority of EASA Member States.

Availability of the methods and of special expertise at EU member state level

The different imaging techniques mentioned above should be available in the majority of the European countries. But there might be differences in the selection of the methods. For example, the choice, which method should be used for the detection of myocardial ischemia, is influenced by site expertise and availability of the methods. Some centres have more experience with cardiac MRI than with nuclear medicine methods, and in other centres it is vice versa. And the number of specialized experts and of specific facilities needed for these methods is probably not sufficient in all countries. Furthermore, the costs also play a role. And as mentioned above, the assessment of the aeromedical fitness of pilots and ATCOs with proven CAD should be performed by the medical assessor and, if necessary, in collaboration with the cardiologist expert consultant, appointed by the national aviation authority of EASA Member States.

Risk classification of the different methods

The different cardiac imaging techniques may contain side effects, but in most cases, the risk of those side effects is very low. Radiation exposure should be mentioned specifically, which is a side effect in nuclear medicine methods. But the radiation dose, when nuclear medicine methods are used, has been reduced enormously within the last few years. If nuclear medicine methods are not used very often, then the radiation exposure can be well accepted.

Risk classification for pilots and ATCOs and aeromedical assessment related to the outcome of the applied cardiac imaging techniques

The results of the applied cardiac imaging techniques represent a wide spectrum of CAD presentation. The risks of the different CAD situations vary enormously. More information is given in the task 2 subchapter “Coronary artery disease (CAD), definitions and therapeutic procedures”, and further detailed information will especially be provided in task 4 and 5.

Advantages and disadvantages of the methods

Advantages: The cardiac imaging techniques allow to evaluate if relevant CAD is present, and if yes, to assess quite precisely which is its manifestation. This is the basis for therapeutic decisions and also for the aeromedical assessment of pilots and ATCOs. And it is helpful, that there are international guidelines concerning the application of diagnostic methods in the different CAD-situations or in the situation, in which CAD is suspected. And the great variety of diagnostic options allows a targeted approach to each patient.

Disadvantages: On the other hand, just because of this huge variety of cardiac imaging methods, it is a challenge to make an optimal choice of the method, despite the existing guidelines.

Bleeding risks of antithrombotic medications, especially after PCI and AFTER CABG

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 4.4.

Importance of this issue, especially for use in aeromedical fitness assessment

The issue is important, because most patients with established coronary artery disease (CAD) have some form of antithrombotic medication. For example, all patients having had a coronary artery intervention (percutaneous coronary intervention = PCI or coronary artery bypass graft surgery = CABG) need an antithrombotic medication for the rest of their life. And as CAD is a very important issue when checking pilots and ATCOs having CAD, the evaluation of the bleeding risks of antithrombotic medications also plays an important role in the aeromedical fitness assessment, and the same is true for other forms of cardiac diseases, in which antithrombotic medications are also used like in atrial fibrillation (AF).

Differentiation of the different categories of antithrombotic medications

All antithrombotic medications are related with an increased bleeding risk, but there are huge differences between the drugs or drug combinations. Here we concentrate only on the bleeding risks of antithrombotic medications, but it is clear, that in each case, the overall risk related to the whole cardiovascular situation has to be considered. - The bleeding risk under aspirin-therapy and under antiplatelet drugs $P2Y_{12}$ receptor blockers as monotherapy can be considered as low, and this situation should not lead to a limitation of the fitness for pilots and ATCOs to fulfil their duties. - The use of dual antiplatelet therapy (DAPT) has a higher bleeding risk than the intake of a single antiplatelet drug. Patients who need DAPT have also an underlying disease which is not negligible. The risk of patients with DAPT should be analysed on an individual basis, the result of it might lead to a limitation of aeromedical fitness or to unfitness. - Triple antithrombotic medication (anticoagulation included) has a very high risk and is not compatible with fitness for pilots and ATCOs to fulfil their duties. - The bleeding risk of anticoagulation with vitamin K antagonists (VKA) and with non-vitamin K oral anticoagulants (NOAC) is in general equal or increased only to a small degree compared with the bleeding risk of aspirin. These situations are compatible with a restricted aeromedical fitness, and, considering the data of the recent literature, they might be even compatible with an unrestricted fitness in many cases. Concerning the situation of VKA-treatment, there must be special requirements in regard to the international normalized ratio (INR) values, maybe similar to those which found in the current EASA medical requirements.

Methods which can be used for screening and for monitoring purposes and frequency of the assessments

The method to analyse the antithrombotic effect of the VKA is defined (checking INR). For the other antithrombotic medications, there is no need to directly measure the antithrombotic effect of the drug used. Important is the evaluation if bleeding events have occurred. In order to prove a bleeding event, clinical and specific analysing methods are used which are chosen according to the kind of bleeding in request. Those methods can be used for initial analysis (screening) as well as for monitoring purposes, the frequencies of which must be defined according to an individual basis.

Costs and cost-effectiveness

The therapy with antithrombotic medications is followed by clear indications, the costs have to be accepted, they are acceptable, but - of course - there exist national variations. But the costs of methods used for analysing possible or proven bleeding side effects of antithrombotic medications must be considered by a cost-benefit evaluation.

Availability of the method

Checking of antithrombotic medications is usually an issue for general practitioner/ AMEs. Testing for bleeding side effects of antithrombotic medications is primarily also performed by general practitioner/AMEs. If there is a need for specific methods, then smaller or higher qualified hospitals/specialized centres are involved.

Availability of the methods and of special expertise at EU member state level

All diagnostic and therapeutic requirements in respect to the issue given in this document can be fulfilled in all EU member states.

Classification of the bleeding risks of antithrombotic medications

As stated above, the bleeding risks vary between very low until very high risk according to the used medication. This variation must be considered in the aeromedical checking of pilots and ATCOs. Pilots and ATCOs being in a very low and low risk situation should have no limitation of the fitness to fulfil their duties. Those with a very high-risk situation should be declared as unfit. The risk categories in between (moderate or high) might be declared as fit with restriction. - In presence of a bleeding side effect, the determination of fitness must be declared on an individual basis (it depends on the severity of such a side effect).

Advantages and disadvantages of antithrombotic medications and of the methods used for analysing bleeding side effects of those drugs:

Advantages are, that there are many treatment options for the selection of antithrombotic medication in the different cardiovascular situations. This means, that drugs or drug combinations can be chosen by weighing the antithrombotic effect against the risk of bleeding side effect, similar as evaluating the cost-benefit, as described above.

Disadvantages: Disadvantages of antithrombotic medications are evident. - Disadvantages of the methods which are used to analyse possible or proven bleeding side effects might be the costs of the method chosen. And there are specific risks of those methods, which contain an invasive procedure. How much those situations influence the assessment of aeromedical fitness; this must be decided on an individual basis.

COVID-19

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 4.12.

