Aeromedical Certification Following Mechanical Aortic and Mitral Valve Implants in the United Kingdom

Tania Jagathesan; Sean O'Nunain; Michael O'Brien

BACKGROUND: For many years, anticoagulant therapy had been deemed unacceptable for civilian pilot medical certification in the United Kingdom under the Joint Aviation Authorities Requirements and, therefore, mechanical valve implants were disqualifying. In 2012, this restriction was removed by implementation of the European Union requirements. This study was undertaken to assess the medical evidence available to develop a certificatory policy following mechanical valve implants in the United Kingdom.

METHODS: A literature review was performed for complication rates following the implantation of mechanical aortic and mitral valves. This study was confined to the three major types of valve commonly used in current clinical practice: the ATS, the Carbomedics, and the St. Jude Medical valves.

RESULTS: We identified 28 papers on aortic valve replacements and 22 papers on mitral valve replacements. Data were extracted for the late complication rates for endocarditis, paravalvular leak, thromboembolism, hemorrhage, and structural valve dysfunction. The total calculated incidence of a late complication was 3.8% per annum for aortic valves over a mean follow-up period of 57 mo and 5.2% per annum for mitral valves over a mean follow-up period of 61 mo. Both of these exceed the maximum 1% per annum medical incapacitation risk considered acceptable for professional multicrew pilot operations.

CONCLUSION: Confounders and sources of error in estimating the risks and methods to mitigate these are considered. A certificatory policy is proposed and the UK experience of mechanical valve replacements is described.

KEYWORDS: anti-coagulation, fitness to fly, incapacitation risk, regulations, pilots.

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The aortic valve is the most commonly replaced cardiac valve, with about 5000 operations undertaken each year in the United Kingdom and about 85,000 in the United States. European and American guidelines have been published for the management of valvular heart disease.[33,44] The commonest clinical indication for an aortic valve implant is severe aortic stenosis in the elderly, while in younger individuals it is more likely to be associated with a congenital bicuspid valve, aortic dilatation, and aneurysm formation. The commonest indication for isolated mitral valve replacement is severe mitral regurgitation due to mitral valve prolapse, where a valve repair procedure is not technically feasible. The demographic of the pilot population includes young adults for whom mechanical prosthetic valves are often recommended over tissue valves, due to the greater durability and longer life of the implant. The main disadvantage of mechanical valves is the need for lifelong anticoagulant therapy, which was previously unacceptable under the European Joint Aviation Requirements (JAR) and, therefore, mechanical valve implants were disqualifying for certification in pilots. In 2012, the United Kingdom implemented the European Union (EU) Requirements set out by the European Aviation Safety Agency (EASA) which removed this bar on mechanical valve replacements. This study was undertaken to develop an evidence-based policy for the certification of UK civilian pilots following mechanical valve implants.

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There are many types of aortic valve implant in existence; however, for the purposes of developing a certificatory policy for aircrew, this study was confined to the three major types of valve used in common clinical practice: the St. Jude Medical, Carbomedics, and ATS Medical Inc. valves, each with different characteristics. The St. Jude Medical (SJM) valve was first implanted in 1977 and has a bileaflet central flow design that provided a lower transvalvular pressure gradient than other mechanical valves of the time. It was claimed that its pyrolytic carbon construction gave greater durability and thrombo-resistance. The Carbomedics (CM) valve, which first became available in 1986, is a second generation bileaflet valve that was claimed to have improved hemodynamic performance by the removal of pivot guard struts which impeded blood flow, less thrombo-resistance at the hinge mechanism, and a carbon covering to reduce tissue overgrowth. The ATS Open Pivot heart valve was first introduced in 1992 and is a full pyrolytic carbon valve, which claimed to have fewer thrombo-embolic events as a result of the convex spherical hinge mechanism without projecting pivot guards.

METHODS

A PubMed search of the literature was performed for English language publications with complication rates following the implantation of SJM, CM, and ATS valves. The search was confined to aortic and mitral valve replacements, as pulmonary and tricuspid replacements are rarely seen in the pilot population. Data was extracted for the valve type, number of patients, mean age, mean follow-up, and total follow-up period in patient years. The linearized incidence was recorded for the complications of structural valve dysfunction, endocarditis, paravalvular leak, valve thrombosis, thrombo-embolism, and anticoagulant-related hemorrhage. Only papers with complication rates expressed as linearized incidences in percentage per patient year were included to allow the collective analysis of the data.

