REVIEW

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Atrial tachyarrhythmia after cardiac surgery

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Introduction

Today an increasing number of patients require cardiac surgery. They are often elderly and have severe cardiac disease, thus constituting an important risk for perioperative complications. Atrial tachyarrhythmia, such as atrial fibrillation, atrial flutter, or atrial tachycardia, frequently complicates cardiac surgery and is now recognized as a major cause of morbidity. Hypotension, hemodynamic instability, congestive heart failure, and thromboembolic complications due to postoperative atrial tachyarrhythmias may lengthen the period of hospitalization and increase costs.

Here we review risk factors and pathophysiological mechanisms of postoperative atrial tachyarrhythmia. Prophylactic and therapeutic measures are discussed.

Incidence and time occurrence of atrial tachyarrhythmias

The reported incidence of atrial tachyarrhythmias following cardiac surgery varies from 10 to 40 % in the postoperative period [1-19]. This wide range is at least in part due to differences in the protocols of the studies cited. Patient populations, type of cardiac surgery, definition, duration, and hemodynamic effect of atrial tachyarrhythmia, withdrawal of antiarrhythmic drugs used preoperatively, and duration and type of postoperative rhythm monitoring frequently vary, making it difficult to indicate precisely the true incidence of this complication. Despite increasing expertise in managing patients undergoing cardiac surgery, the incidence of these arrhythmias seems not to have declined in the past 10–15 years [17, 20]. Atrial tachyarrhythmias can develop immediately or several days after surgery. They are most often observed during the second to fourth postoperative day [1–3, 6, 10–12, 15, 18, 21–28]. Sustained atrial fibrillation and flutter are often preceded by atrial ectopic activity, atrial tachycardia, or nonsustained atrial fibrillation [13, 25].

Etiology and risk factors of atrial tachyarrhythmias

In patients who have not had cardiac surgery, the mechanisms underlying atrial fibrillation have been studied extensively. Several models have been developed. Based on mathematical modelling the "multiple wavelet hypothesis" has been proposed [29], which suggests that excitation of the atrium during fibrillation is the consequence of multiple, self-sustaining re-entrant wavelets. The electrophysiological basis for this model was described as the "leading circle reentry" in a rabbit model [30], in which electrical activation becomes fractionated as it divides about islets of refractory tissue (circular movement around an area of functional block). Further support for the re-entrant mechanism resulted from the demonstration of local entrainment of the arrhythmia during rapid pacing [31].

In some patients without structural heart disease the surface electrocardiographic pattern of atrial fibrillation is due to a focal, rapidly firing source of activity. These sources have been identified and successfully eliminated by radiofrequency ablation [32].

Much less is known of the pathophysiology of postoperative atrial fibrillation. Whether the responsible factors lead either to abnormally high inducibility or to abnormally high stability of established atrial fibrillation is unclear. A number of cardiac-associated perioperative problems are thought to be responsible: postoperatively raised levels of catecholamines [33] (in some cases intensified by withdrawal of beta blockers) or pericarditis [34] may be involved. With increasing age, atrial dilatation [35, 36], enlarged left ventricular mass [35], and calcification of the mitral annulus [36, 37] are more common. It is possible that these are responsible for atrial conduction delay, and they probably represent in many patients a critical prerequisite for atrial re-entry and arrhythmia. Thus, the signal-averaged electrocardiogram is a potent predictor of atrial fibrillation after cardiac surgery [11].

Whereas hypokalemia is known to be related to ventricular arrhythmia, a correlation to supraventricular arrhythmia in patients after cardiac surgery is controversial [38, 39]. Thus, myocardial potassium concentration in the right atrium was similar in patients experiencing atrial fibrillation compared to patients with sinus rhythm [28].

It is clearly desirable to identify risk factors for atrial tachyarrhythmias. Several important studies have found increasing age [6, 16, 17, 20, 25, 28, 40, 41], heart valve surgery [16, 42], a history of atrial fibrillation [16, 41, 42], and prolonged signal-averaged *p*-wave duration [11, 43] to be predictive of postoperative atrial tachyarrhythmia. Conflicting results have been published for: sex [6, 16, 17, 20, 40, 43, 44], left ventricular end-diastolic pressure [20, 40, 41], aortic cross-clamp time [16, 20, 25, 28, 40, 43-45], arterial hypertension [17, 20, 43], ejection fraction [20, 40, 43, 45], and chronic obstructive pulmonary disease [16, 20]. Postoperative withdrawal of beta blockers has been identified as a possible risk factor for atrial tachyarrhythmia, but no controlled study has addressed this question. The number of bypass grafts [25, 40, 43, 44] and a prior history of myocardial infarction [16, 40, 43, 44] are not risk factors.