Importance of this issue (clinical presentation of the COVID-19 disease, its possible clinical complications, the aspects of vaccination and the use of specific diagnostic methods), especially for use in aeromedical fitness assessment

The issue is important, because COVID-19 disease is still relevant and the disease can affect everyone. In the acute phase of COVID-19 the person (pilot/ ATCO) must be considered as not able to perform his duties. When he has recovered without complications, then the person can be considered as healthy/fit. In most cases, the vaccination is not related with harm, and if yes, then the case has to be evaluated on an individual basis. Also, on an individual basis, a person has to be assessed if there is a suspicion of long COVID syndrome.

Which methods can be used for screening and which for monitoring purposes and frequency of the assessment

The clinical evaluation is the most important diagnostic point, as well for initial screening as well as for follow-up (monitoring) checking. If suspicion of peri- and/or myocarditis is given, then cardiac imaging techniques such as echocardiography or cardiovascular magnetic resonance imaging (CMR) might be required. The time intervals between monitoring checking have to be defined on an individual basis.

Costs and cost-effectiveness

As long as no hospitalization is required, and as long as no cardiac imaging techniques are used, the costs related to COVID-19 disease and its complications are relatively low.

Availability of the method: by AME, by specialist (cardiologist), smaller or middle-sized hospitals, only center hospitals?

The main contact point is the general practitioner/ AME. Severe cases might be hospitalized, in general, a regional hospital is sufficient for this purpose. Of course, special methods such as echocardiography, CMR or other techniques must be performed by specialists/ specialized centers.

Availability of the methods and of special expertise at EU member state level

See section above. All requirements for checking patients and for applying specific methods can be fulfilled by all EU member states.

Classification of the risk of the methods which might be used for checking patients with suspicion of COVID-19 disease or with proven COVID-19 disease with or without complications and for vaccination

These methods can be classified as “no risk” or, as an exception, as “low risk” (see below concerning therapeutic options) for patients as well as for pilots and ATCOs. For pilots and ATCOs the evaluated risk - done on an individual basis - is the basis for the decision about their fitness to fulfil their duties.

Advantages and disadvantages of the disease and the applied methods

Advantages: The diagnosis of COVID-19 infection is quite easy, and the therapeutic and the behaviour measures are clearly defined. In most cases, vaccination and complications of vaccination have neither specific diagnostic nor therapeutic problems. In severe cases of COVID-19 disease, a hospitalization is required, and in this case, there are also quite well-defined therapeutic procedures.

Disadvantages: But the diagnosis of long COVID syndrome can be very challenging. Symptoms which could be suspicious for long COVID syndrome could be caused by a clinical situation, which is not related to an undergone COVID-19 infection.

Risk classification of the therapeutic measures

Treatment options of manifested COVID-19 disease, of side effects of vaccination or of long COVID syndrome are dependent on the clinical manifestation. In most situations, the treatment corresponds to a symptomatic treatment, and those treatments are without risks. For example, acute pericarditis is treated in the same way as pericarditis of other than COVID-19 origin. But there are some established treatment options for patients with severe COVID-19 disease (mainly hospitalized patients), including classical medication like dexamethasone or anticoagulation etc. And there exist also several specific new drugs for severe cases. Those medications are related with some risks (for example bleeding risk). For the aeromedical evaluation, this is not a problem, because those pilots/ATCOs are unfit to fulfil their duties at that moment because they are severely ill.

5. Arrhythmias

Atrial Fibrillation

The issue and comments in this document are related to the following corresponding subchapters in Report CaVD D-1.1/D-1.2:

5.1 Atrial fibrillation
5.2 Indication of anticoagulation in atrial fibrillation

Importance of this issue, especially for use in aeromedical fitness assessment

Atrial fibrillation (AF) is the most common tachyarrhythmia. Its incidence increases with age. Therefore, many pilots and ATCOs will certainly develop AF during their career. These pilots and ATCOs have to be examined for diseases and risk factors leading to AF. This will include cardiological examinations for coronary artery disease, valvular heart disease, cardiomyopathies etc., but also non-cardiological testing for hypertension, hyperthyroidism, electrolyte disorders etc. Treatment could include antiarrhythmic drug treatment, catheter ablation or both in combination. Additionally, anticoagulation might be required depending on risk score results.

Differentiation of therapeutic options for AF

Basic therapeutic strategies for AF are rate control with the aim of normalizing heart rate during AF, and rhythm control with the aim of establishing and maintaining sinus rhythm. In most pilots and ATCOs, rhythm control will be the strategy of choice. This can be achieved by antiarrhythmic drug therapy and/or catheter ablation. As class IC and class III antiarrhythmic drugs are often not compatible with flying because of their side effects, catheter ablation will be the adequate treatment for many pilots and ATCOs with recurrent symptomatic AF. The main indication of catheter ablation is symptom relief. Although catheter ablation has shown superiority in arrhythmia-free survival as compared to antiarrhythmic drug treatment, significant advantages concerning outcomes such as death, stroke, or major bleedings in comparison to antiarrhythmic drug treatment have not been proven so far.

Differentiation of options for anticoagulation in AF

The decision if anticoagulation is indicated depends on certain risk scores. Options for oral anticoagulation are direct oral anticoagulants (DOAC) and vitamin K antagonists (VKA). DOAC are preferred in most cases. The most important contraindications for DOAC are mechanical heart valves and moderate to severe mitral valve stenosis which is usually not compatible with flying. If anticoagulation per se is not possible in those with a clear indication, e. g. because of a high bleeding risk, interventional left atrial appendage occlusion may be an alternative. But this will very seldom be indicated in pilot and ATCOs.

Methods which can be used for screening and for monitoring purposes and frequency of the assessments

Pilots and ATCOs with AF will often report symptoms which can be classified by the EHRA classification (European Heart Rhythm Association). However, many pilots and ATCOs with AF are asymptomatic or have symptoms which are not specific for AF. Methods for screening and monitoring of AF are resting ECG, Holter ECG, telemetry ECG or telemetry monitoring, event or loop recorders which can be external or implantable. Additionally, different wearables including watches and belts are available and are gaining importance along with their increasing reliability. The frequency of screening and monitoring is very much case-dependent. It depends on the long-term stability of pilots and ATCOs with a history of AF, and on the history of treatments

such as catheter ablations. - For anticoagulation with VKA monitoring of the international normalized ratio (INR) is the appropriate method, which can be performed by the treating physician or by means of near-patient measurement systems. A regularly applicable monitoring option for DOAC does not exist. The frequency of INR monitoring during VKA treatment is case-dependent. Using near-patient systems should generally be preferred, as measurements are usually performed in closer time intervals and could be done shortly prior to flight if required, and as patients usually have a better knowledge, and are more involved in the management of their anticoagulation.