A search of the UK Civil Aviation Authority (CAA) computer medical records database for the diagnostic terms 'mitral/aortic mechanical valve replacement' and 'anticoagulant therapy' between 1990 and 2017 was performed. The type of valve implant, age at time of implant, follow-up period, and any reported complications were recorded.

RESULTS

Five papers were found that had data for aortic and mitral valves only expressed as a combined figure and these were excluded from data analysis.[11,35,37,45,46] There were 28 aortic valve papers and 22 mitral valve papers which met the criteria for inclusion. Some of these contained data for more than one valve type. The demographic of these papers is shown in **Table I.**

Complications following mechanical valve replacement surgery are typically classified into early and late. Early complications are defined as those arising within 30 d of surgery. As a pilot would not be permitted to return to flying so soon after such a major operation, early complications were excluded from our analysis. This appears justified as the calculated mean 30-d mortality for aortic valves was 2.9% and for mitral valves was 3.4%. Late complications are defined as those occurring more than 30 d postoperatively. Structural valve dysfunction is a recognized late complication but is exceptionally rare, with a rate of 0.06% per patient year reported for mitral valves in only one paper.[16] There are five other well-recognized late complications: endocarditis, paravalvular leak, valve thrombosis, thrombo-embolism, and anticoagulant-related hemorrhage.

The linearized incidence rate is the number of observed events divided by the total number of patient years of follow-up and is expressed as a percentage per patient year. However, to simply calculate a mean of the linearized incidences from the papers would not take into account the differing contributions from the various numbers of patients in each study. The linearized incidence is, therefore, first multiplied by the number of patient years to give the number of observed events for each study. This is summed for all the studies to give the total

Table I. Valve Literature.

VALVE TYPE	NUMBER OF PAPERS	NUMBER OF PATIENTS	MEAN AGE (YEARS)	MEAN FOLLOW-UP PERIOD (MONTHS)	TOTAL FOLLOW-UP (PATIENT YEARS)
Aortic*					
SJM	9	3777	51	70	27,402
CM	14	4794	54	55	10,323
ATS	9	2528	61	49	12,569
Total	28	11,099	55	57	44,670
		Average target INR range 2.1 to 2.9 (minimum 1.5, maximum 2.1)			
Mitral**					
SJM	7	2478	54	63	21,073
CM	9	2802	58	69	8835
ATS	7	1031	61	49	13,377
Total	22	6311	58	61	38,068
		Average target INR range 2.2 to 3.1 (minimum 1.5, maximum 4.5)			

SJM: St. Jude medical valve; CM: Carbomedics valve; ATS: ATS Medical Inc. valve; INR: international normalized ratio.
* References: 1,2,3,7,8,9,10,12,13,16,18,19,22,24,26,28,30,31,32,34,36,38,40,41,42,43,47,49.
** References: 1,3,7,8,9,10,12,16,18,19,22,23,28,31,32,34,36,38,40,41,43,49.

number of observed events, which is then divided by the total number of patient years from all the studies to give a complication rate expressed as % per patient year:

$$\text{Linearized incidence rate} \times \text{number of patient years} = \text{Number of observed events}$$

$$\text{Complication rate} = \sum \frac{\text{Number of observed events for each study}}{\text{Total number of patient years for all studies}}$$

Aortic and mitral valve complication rates were calculated (**Table II**). Although there are small differences in the published complication rates for each of the three valve types, it would be impractical to have a separate policy for each type of valve and, therefore, a mean across all three valve types was calculated.