Consequences of postoperative atrial tachyarrhythmia

Atrial tachyarrhythmia may be of short duration and is often well tolerated [3, 24, 45]. By contrast, it can lead to important hemodynamic deterioration with a significant decline in cardiac output leading to congestive heart failure [16]. This complication is frequently observed in patients with pre-existing cardiac ischemia, poor left ventricular function, rapid ventricular rate, or reduced ventricular compliance. The poorly compliant ventricle needs atrial contraction in order to gain sufficient preload. A significant increase in cardiac index from 2.7 to 3.4 l/min per m² as well as a decrease in pulmonary arterial diastolic pressure have been observed in patients who converted from postoperative atrial fibrillation to sinus rhythm [46]. A rapid conversion to sinus rhythm is therefore imperative in patients with hemodynamic instability.

Atrial tachyarrhythmia can lead to systemic thromboembolism and cause transient, or severe and persistent, neurologic deficit [6, 20, 47–49]. After coronary artery bypass in 453 patients, atrial fibrillation alone increased the probability of stroke or transient ischemic attack from 0.78 to 3.9% during the postoperative period [49]. In 108 patients with carotid bruits, postoperative atrial fibrillation was an important risk factor for stroke or transient ischemic attack [47]. Patients with a previous history of cerebrovascular events were at highest risk for this severe complication.

Patients with atrial tachyarrhythmia stay significantly longer in the intensive care unit (ICU), are more often readmitted to the ICU [16, 19, 20, 50], and have a longer total duration of hospitalization [3, 12, 16, 51], resulting in additional costs estimated variously at U.S. \$ 1600 etc. [16], U.S. \$ 4500 [7], U.S.\$ 8000 [19], or U.S.\$ 10000 [17]. Whereas other factors often associated with postoperative atrial tachyarrhythmia (such as age and postoperative complications) contribute to prolonged hospitalization, atrial fibrillation is independently associated with an increased length of stay of 4.9 days [17]. Postoperative atrial fibrillation is therefore an important drain on hospital resources, contributing significantly to the escalating health costs associated with coronary artery bypass grafting.

Prevention of postoperative atrial tachyarrhythmias

It has been suggested that routine pharmacological prophylaxis of postoperative atrial tachyarrhythmia may lead to the administration of unnecessary medication to a majority of patients, with a financial burden and risk of pharmacologic side effects [3, 50]. However, considering the medical and financial consequences of postoperative atrial tachyarrhythmias, it is obvious that an effective, nontoxic prophylactic drug regimen, at least for patients at risk, would be highly desirable. An overview of trials evaluating the efficiency of drugs in preventing postoperative atrial tachyarrhythmias is presented in Table 1. Summarized are only prospective randomized trials including at least 50 patients.

Propafenone has been compared in a double-blinded study with atenolol in 207 patients [14]: the incidence of atrial tachyarrhythmias was the same in both groups, although preoperative beta blockers were stopped in the propafenone group.

Beta blockers are the most widely studied agents applied for prophylactic purposes: propranolol [1, 3, 15, 52], acebutolol [22], atenolol [5], metoprolol [2], and nadolol [4] have all been compared to placebo. In all trials,