Costs and cost-effectiveness

Comparing antiarrhythmic drug treatment and catheter ablation for rhythm control treatment, catheter ablation appears to be more expensive on short-term. But there have been studies indicating that the costs of antiarrhythmic drug treatment outweigh the costs for catheter ablation after about five years for certain patient groups, and that catheter ablation is therefore a potentially cost-effective treatment option. - Anticoagulation is mandatory in pilots and ATCOs with a clear indication. The aim of anticoagulation is to prevent thromboembolic events and especially stroke. Therefore, the costs for oral anticoagulants cannot be avoided if there is a clear indication for anticoagulation. There have been comparisons between DOACS and VKA concerning cost-effectiveness showing that DOAC are cost-effective especially in high-income countries.

Availability of the method

The evaluation of pilots and ATCOs with AF and their treatment initiation should be done in specialist centres for cardiology or even electrophysiology. If catheter ablation is indicated, it should be performed in specialized electrophysiological department of big heart centers or university hospitals. AF screening and the continuation of antiarrhythmic drug treatment or anticoagulation can be done by outpatient care in a practice.

Availability of the methods and of special expertise at EU member state level

Most diagnostic and treatment options for AF are available in all the EU member states. Catheter ablation with certain techniques might not be available in all the countries, but in such cases, electrophysiologists usually know where these could be done in neighbour countries.

Classification of risk

The risk of AF itself depends very much on the symptomatology, on potentially underlying diseases, and especially on the stroke risk, which can be estimated by means of risk scores (currently the CHA_2DS_2Vasc score). In case of antiarrhythmic drug treatment, their side effects have also to be considered. Pilots and ATCOs with a high risk may be unfit for performing their duties, pilots with moderate risk may be fit with limitations.

The bleeding risk during anticoagulation can also be estimated by certain risk scores (currently the HAS-BLED score) in the general population. Additionally, it depends on the used medication and the quality of therapy adjustment (e. g. time in therapeutic range (TTR) in those treated with VKA). In those treated with VKA, the bleeding risk is usually lower in those using a near-patient measurement system. Pilots and ATCOs with low bleeding risk can usually fly without limitation, those with moderate risk might need restrictions, and those with high bleeding risk are unfit for flying.

Advantages and disadvantages of the methods

Regarding AF treatment, the main disadvantage of catheter ablation in comparison to antiarrhythmic drug treatment is its invasiveness and the periprocedural risk. In many cases, more than one catheter ablation is needed for long-term success. The main advantage of catheter ablation is the potential to avoid the side effects

of antiarrhythmic drugs. Long-term success has been shown to be better for catheter ablation than for antiarrhythmic drug treatment.

Regarding anticoagulation, advantages of DOAC in comparison to VKA are that there is no need for monitoring this treatment, the better stability of therapy adjustment, and a lower overall bleeding risk, especially for intracerebral bleedings. In patients treated with VKA, therapy adjustment has been shown to be more stable in those using a near-patient system in comparison to those with INR monitoring performed by the treating physician.

Ventricular and supraventricular ectopy

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 5.3.

Importance of this issue, especially for use in aeromedical fitness assessment

This issue "Ventricular and supraventricular ectopy" is of great importance in aeromedical fitness assessment, because premature ventricular complex (PVC) and premature atrial contractions (PAC) are common electrocardiographic phenomena which often lead to broad discussions about their relevance. The overall terms of PVC and PAC are ventricular ectopy (VE) and atrial ectopy (AE) respectively. Although a majority of PVC and PAC has not a negative significance, there are forms, especially concerning VE like ventricular tachycardia (VT), which are related with a nonnegligible risk, which has an influence when checking pilots and ATCOs for the fitness to fulfil their duties. The aetiology, the pathophysiology, the different electrocardiographic and clinical presentations and the risks of the different forms of VE and AE are well described in the corresponding subchapter in Report CaVD D-1.1/D-1.2.

Which methods can be used for screening and which for monitoring purposes and frequency of the assessment

VE and AE are detected in the electrocardiogram (ECG), often in a resting 12-lead ECG. Sometimes they are discovered on an ECG Holter monitoring, or they are an incidental finding in a routine physical examination. In rare cases, AE might have a risk of incident atrial fibrillation (AF); and very rarely, it might have a risk of other adverse outcomes such as stroke and all-cause mortality. And advanced forms of VE have an increased risk for fatal arrhythmias and sudden cardiac death, respectively. These forms of VE might be related to an underlying cardiac disease. They require further cardiological investigations, such as exercise tests, cardiac imaging techniques, and in specific cases even electrophysiologic studies (EPS). Very frequent PVC can lead to PVC-induced cardiomyopathy and require monitoring of the left ventricular ejection fraction. For advanced VE, there is a huge variety of treatment options, such as antiarrhythmic drugs and catheter ablation techniques. As mentioned above, more detailed comments are given in the corresponding subchapter in Report CaVD D-1.1/D-1.2. The methods and the time intervals for monitoring proven and relevant VE or AE in the long term follow up must be defined on an individual basis.

Costs and cost-effectiveness

As long as PVC and PAC present as nonsignificant electrocardiographic features, the costs are minimal (rest-ECG, maybe an ECG Holter, maybe exercise test). The costs become higher if advanced methods and/or therapeutic procedures are required. But if there is a clear indication for these not avoidable examinations and therapies, and if they are well chosen, the overall cost-effectiveness should still be guaranteed.

Availability of the method

The mentioned basic examinations are widely available. Resting ECGs are usually done by every AME; ECG Holter monitoring, and exercise ECG are available in cardiological practices. If advanced cardiological methods like cardiac imaging techniques are necessary, then these methods are available in many hospitals of medical centers with a cardiological department. If an EPS or a catheter ablation must be performed, there is a need for a cardiological center which has an electrophysiological section, like for example university hospitals.

Availability of the methods and of special expertise at EU member state level

The required testing for VE and AE should be available in all EU member countries. This is true for the different ECG-methods, but also for advanced cardiological evaluation. The latter examinations should at least be offered in big hospitals with cardiological departments. And - as mentioned above - for EPS and catheter ablation, there is a need for an electrophysiological section. There might be some differences in the different EU member countries concerning the amount of such specialized electrophysiological centres and concerning the expertise to perform the high specialist examinations/interventions, but it is difficult to know how big these differences are, and to know how much these differences might influence the diagnostic and therapeutic procedures in the individual case.