A total of 18 pilots have been certificated by the UK CAA following a mechanical aortic valve implant. Five were professional pilots (Class 1) with a mean age at implant of 49 yr (33–57) and a mean follow-up period of 54 mo (17–84), four were private pilots (Class 2) with a mean age at implant of 48 (30–49) and mean follow-up period of 16 mo (3–27) and nine were Light Aircraft Pilot License (LAPL) holders with a mean age of 61 (34–70) and mean follow-up period of 34 mo (11–84). The only reported complication was in a professional pilot who developed minor hemoptysis following prolonged coughing, with international normalized ratio (INR) readings within the target range. The pilot underwent full respiratory investigation which did not reveal any underlying pathology. There have been no pilots certificated by the UK CAA with mechanical mitral valve implants.

DISCUSSION

The calculated annual complication rate was 3.79% for aortic valve replacements and 5.19% for mitral valve replacements (Table II). This figure is greater for mitral valve replacements due to the increased incidence of thromboembolism and hemorrhage, possibly related to the larger valve size and higher target INR in these patients, who are often also on treatment for coexisting medical conditions such as atrial fibrillation.[5] Both of these figures exceed the criteria used by the UK CAA of a 1% per annum maximum acceptable medical incapacitation risk for the certification of pilots undertaking multicrew professional operations.[25] However, these rates are only estimates and there are confounders and sources of error in deriving a risk in this way.

Complication rates for valve procedures in the literature were expressed as linearized incidence rates. These assume that the incidence of developing a complication is constant throughout the follow-up period; however, this may not apply to all complications, some of which may occur earlier than others in the postoperative period.

Complications such as major and minor bleeds were categorized together and not differentiated in some papers.[42] The definition of major and minor hemorrhages also varied between studies. In one paper, examples of minor bleeds were rectal bleeds and hematuria, while major bleeds were those requiring hospitalization or transfusion.[18] From a certificatory point of view, any hemorrhage that could cause a medical incapacitation in a pilot would be of aeromedical concern.

Some studies included emergency operations in addition to elective procedures, which would worsen the overall outcome data.[8] Pilots are more likely to have elective procedures and, therefore, better outcomes.

The majority of the papers included patients with comorbidities that were mainly cardiovascular, which were likely to have been contributory to the complication rates. Myocardial infarction was seen in some patients undergoing aortic valve implants and preoperative atrial fibrillation was present in many patients with mitral valve disease.[36] Other patients had chronic renal failure, chronic obstructive airways disease, atrioventricular block,[47] and permanent pacemakers.[24] Patients had also undergone more than one surgical procedure; for example, coronary artery bypass grafting, multiple valve implants, repair of intracardiac anomalies, and redo operations.[22,42] These were present in the majority of the published data, which is taken from the general population. In contrast, pilots undergo regular screening for other medical conditions by periodic medical examinations throughout their flying career, resulting in the 'healthy worker' effect and fewer comorbidities than the general population.

Table II. Aortic and Mitral Valve Complication Rates as Linearized Incidence (% per Patient-Year).

VALVE	ENDOCARDITIS	PARAVALVULAR LEAK	VALVE THROMBOSIS	THROMBO-EMBOLISM	HEMORRHAGE	TOTAL RATE	MEAN TARGET INR RANGE
Aortic*							
SJM	0.30	0.33	0.06	1.56	1.95	4.20	1.8–4.5
CM	0.19	0.32	0.02	1.16	1.78	3.47	1.4–4.0
ATS	0.08	0.47	0.45	1.05	0.59	2.64	1.6–3.0
Mean	0.24	0.36	0.036	1.42	1.74	**3.79**	
Mitral**							
SJM	0.27	0.30	0.25	2.61	2.20	5.63	2.3–3.5
CM	0.28	1.05	0.06	1.28	2.03	4.70	2.3–3.0
ATS	0.07	0.41	0.48	0.98	0.28	2.22	2.1–2.9
Mean	0.24	0.55	0.57	2.02	1.76	**5.19**	

SJM: St. Jude medical valve; CM: Carbomedics valve; ATS: ATS Medical Inc. valve; INR: international normalized ratio.
* Total follow-up period 44,670 patient-years; mean follow-up period 57 mo.
** Total follow-up period 38,068 patient-years; mean follow-up period 61 mo.