Authors	Type of study	Number of patients	Type of operation	Proceeding A and effi	ciency ^a	Proceeding B
Johnson et al. [23]	Open	120	CABG	Digitalis	>	No prophylaxis
Tyras et al. [48]	Open	140	CABG	Digitalis	<	No prophylaxis
Csicsko et al. [57]	Open	407	CABG	Digitalis	>	No prophylaxis
Hammon et al. [52]	Double-blinded	50	CABG	Propranolol	>	Placebo
Matangi et al. [1]	Open	164	CABG	Propranolol	>	No prophylaxis
Williams et al. [27]	Double-blinded	141	CABG	Verapamil	=	Placebo
Smith et al. [24]	Open	100	CABG	Verapamil	=	No prophylaxis
Davison et al. [55]	Double-blinded	200	CABG	Verapamil	=	Placebo
Daudon et al. [22]	Open	100	CABG	Acebutolol	>	No prophylaxis
Janssen et al. [2]	Open	1251	CABG	Sotalol Metoprolol Sotalol	> > >	No prophylaxis No prophylaxis Metoprolol
Rubin et al. [3]	Open	123	CABG	Propranolol Digitalis	> =	No prophylaxis No prophylaxis
Khuri et al. [4]	Double-blinded	148	CABG	Nadolol	>	Placebo
Lamb et al. [5]	Open	60	CABG	Atenolol	>	No prophylaxis
Suttorp et al. [44]	Double-blinded	300	CABG	Sotalol	>	Placebo
Hohnloser et al. [54]	Open	77	CABG	Amiodarone	>	Placebo
Fanning et al. [8]	Double-blinded	99	CABG	Magnesium	=	Placebo
England et al. [9]	Double-blinded	100	CABG, AVS, MVS	Magnesium	=	Placebo
Parikka et al. [56]	Open	140	CABG	Magnesium	=	Placebo
Nyström et al. [26]	Open	101	CABG	Sotalol	>	Half dose of preoperative β-blocker
Merrick et al. [14]	Double-blinded	207	CABG, AVS, MVS	Propafenone	=	Atenolol
Babin-Ebell et al. [15]	Open	103	CABG	Propranolol Diltiazem	> =	No prophylaxis No prophylaxis
Kowey et al. [19]	Double-blinded	157	CABG	Digitalis + acebutolol	=	Digitalis + placebo

 Table 1
 Drug efficiency in prophylaxis of postoperative atrial tachyarrhythmia (randomized, prospective studies published from 1976 to 1997 including at least 50 patients)

^a >: Proceeding A significantly more efficient in preventing postoperative atrial tachyarrhythmia compared to proceeding B; =: no significant difference; <: proceeding A significantly less efficient in preventing postoperative atrial tachyarrhythmia compared to drug B (*CABG* coronary artery bypass grafting, *AVS* aortic valve surgery, *MVS* mitral valve surgery)

postoperative atrial tachyarrhythmia was significantly reduced, although preoperative therapy with beta blockers was sometimes suspended in the control groups. This withdrawal may be a risk factor for postoperative atrial tachyarrhythmia and may lead to a false high incidence in the placebo groups.

A meta-analysis of 14 studies incorporating a total of 2585 patients treated either with prophylactic beta blockers (n = 675), digitalis (n = 375), a combination of both (n = 139), or placebo (n = 1414) revealed the combination of beta blockers and digitalis to be significantly more effective than beta blockers alone, which in turn was significantly superior to placebo [53]. Digitalis alone had no significant effect and showed only a trend toward benefit. However, meta-analyses can never be

used as final statements, as the nonuniformity of the different studies may make comparison difficult. Furthermore, in a recent study, no significant additional effect of acebutolol could be demonstrated when given in conjunction with digitalis [19].

Amiodarone [54] and sotalol [2, 26, 44] have been compared to placebo in several open and double-blinded trials. In all studies, a significant reduction in postoperative atrial tachyarrhythmia was observed. Again, in the placebo groups preoperative beta blockers or other cardiac medication were reduced or completely stopped, which may have led to a false high incidence of postoperative atrial tachyarrhythmias in these groups. In a study comparing sotalol with metoprolol, sotalol was significantly more effective [2].

Authors	Type of study	Number of patients	Type of operation	Proceeding A and efficiency of conversion ^a		Proceeding B
Plumb et al. [68]	Double-blinded	28	CABG, AVS, CC	Verapamil	=	Placebo
Hwang et al. [58]	Double-blinded	14	CABG, ASD	Verapamil	=	Placebo
Campbell et al. [66]	Open	40	Not specified	Sotalol	=	Digitalis + disopyramide
Connolly et al. [21]	Double-blinded	14	CABG, ASD, AVS	Propafenone	>	Placebo
Gavaghan et al. [64]	Open	56	Not specified	Flecainide	=	Digitalis + disopyramide
Wafa et al. [63]	Open	29	CABG	Flecainide	>	Digitalis
McAlister et al. [42]	Open, crossover	80	CABG, AVS, MVS	Quinidine	>	Amiodarone
Hjelms et al. [61]	Open	30	CABG, VSD, AVS	Procainamide	>	Digitalis
Ollitrault et al. [65]	Double-blinded	86	CABG, AVS, MVS, CC	Cibenzoline	>	Placebo
Cochrane et al. [10]	Open	30	CABG, AVS, MVS	Amiodarone	=	Digitalis
Larbuisson et al. [62]	Open	40	CABG, AVS	Propafenone	=	Amiodarone
Frost et al. [67]	Double-blinded	98	CABG	Dofetilide	=	Placebo