Classification of risk of the methods used in the evaluation of VE and AE and of the risk of VE and AE per se

Concerning the risks of the applied methods, there is almost no risk in the non-invasive ECG-examinations and in cardiac imaging-scanning if such a method is necessary. Invasive cardiological diagnostic methods like EPS and invasive therapeutic methods such as catheter intervention are related with a certain risk of nonnegligible complications. - As mentioned above, although PVCs are generally considered benign, they can lead to the development of cardiomyopathy, and they can be associated with VT, with syncope or even with sudden cardiac death. AE might also be related with significant adverse outcomes, even if this occurs rarely. Furthermore, possible side effects of drugs must be taken into account in cases where antiarrhythmic medical treatment has been established. - Concerning aeromedical fitness assessment, the different situations must be evaluated on an individual basis. Many situations of VE and AE do not influence negatively the fitness of pilots and ATCOs, others might lead to a complete unfitness or a restricted fitness. The international guidelines should be respected when evaluating the individual ectopy situation. Whenever possible, the assessment of the aeromedical fitness of pilots and ATCOs with advanced ectopy disease should be performed by cardiologists who are appointed as cardiologist consultants by the national aviation authorities. - More detailed information concerning the aeromedical fitness assessment will be presented in the subchapters of task 4 and task 5.

Bundle branch and fascicular blocks

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 5.4.

Importance of this issue, especially for use in aeromedical fitness assessment

Left bundle branch block (LBBB), right bundle branch block (RBBB), and fascicular blocks (FB) are of great importance in pilots and ATCOs, as they are very common, and as these findings could be a sign of structural heart disease. There are complete and incomplete bundle branch blocks (BBB) with a cut-off in QRS-duration of 120 ms. While incomplete BBB are usually less important, complete BBB usually require cardiological evaluation. Left anterior fascicular block (LAFB) is also very common, while left posterior fascicular block (LPFB)

is rare. A combination of RBBB and LAFB is called bifascicular block (BFB). Ruling out structural heart disease if indicated is crucial for the aeromedical fitness assessment of pilots and ATCOs.

Differentiation of diagnostic options for BBB and FB

The most important screening and monitoring examination for BBB and FB is a 12-lead resting electrogram (ECG). Holter monitoring is helpful to identify intermittent BBB or FB, exercise-induced BBB or FB can be identified by exercise-ECG. - If cardiological evaluation is indicated, e. g. in complete LBBB or RBBB detected for the first time, transthoracic echocardiography is usually the first and widely available option. Cardiomyopathy (CM), coronary artery disease (CAD), or valvular heart disease (VHD) could lead to BBB and have to be ruled out. Magnet resonance imaging (MRI) may also be helpful for this purpose. And coronary computed tomography angiography (CCTA) or invasive coronary angiography (ICA) are often required for the examination of coronary arteries, especially in those above 40 years of age. The new development of LBBB in combination with symptoms and/or laboratory findings could indicate acute myocardial infarction.

Differentiation of therapeutic options for BBB and FB

BBB or FB themselves do not require treatment. However, underlying cardiac disease has to be treated if identified. The combination of BFB plus first-degree atrioventricular block (AVB) can indicate a risk of progression to trifascicular block in some cases, which might eventually require pacemaker implantation.

Methods which can be used for screening and for monitoring purposes and frequency of the assessments

A resting ECG is the most important examination for screening and monitoring of BBB and FB. It should be performed in regular time intervals, usually at least annually. ECG Holter monitoring and exercise ECG can be used for intermittent or exercise-induced BBB and FB, respectively. Even if structural heart disease has been excluded initially, echocardiography should be performed in certain time intervals, as ECG changes can precede changes in cardiac imaging methods such as echocardiography or MRI. Cardiac imaging with MRI, CCTA, or even invasive testing, are usually only required during initial diagnostic work-up, when BBB has been detected.

Costs and cost-effectiveness

Resting ECG, ECG Holter monitoring, and exercise ECG are non-invasive cardiological examinations, which are available at low cost. They are used for screening and monitoring of BBB or FB, and their cost-effectiveness is very high. This is also true for transthoracic echocardiography. More expensive examinations including MRI, CCTA, or invasive examinations are usually only needed for the initial examination when structural heart disease has to be excluded. These examinations, however, are absolutely necessary in the interest of individual health and flight safety.

Availability of the method

Resting ECG is widely available and is usually performed by every AME. Exercise ECG, ECG Holter monitoring, and echocardiography are available in most cardiological practices, and of course in hospitals and heart centers. CCTA and MRI for cardiological imaging can be done in radiological institutes or in hospitals with radiological or big cardiological departments. Invasive examinations are rarely needed but can also be done in heart centers or hospitals with cardiological departments.

Availability of the methods and of special expertise at EU member state level

The above-mentioned diagnostic methods for screening and monitoring of BBB and FB, and for initial diagnostic work-up should be available in nearly all EU member states. All these countries will at least provide big heart centers or university hospitals where all the required examinations can be done.

Classification of risk

There is no real risk caused by the diagnostic methods used for cardiological evaluation in case of BBB or FB, as long as no invasive method are used which is only used in rare cases. - But there is a certain risk especially in complete LBBB that these ECG changes are an early indication for the development of cardiac disease including CM, CAD, or VHD. The detection of cardiac disease could lead to the denial of aeromedical fitness of pilots or ATCOs. The risk is slightly lower in complete RBBB, but it also exists. In a number of cases, the combination of BFB and first-degree AVB (in case of infrahisian block) can progress to complete AVB, which then has to be treated by pacemaker implantation. In the literature, significant associations between RBBB, LBBB, non-specific intraventricular conduction delay and the hazard of incident heart failure (HF), myocardial infarction as well as pacemaker implantation has been described. Absolute risk predictions of HF and pacemaker implantation revealed clinically relevant differences between having various BBB subtypes versus no BBB. The presence of LAFB can predict obstructive stenoses of the left main and/ or proximal left anterior descending coronary artery in patients with stable angina pectoris. LAFB carries no appreciable risk of progression to higher degrees of block. However, it may be associated with myocardial ischemia, and if newly acquired over age 40, underlying CAD should be excluded with CCTA. Isolated LPFB is an extremely rare ECG finding, and could be a valuable tool for arrhythmic risk stratification in young people, should be recognized as a pathological finding, and should prompt further investigation to detect underlying structural abnormalities.

Advantages and disadvantages of the methods

The described methods for screening and monitoring of BBB and FB, and for cardiological evaluation in order to examine for underlying cardiac disease have no disadvantages. They are of great importance for aeromedical decision making in pilots and ATCOs with BBB and FB in their ECG. The advantages are their wide availability, their good cost-effectiveness and their value for the identification of underlying cardiac disease leading to the respective ECG findings and being highly relevant for aeromedical decision making. - Whenever possible, the assessment of the aeromedical fitness of pilots and ATCOs, in which the evaluation of BBB and FB has led to significant underlying cardiac disease should be performed by cardiologists who are appointed as cardiologist consultants by the national aviation authorities.

More detailed information concerning the aeromedical fitness assessment will be presented in the subchapters of task 4 and task 5.

Atrioventricular block

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 5.5.