The mean age was 55 yr for aortic valves and 58 for mitral valves (Table I), with patients in some papers reaching 79 yr of age.[43] This is an older age group than the professional pilot population and the UK CAA experience. Increasing age was in itself associated with an increased risk of death.[10] Ikonidis et al.[22] found that concomitant coronary artery bypass grafting (CABG) of more than three vessels, heart failure (NHYA Class IV), increased age, and African American ethnicity in aortic valve replacements were independent predictors of mortality. They suggested that survival may be more strongly influenced by pre-existing comorbidities than by the presence of the mechanical valve itself.

Patients from the literature were usually symptomatic, with dyspnea, angina, heart failure and syncope, as their condition had already progressed to a much more advanced stage than would be allowed to develop in a pilot. A pilot would have been grounded when initial symptoms were reported or when the certificatory parameters for valve disease had become disqualifying, which typically precedes the point when the clinical criteria for an operation in the general population is reached. In the United Kingdom, the European Society of Cardiology Guidelines[44] usually form the basis for the timing of valve replacements. In pilots, the condition is treated earlier in the natural course of the disease, improving the prognosis. For all these reasons, the complication rates that have been derived from the literature in this study are likely to be an overestimate of that applicable to the pilot population.

Mitigation of Risk

Although each complication may produce symptoms, the likelihood of a medical incapacitation will depend on the clinical presentation of each event. Endocarditis typically manifests with fevers, rigors, and shortness of breath. A paravalvular leak can present with fatigue, dyspnea, and sometime severe anemia from intravascular haemolysis.[47] Valve thrombosis can result in symptoms of partial valve obstruction, such as shortness of breath and fatigue. In instances where valve thrombosis had occurred, the average INR was found to be well below the therapeutic range, falling to as low as 1.3 in one paper.[45] These symptoms usually develop gradually over a period of time before leading to an incapacitating event. It therefore may be possible to detect these prior to the onset of symptoms by undertaking regular clinical monitoring with appropriate investigations.

Thromboembolic complications included transient cerebral ischemic events[17,45] and complete strokes.[35] In contrast, these events are sudden in onset, without warning, and would be incapacitating in a pilot. Most episodes of thromboembolism occurred within the first 5 yr of the implant[45] when INR values were below the therapeutic range; for example, in two studies with such episodes the mean INR values were 1.97[45] and 1.8.[46]

Anticoagulant-related hemorrhage was sometimes classified as major when requiring hospitalization and/or transfusion and minor when not. Major events were gastrointestinal bleeds,[18,43] cerebral bleeds,[43,47] retroperitoneal bleeds, pericardial effusions, subdural hematoma,[18] extradural hematomas,[35] subarachnoid bleeds,[17] and traumatic bleeds.[45] Such bleeding episodes may develop suddenly and can cause incapacitation. Unsurprisingly, these were also associated with the highest mortality. Hemorrhagic events were reported to occur later, usually after the first 5 yr of the implant[45] and mostly when the INR was outside the target range.[46]

Although thrombo-embolism and hemorrhage are unlikely to occur together in the same patient at the same time, it is possible that both these complications could affect the same patient over a 1-yr period at different times. Even though all these complications can present clinically with symptoms, the greatest potential to cause a sudden incapacitation arises from thromboembolism and anticoagulant-related hemorrhage. By summing these two risks, the combined risk for aortic valves is 3.16% (1.42 + 1.74) per annum. As the total risk is 3.79% per annum, the remaining risk is attributable to endocarditis, paravalvular leak, and valve thrombosis, and amounts to only 0.63% per annum. For aortic valves, if it were theoretically possible to eliminate the risk of thromboembolism and hemorrhage, the risk of the other complications would fall to below the critical figure of 1% per annum. For mitral valves, the combined risk for hemorrhage and thromboembolism is 3.78% (1.76 + 2.02) per annum. As the total risk is 5.19% per annum, the remaining risk due to endocarditis, paravalvular leak, and valve thrombosis would be 1.41% per annum, which by itself would exceed the critical figure of 1% per annum, precluding medical certification following mitral valve replacement.