Importance of this issue, especially for use in aeromedical fitness assessment

The issue atrioventricular block (AVB) is of great importance in aeromedical fitness assessment, first because some forms of AVB can often be detected at initial examination of pilots and ATCOs, and second because the higher degrees of AVB have significant consequences (see below). - First degree atrioventricular block (AVB) and second degree AVB Mobitz type I (Wenckebach) are common findings in pilots and ATCOs, especially in young individuals with a high vagal tone. First-degree AVB in asymptomatic pilots and ATCOs can be regarded as a normal variant up to 300 ms with no further examinations needed. If the PR interval exceeds 300 ms, further evaluation is necessary. In case of normal results most pilots and ATCOs can remain fulfilling their duties. In asymptomatic pilots and ATCOs with second-degree AVB Mobitz type I (Wenckebach) as an incidental finding further examination is usually not required. As with first degree AVB, further investigation is only required in pilots and ATCOs with symptoms, diurnal occurrence or in those aged over 40 years at first presentation. Most pilots and ATCOs with Mobitz type I may be returned to unrestricted duties. - In contrast

to Mobitz type I, Mobitz type II is rarely seen in pilots and ATCOs. Individuals with AVB Mobitz type II and complete AVB must be investigated for underlying structural heart disease and, although often asymptomatic, pilots and ATCOs are unfit for performing their duties because of the risk of sudden cardiac death (SCD), syncope, bradycardia-related hemodynamic symptoms, and heart failure. In most cases pacemaker (PM) therapy is indicated. A review by an electrophysiologist is recommended.

Differentiation of diagnostic options for AVB

The screening test for AVB is usually a 12-lead resting ECG. After detection of AVB in a resting ECG or in case of symptoms, an ECG Holter monitoring is usually carried out to look for the degree of AVB during day and night-time, and to measure the length of pauses by AVB. An exercise ECG is important to evaluate if AVB normalizes under exercise, or if it deteriorates. Echocardiography and other cardiac imaging including computed tomography (CT) or magnet resonance imaging (MRI) are performed to look for underlying cardiac disease if indicated. Coronary artery disease should be ruled out in pilots and ATCOs above 40 years of age. Non-cardiac testing including electrolytes and thyroid hormones may also be required. In very rare cases, invasive electrophysiological testing with measurement of the His bundle-ventricular (H-V) interval might be helpful to discriminate between second degree AVB Mobitz I and II.

Differentiation of therapeutic options for AVB

In asymptomatic first and second degree AVB Mobitz type I, a treatment is usually not required. In second degree AVB Mobitz type II and third degree AVB, PM implantation is often required. This therapeutic option is pointed out in the task 2-subchapter “Cardiac Pacing”/”ICD”.

Methods which can be used for screening and for monitoring purposes and frequency of the assessments

A resting ECG is usually used for screening. It is performed in every initial examination for pilots and ATCOs, and in periodic medical examinations (PME) in certain time intervals defined in the regulations. In pilots and ATCOs with known AVB, monitoring is carried out by resting ECGs, ECG Holter monitoring, and exercise ECG. These assessments can be performed in every PME, shorter time intervals can be defined. Other methods for screening and/or monitoring are telemetric ECG monitoring, external/implantable event/loop recorders, and/or wearables including smart watches, belts or patches, and in specific cases other cardiovascular (CV) methods, especially CV imaging methods, which are used to define a possible or proven underlying cardiac disease.

Costs and cost-effectiveness

Resting ECG, ECG Holter monitoring, and exercise ECG are non-invasive cardiological examinations, which are available at low cost. Their effectiveness is very high. More extensive evaluation is rarely required in pilots and ATCOs, mostly in cases with second degree AVB Mobitz type II or third degree AVB. In those cases, more expensive cardiac imaging or even invasive cardiological examinations might be required. But these examinations are still very effective and cannot be avoided if there is a clear indication.

Availability of the method

The mentioned non-invasive examinations are widely available. Resting ECGs are usually done by every AME; Holter monitoring, and exercise ECG are available in cardiological practices. If cardiological imaging by CT or MRI or invasive testing should be required, these methods are available in many hospitals of medical centers with a cardiological department.

Availability of the methods and of special expertise at EU member state level

The required testing for AVB should be available in all EU member countries. This is true for non-invasive testing, but also for cardiac imaging and invasive cardiological evaluation. The latter examinations should at least be offered in big hospitals with cardiological departments and/or university hospitals.

Classification of risk

The risk of first degree AVB and second degree AVB Mobitz type I is very low. Pilots and ATCOs are mostly asymptomatic. AVB is often caused by increased vagal tone in young and sportif individuals. In cases with second degree AVB Mobitz type II or third degree AVB, the risk is much higher, but such cases are rare in pilots and ATCOs. AVB in those cases can lead to sudden cardiac death, syncope, bradycardia-related hemodynamic symptoms, and heart failure. Therefore, PM implantation is often required in those individuals, which can safely and effectively treat such higher degrees of AVB. Concerning the risks of the applied methods, there is no risk of the non-invasive examinations and almost no risks for CT- or MRI-scanning if such a method is necessary. The implantation of a PM and the situation of having a PM is related with a nonnegligible risk. This is further described in the task 2-subchapter “Cardiac Pacing”/ ”ICD”.

Advantages and disadvantages of the methods

The advantage of screening for AVB, evaluating and monitoring pilots and ATCOs with known AVB is the detection of higher degree AVB, and to mitigate the risk of sudden cardiac death, syncope, bradycardia-related hemodynamic symptoms, and heart failure as well as the risk of sudden incapacitation. Pilots and ATCOs at risk should be assessed as unfit and treated by PM implantation if indicated. A return to pilot and ATCO duties after PM implantation is possible in many cases. Pilots and ATCOs with first degree AVB and second degree AVB Mobitz type I can usually assessed as fit and do not need a specific treatment. - There are no disadvantages of the screening and monitoring methods mentioned in this document.

Asymptomatic ventricular pre-excitation

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 5.6.

Importance of this issue, especially for use in aeromedical fitness assessment

Asymptomatic ventricular pre-excitation is of great importance in aeromedical fitness assessment, especially because it can contain a high risk in specific cases. It is characterized by a delta wave and a short PR interval in the ECG. It shows the presence of an antegrade or both, antegrade and retrograde conducting accessory pathway (AP). As it is estimated that 1 in 1000 people will exhibit such a pattern, it will also be detected in initial applicants for pilot and ATCO careers. There are two main risks of asymptomatic pre-excitation, the development of atrioventricular re-entrant tachycardia (AVRT) and fast antegrade conduction over the AP in case of atrial fibrillation (AF), potentially leading to ventricular fibrillation (VF) sudden cardiac death (SCD). In former studies, the risk of cardiac arrest/VF has been estimated at 2.4 per 1000 person years (95% confidence interval 1.3 - 3.9**).** Therefore, an electrophysiological risk assessment is required at the initial examination and at periodic medical examinations.

Differentiation of diagnostic options for asymptomatic ventricular pre-excitation

The most reliable diagnostic test for asymptomatic ventricular pre-excitation is an invasive electrophysiologic study (EPS) with testing for certain high-risk features including conduction properties of the AP, multiple APs,

and the inducibility of AVRT. Antegrade conduction of an AP can be examined measuring the effective refractory period (ERP). An ERP below 250 ms would mean a fast conduction from atria to ventricles in case of AF and a high risk of SCD. During an AF episode, the shortest pre-excited RR interval (SPERRI) can be measured. A SPERRI ≤ 250 ms would also mean a high risk of VF and SCD. A retrograde conduction or even multiple APs with retrograde conduction can facilitate AVRT. A fast antegrade conduction of an AP is very unlikely in individuals with intermittent delta waves, or of the delta waves which disappear during exercise. Invasive testing by EPS would usually only be required for the initial examination of pilots and ATCOs. For the following periodic medical examinations, non-invasive testing is mostly sufficient.

Differentiation of therapeutic options for asymptomatic ventricular pre-excitation

In case of high-risk features and of course in symptomatic individuals with a Wolff-Parkinson-White syndrome, catheter ablation of the APs is the only reliable option with good long-term success.

Methods which can be used for screening and for monitoring purposes and frequency of the assessments

A resting-ECG is the adequate screening examination for asymptomatic pre-excitation. Once it has been detected, an exercise ECG can be used to evaluate the presence of the delta wave during exercise, an ECG Holter monitor could detect intermittent delta waves, and perhaps short episodes of AF and/or AVRT. Echocardiography should be performed to look for associated cardiac disease like Ebstein´s Anomaly.

Costs and cost-effectiveness

EPS and especially catheter ablation are more expensive than the non-invasive examinations mentioned above. But there is no alternative for a reliable risk stratification. In former times, ajmaline was used to assess conduction properties of accessory pathways. But studies have shown that ajmaline is not useful to assess electrophysiological characteristics of APs. In high-risk individuals, catheter ablation is the only reliable treatment option of APs.

Availability of the method

EPS and catheter ablation are available in hospitals with invasive cardiological departments including invasive electrophysiology. Non-invasive testing including ECG, exercise-ECG and ECG Holter monitoring can be done in centres for cardiological outpatient care, sometimes even by AMEs.

Availability of the methods and of special expertise at EU member state level

Invasive electrophysiological departments with the ability of ablating APs should be available in nearly all, if not all, EU member countries. This is of course also true for non-invasive cardiological testing.

Classification of risk

The risk of developing AVRT or AF with FBI tachycardia (fast, broad, irregular), VF or even SCD should initially be assessed by EPS in pilots and ATCOs. For reasons of greater caution in those groups the limit of ERP and SPERRI might be set to 300 ms instead of 250 ms in the general population. In high-risk individuals, catheter ablation of the AP is indicated. - The risk of EPS for risk stratification is very low. It might be higher if catheter ablation is required for APs near the AV node. A certain risk of iatrogenic AV block might exist in those cases. Additionally, there might be a very small risk of pericardial effusion if an AP at the free wall of an atrium needs to be ablated. However, there is no reasonable alternative for this procedure.

Advantages and disadvantages of the methods

The advantage of invasive risk assessment in initial applicants for a pilot or ATCO career is the avoidance of a sudden incapacitation in flight by a AVRT or rapidly conducted AF. Catheter ablation is a curative approach for symptomatic or asymptomatic high-risk individuals, a reasonable alternative does not exist for those individuals. - A small disadvantage of catheter ablation as a treatment option is the small periprocedural risk, which depends on the localization of the AP.

Channelopathies

The issue and comments in this document are related to Report CaVD D-1.1/D-1.2 subchapter 5.7.

Importance of this issue, especially for use in aeromedical fitness assessment

This issue "Channelopathies" is of great importance in aeromedical fitness assessment, even if these diseases are quite rare in the general population. But they are mostly diagnosed in younger people, and they can be related to severe complications. As the electrocardiogram (ECG) can show a wide variety between normal and clearly abnormal features compatible with one of the different channelopathies, there is often a discussion if an ECG-finding is already pathologic and as such compatible with a defined channelopathy or not. AMEs are not seldom confronted with this dilemma when performing the initial aeromedical examination of pilots and ATCOs. And the same is true for cardiologists, when pilots and ATCOs with a suspicious ECG are sent to them. First, it is a challenge to make a clear diagnosis: Can a given ECG still be considered as normal, or is there a real suspicion of the presence of a channelopathy disorder. Second, if a suspicion or the diagnosis of a channelopathy is given, there is also a challenge to classify the severity of the given channelopathy. Brugada syndrome (BrS) and Early repolarization syndrome (ERS) are good examples showing that some ECG presentations can be declared as acceptable or as being still in the range of normal, whereas others ECG presentations must be considered having a probably high risk for fatal arrhythmias and sudden cardiac death. ERS-ECGs are often found in young persons and athletes, and most of them correspond to a benign situation, but a small part of them can be related with a high risk. For the aeromedical fitness assessment, in presence of suspicious or proven disease of channelopathy, it is of utmost importance to make a clear diagnosis and classification of the severity of the disease in order to make a distinct assessment concerning the fitness of pilots and ATCOs to fulfil their duties. A clear evaluation is also important for all those persons in order to install adequate therapeutic procedures. The list of the most important channelopathies, the different ECG-criteria, the pathophysiology, the clinical presentations, the significance and the indications of genetic testing, the risks of the different forms of channelopathies and the therapeutic options are well described in the corresponding subchapter in Report CaVD D-1.1/D-1.2.

Which methods can be used for screening and which for monitoring purposes and frequency of the assessment?

Channelopathies are detected in the resting 12-lead ECG. Concerning pilots and ATCOs, the first ECG in their life is often performed at the time when they present as initial applicants (most of them being young) at the AME; at that moment, the suspicion of a channelopathy is raised. Then, suspicious ECGs are discussed in general with a cardiologist, who has to decide if additional examinations shall be performed in order to come to a clear diagnosis which might have also therapeutic consequences. For the choice of additional examinations and for the consequences which result out of the findings of this further evaluation, there are clear recommendations in the already cited corresponding subchapter in Report CaVD D-1.1/D-1.2. And it is practical if the chosen cardiologists are appointed as cardiologist consultants by the national aviation authorities, who are familiar

with aeromedical assessments and decision making for the fitness of pilots and ATCOs to fulfil their duties. According to the classification of the given channelopathy, the amount of monitoring examinations which shall be undertaken in the long term follow up and the corresponding time intervals can be defined.