The most effective measure to mitigate the risk of both thrombo-embolism and hemorrhage complications is the stringent control of anticoagulation. The Time in Therapeutic Range (TTR) is a strong predictor of thrombotic and, to a lesser extent, hemorrhagic events for patients on anticoagulants. One study with warfarin showed each 10% increase of TTR correlated with a decrease in the embolic rate of 0.32% per patient year ($P < 0.001$) and a decrease in the major bleed rate of 0.035% per patient year ($P = 0.63$).[6] A systematic review of patients with atrial fibrillation on warfarin showed an inverse relationship with both major hemorrhage and thromboembolic events: a 7% improvement in TTR led to a reduction of one major hemorrhage per 100 patient years and a 12% improvement in TTR led to a reduction of one thromboembolic event per 100 patient years.[48]

The European Union medical requirements set by EASA stipulate that pilots must be grounded for 6 mo following mechanical valvular surgery.[4] Pilots must be asymptomatic with a satisfactory exercise electrocardiogram (ECG) and echocardiogram. For recertification, anticoagulation must be stable, which is defined as 6 mo with at least five documented INR values, of which at least four are in the target INR range. Ongoing certification requires cardiac follow-up with exercise electrocardiogram testing and echocardiography.

The grounding period for 6 mo following surgery appears to be justified by the risk of thromboembolism, which is up to seven times higher in the first 6 mo.[5,29] On the basis of the results of this study, our proposed policy has an additional certificatory measure to that stipulated in the EU Requirements,

namely an INR test must be performed within the 12-h period preceding a flight. The target INR range should be set by the treating physician and if the INR should fall outside the range, the pilot must not fly. Although the INR is generally considered stable for 48 h after a maintenance dose, 12 h is a practical time to undertake testing prior to a flight to allow for the preparation and the duration of a long-haul flight. This would ensure that anticoagulation is within the therapeutic range while flying. To achieve this, the pilot must use a portable INR testing machine to allow testing down-route. There are various types of INR testing machines available and the type is not stipulated, but it must undergo regular calibration. The pilot should record the INR values in their logbook prior to each flight and this must be checked at each periodic aviation medical examination. With this additional measure, the proposed policy would allow certification with a multicrew restriction for Class 1 (professional) pilots and unrestricted certification for Class 2 (private) pilots.

Positive results have been achieved with the use of near point INR self-monitoring devices. The Early Self Controlled Anticoagulant Trial 1 (ESCAT 1) demonstrated that self-management of oral anticoagulants improved the percentage of INR values within the target range, reducing thrombo-embolic events and improving long-term survival compared with the management of oral anticoagulants by a General Practitioner.[27] In another study, self-managed anticoagulation achieved significantly better control with a greater TTR (76.5% vs 63.8%) than in a conventionally General Practitioner and hospital managed group.[39]

As the risk of incapacitation from comorbidities (e.g., coronary artery disease) is not mitigated by INR near point testing, additional medical conditions would not be permitted in pilots seeking recertification following mechanical aortic valve implants. The complication risk is too high to permit certification after mechanical mitral valve replacements.

Wide variations exist across different aviation authorities in their certificatory policies. The U.S. Federal Aviation Administration allows recertification following mechanical valve replacements with INR values within an acceptable range at least monthly during the past 6-mo period of observation.[20] Transport Canada may consider a return to flying only where the cumulative risk of incapacitation due to complications can be shown to be less than 2% per year.[21] The Australian Civil Aviation Safety Authority permits certification 6 mo following surgery with demonstrated stability on warfarin.[14]

Novel oral anticoagulants are not licensed for use with mechanical valves. Indeed, one clinical trial with dabigatran was terminated early due to the increased thromboembolic and bleeding event rate compared with warfarin.[15]

In conclusion, it is proposed that professional pilots could gain medical certification with a multicrew restriction and private pilots could gain unrestricted certification 6 mo after a mechanical aortic valve replacement provided there has been a satisfactory cardiac assessment, evidence of INR stability, and the exclusion of all comorbidities that might adversely affect long-term outcome. As the estimated risk of total complications exceeds 1% per annum, there would be an additional requirement for an INR measurement within the therapeutic range in the 12-h period preceding a flight. Mechanical mitral valve implants would not be permitted for medical certification, as the total complication risk exceeds acceptable limits.

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