Costs and cost-effectiveness

Of course, the cost of the main diagnostic element, the ECG, is minimal. As soon as additional methods including genetic testing or invasive procedures such as electrophysiologic study (EPS) or implantation of an implantable cardioverter defibrillator (ICD) must be undertaken, the costs become relevant. But if there is a clear indication for these not avoidable examinations and therapies, and if they are well chosen considering the international guidelines, the overall cost-effectiveness should still be guaranteed.

Availability of the method

A resting ECG can be performed by every AME. The analysis of a suspicious ECG will be performed by a cardiologist. Additional methods or invasive procedures must be performed in specialist centres. These methods are first of all genetic testing, EPS and implantation of ICD, and often also cardiac imaging techniques are used in the diagnostic procedure.

Availability of the methods and of special expertise at EU member state level

The required method for diagnosing and treating persons with the one or other form of suspected or proven channelopathy should be available in all EU member countries. Advanced cardiological evaluation including genetic testing and invasive procedures like EPS or ICD-implantation must be performed in specialized hospitals with cardiological departments including an electrophysiological section, and in case of genetic testing, in specialized genetic centres. There might be some differences in the EU member countries concerning the amount of such specialized electrophysiological centres and concerning the expertise to perform the high specialist examinations/interventions, but it is difficult to know how big these differences are, and to know how much these differences might influence the diagnostic and therapeutic procedures in the individual case. If one country has no specialized genetic centre, there is no problem to send the probe, which must be genetically tested, to another country which has the required genetic centre and expertise for such sophisticated examinations.

Classification of risk of the methods used in the evaluation of channelopathies and of the risk of channelopathies per se

Concerning the risks of the applied methods, to perform an ECG has of course no risk. But advanced cardiological methods are related to certain risks. This is especially the case for invasive procedures such as EPS or ICD-implantation. The specific medications which might be introduced have in general no relevant side effects. - As stated above some forms of the different channelopathy diseases must be considered as high-risk situations needing specific attention and often the implantation of an ICD. It is important that international guidelines are respected in the evaluation of the abnormal findings and in the choice of the therapeutic options. - Concerning aeromedical fitness assessment, the different situations must be evaluated on an individual basis. Many forms of channelopathies do not negatively influence the fitness of pilots and ATCOs, but those with higher risks lead to a complete unfitness or a restricted fitness. Whenever possible, the assessment of the aeromedical fitness of pilots and ATCOs with advanced channelopathy disease should be performed by cardiologists who are appointed as cardiologist consultants by the national aviation authorities. More detailed information concerning the aeromedical fitness assessment will be presented in the subchapters of task 4 and task 5.

Cardiac Pacing, Implantable Cardioverter Defibrillator

The issue and comments in this document are related to the following corresponding subchapters in Report CaVD D-1.1/D-1.2:

5.8. Cardiac pacing
5.9. Implantable Cardioverter Defibrillator (ICD)

Importance of this issue, especially for use in aeromedical fitness assessment

The issues Cardiac pacing and Implantable cardioverter defibrillator (ICD) are of great importance in aeromedical fitness assessment, first because the number of patients and as such also of pilots and ATCOs who need a pacemaker (PM) or an ICD is not negligible, and second because the presence of a PM and/or ICD has significant consequences (see below). - For pilots and ATCOs it is possible to perform their duties with implanted PM under certain preconditions. Patients with bradycardia or conduction system disease should be evaluated properly according to the ESC guidelines. Most important indications for cardiac pacing are bradycardia because of sinus node disease (SND) and/or atrioventricular block (AVB). One of the new developments in cardiac pacing is conduction system pacing (CSP) with either His bundle pacing (HBP) or left bundle branch area pacing (LBBAP) in lieu of right ventricular pacing (RVP) to prevent pacing-induced cardiomyopathy, or in lieu of biventricular pacing (BiV) in cardiac resynchronization therapy (CRT). LBBAP is regarded as the preferred method compared to HBP in most cases. As CRT is used in patients with heart failure, this indication for CSP is not relevant for pilots and ATCOs. To avoid complications caused by transvenous leads and being able to treat patients with difficult or without transvenous access, leadless pacing (LP) has been developed with devices implanted by percutaneously inserted femoral venous catheters. LP might rarely be an alternative for pilots and ATCOs with difficult transvenous access. - ICDs, however, have not been compatible with flying or ATCO duties. Ventricular tachycardia or ventricular fibrillation can lead to a short incapacitation or even unconsciousness while the capacitor charges and the shock is delivered. After the shock is delivered, a few seconds can elapse until the individual is fully oriented. The same is true for subcutaneous ICD (S-ICD) or extravascular ICD (EV-ICD). Furthermore, the risk of inappropriate delivery of an ICD-shock must also be considered.

Differentiation of therapeutic options of cardiac pacing

Cardiac pacing is usually used as a treatment for pilots and ATCOs with SND, AVB, or bradyarrhythmia in individuals with atrial fibrillation (AF). While in permanent AF, which is very rare in pilots and ATCOs, only a ventricular lead is implanted, and in SND without AVB a single lead might be implanted in the atrium, in most other cases an atrial and a ventricular lead is required. Ventricular pacing should be reduced as much as possible to reduce pacemaker-induced cardiomyopathy. For this purpose, CSP as described above can be used in lieu of RVP. For individuals with difficult transvenous access, LP might be an option. CRT is usually not an option for pilots and ATCOs, because heart failure requiring CRT is not compatible with flying. - The requirements of the PM modalities for pilots and ATCOs will be discussed in detail in tasks 4 and 5. Those requirements are important in order to avoid electromagnetic interferences.

Differentiation of options for ICD treatment

As described above, ICD is usually not an adequate therapeutic option for pilots and ATCOs. For the general population, an ICD is a well-established treatment option for ventricular tachyarrhythmia and the primary and secondary prevention of SCD. There are clear recommendations concerning the different indications for implantation of ICD. S-ICD has been introduced to address problems related to transvenous leads. S-ICD has no intravascular lead and therefore cannot deliver anti-tachycardia pacing (ATP). EV-ICD systems provide an

alternative to the transvenous ICDs in patients without the need for bradycardia pacing. Placement of EV electrodes in closer proximity to the heart requires less shock energy for defibrillation, and therefore smaller pulse generators, compared with the S-ICD. Delivery of ATP is possible.

Methods which can be used for screening and for monitoring purposes and frequency of the assessments

Cardiac implantable electronic devices (CIED) have to be checked in regular follow-up examinations, usually at least once per year. For this purpose, special programmers and monitoring devices are required which are company specific. Additionally, most CIEDs have a remote monitoring option allowing CIEDs to be monitored via internet by the treating physician is his practice or heart centre.

Costs and cost-effectiveness

CIEDs are comparatively expensive treatment options requiring not only the device itself, but also a programmer and/or a remote monitoring system for monitoring and follow-up examinations. But if there is a clear indication for the use of such devices, they are without a reasonable alternative.

Availability of the method

Cardiac PMs and ICDs are usually implanted in heart centres with an electrophysiology department. Especially PM implantations are also possible in adequately equipped cardiological practices. For follow-up examinations, programmer and monitoring devices from the specific company are required, computers and internet access for remote monitoring options should also be available. Therefore, device monitoring and follow-up examinations need to be done in adequately equipped practices, or in heart centres.

Availability of the methods and of special expertise at EU member state level

Currently, treatment with cardiac PMs and ICDs is possible in most EU member states. But in some of them, all the different treatment options are only offered in big heart centres or university hospitals. But there is an increasing number of specialized hospitals or practices even in smaller countries.

Classification of risk

The probability, that complications occur in the procedures PM-implantation and/or ICD-implantation, is moderate, depending on the method chosen and on the experience of the specialist performing the intervention. And specific risks of ICD treatment in the long term follow up have been described above. Therefore, an ICD is usually not compatible with pilot or ATCO duties. - Examples of short-term complications after CIED implantation are pneumothorax, cardiac perforation, cardiac tamponade, early lead-displacement, hematomas, and periprocedural wound infections. Pneumothorax would be particularly dangerous, because the trapped air will expand in flight because of the reduced ambient pressure, even in a pressurized cabin. - Whilst such short-term complications can widely be excluded by a postprocedural three months observation period, pilots and ATCOs with CIED can still be affected by long-term complications, including lead dislodgement, lead failure, lead destruction by subclavian crush, pre-erosion and erosion of the pocket, infection, clinically significant haematoma, early battery depletion of the generator, or even stroke or death. Although these complications are very rare after PM implantation, most of them can lead to sudden incapacitation or at least distraction of pilots and ATCOs and impair the fitness to fulfil their duties. - The risk of electromagnetic interference (EMI) with CIEDs is very low in commercial aircraft but can be higher in military aircraft with radar and communication systems with very strong electrical fields. There are no reports in literature about deleterious effects of EMI on CIEDs in commercial aircraft. - Another possible issue is cyber security because of remote monitoring systems. Although there has yet to be a cyberattack leading to direct patient harm reported in the literature, the theoretical threat has been demonstrated in research laboratory

scenarios and echoed in patient concerns. - Whenever possible, the assessment of the aeromedical fitness of pilots and ATCOs with PMs and ICDs should be performed by cardiologists who are appointed as cardiologist consultants by the national aviation authorities. More detailed information concerning the aeromedical fitness assessment will be presented in the subchapters of task 4 and task 5.

Advantages and disadvantages of the methods

The implantation of cardiac PMs is the only option to keep pilots or ATCOs with SND, AVB, or bradyarrhythmia during AF able to perform their duties. It is therefore without an alternative. Implantation and follow-up have to be performed in specialized treatment facilities. Modern devices are safe, complication rates are very low, although several possible complications exist as described above. - ICDs are usually not compatible with flying and ATC-activity. Exemptions might be possible in class 2-pilots, in LAPL-pilots and maybe also in ATCOs, if the following criteria are fulfilled: 1) The ICD has been implanted as a preventive measure (example: Brugada-syndrome without any previous ventricular tachycardia or ventricular fibrillation), 2) the underlying cardiac disease has not a relevant additional risk besides the arrhythmia risk, 3) there has not been a spontaneous ICD shock delivery for at least one year. An exemption would only be possible with a restriction (for example an OSL-limitation). More detailed information will be presented in the subchapters of task 4 and task 5.

6. Cardiovascular incapacitation risk assessment

For the scientific background and literature references the reader is referred to the corresponding subchapter 6 of report CaVD-Pace D-1.1/D-1.2.

Importance and suitability of recommended risk assessment concept for use in aeromedical certification examinations

In aeromedical fitness examinations it is important to predict incapacitation levels ranging from subtle to complete with variable probabilities of occurrence while taking the operational impact of an incapacitation event and potential mitigation measures into account. This can best be done by using risk matrices, which plot the operational impact of an event (severity) against the probability of occurrence of the event and provide a semi-quantitative assessment of the flight safety impact of a broad spectrum of cardiological conditions with variable probabilities of occurrence. A series of risk matrices that reflect the varying operational risk pertinent to specific aircrew/ATCO roles should be developed for different classes of medical certificates: Class 1 (single pilot, multi-pilot), Class 2, Class 3 (ATCO Area/Terminal control, Tower/ Remote and Virtual tower), and LAPL.

The ICAO standard 5x5 risk matrix as well as the ICAO risk probability categories are recommended. Acceptability of the risk requires careful consideration taking into account the type of operation for which the risk is assessed (multi-crew ops, single pilot ops, different ATC ops). To measure the safety impact of cardiovascular incapacitation events, severity and probability levels have to be defined. It is recommended to use the severity levels as defined by ICAO. For determination of probability levels, it is recommended to use, whenever possible, epidemiological data expressed as the percentage of risk per year, per 5 years, or per 10 years. These data are better suited to be used for an assessment of the probability of a cardiac medical event than probability per flight hour as is used in most risk estimations of technical aircraft failures. To consider the tolerability (acceptability) of the risk it is recommended to follow the levels of tolerability and the associated colours in the matrix as defined by ICAO in their Safety Management Manual.

Comparison with other diagnostic methods

The current commonly used method for risk assessment is the 1% rule which is based on debatable assumptions and does insufficiently address operational aspects and requirements. Although the 1% rule has some value in predicting complete sudden incapacitation during the critical flight phases start, take off, approach, and landing this rule is less suitable for risk prediction of incapacitation levels during the entire flight ranging from subtle to complete with variable probabilities of occurrence and for different classes of medical certificates. It is also not suitable for ATC operations.

Frequency of screening

It is recommended to use the matrix method for each aeromedical risk examination of pilots and ATCOs applying for a medical certificate.

Costs and cost-effectiveness

The method is highly cost-effective and can be used on a computer as well as on paper.

Availability of the method

The matrix method can be made available in all member states and can be used by AMEs, and (aviation) cardiologists.

Advantages

- The matrix method can be used for different pilot roles (multiple crew ATPL, single commercial pilot, leisure pilot) and air traffic control operations.
- The method offers structured and systematic decision making and may lead to optimal evidence-based reasoning.
- The method is focused on cardiovascular incapacitation events and their consequences rather than on cardiological diagnoses and therefore offers clear insight to AMEs about their decision process and clearer communication with pilots and ATCOs about their risk(s).

Disadvantages

- Using the risk matrix requires knowledge of operational consequences of cardiovascular incapacitation events. The method should be used by an AME and, if necessary, assisted by an (aviation) cardiologist and in consultation with operational competence.
- AMEs, and (aviation) cardiologists, will initially need guidance and a brief training to apply the method appropriately.

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