 Table 2 Drug efficiency in conversion of postoperative atrial tachyarrhythmia to sinus rhythm (only randomized and prospective studies, 1982–1997)

^a >: Proceeding A significantly more efficient in converting postoperative atrial tachyarrhythmias to sinus rhythm as compared to drug B; =: no significant difference (ASD atrial septal defect, AVS aortic valve surgery, *MVS* mitral valve surgery, *VSD* ventricular septal defect, *CABG* coronary artery bypass graft, *CC* correction of congenital heart disease)

Diltiazem [15] and verapamil [24, 27, 55] have been compared to placebo in open and double-blinded studies. No prophylactic effect for postoperative atrial tachyarrhythmia of either drug could be demonstrated. Patients given diltiazem experienced exactly the same incidence of supraventricular tachyarrhythmias as those in the placebo group. In addition, the diltiazem group needed significantly more inotropic support. In only one [55] of the three trials comparing verapamil to placebo was ventricular heart rate significantly lowered during atrial tachyarrhythmia. Moreover, a significant incidence of severe side effects, including hypotension and pulmonary edema, was observed [55].

Magnesium has been investigated in several trials. In a controlled study, a significantly higher incidence of atrial tachyarrhythmia was observed in hypomagnesemic compared to normomagnesemic patients [9]. However, prophylactic magnesium supplementation was ineffective. In accordance with this finding, hypomagnesemic patients experienced significantly more episodes of atrial fibrillation, but prophylactic magnesium did not significantly lower the number of patients experiencing atrial fibrillation [8]. Indeed, a nonsignificant increase in atrial fibrillation has been reported with prophylactic magnesium [56]. However, patients in this group were significantly older and more frequently had a history of atrial fibrillation compared with those receiving placebo.

The prophylactic use of postoperative digitalis is controversial. Some studies identified a positive effect [23, 57]. By contrast, others [48] found a significant increase in postoperative atrial tachyarrhythmias with prophylactic digitalization. In a meta-analysis, only a trend toward a benefit was demonstrated [53].

Triiodothyronine, given for 9 h following unclamping of the aorta, was compared to placebo in a double-blinded manner in 131 patients with an ejection fraction of < 40% following coronary artery bypass grafting [18], and this led to a significant decrease in atrial fibrillation after 25–120 h. However, possible mechanisms of action remain speculative.

Therapy of postoperative atrial tachyarrhythmias

The therapeutic goals of correcting atrial tachyarrhythmia are rapid reduction of the ventricular rate and early conversion to sinus rhythm [10]. In cases of hemodynamic instability, acute myocardial ischemia, or hypertrophic cardiomyopathy, for example, associated with severe aortic stenosis, DC cardioversion is the therapy of choice [58].

Even patients with chronic preoperative atrial fibrillation can be converted to sinus rhythm [59, 60], a successful conversion occuring in 60–77 % of patients treated pharmacologically, with or without DC cardioversion. In all of these patients, atrial fibrillation was present for 48 to 72 months. A left atrial diameter less than 45–52 mm, good functional capacity and shorter duration of preoperative atrial fibrillation were predictors of successful cardioversion; 70% remained in sinus rhythm over a mean follow-up period of 17 months [60]. Table 2 summarizes the results of randomized and prospective trials evaluating drug efficiency in converting postoperative atrial tachyarrhythmia to sinus rhythm.

Drugs and efficiency

Procainamide

In a small trial of 30 patients, procainamide (25 mg/min up to 15 mg/kg intravenously) was compared to digitalis (0.75–1.0 mg i. v.) [61]. In the procainamide group significantly more patients (87 vs 60%) converted to sinus rhythm and conversion occurred significantly faster (40 vs 540 min). No serious complication was observed in the procainamide group.

Propafenone

Propafenone (2 mg/kg i.v. over 10 min) was compared to placebo in a small double-blinded crossover study: 43 % of patients converted within 10 min of receiving propafenone, but none after placebo [21]. In addition, the ventricular rate decreased significantly in the propafenone group, the only side effect being a decrease in systolic blood pressure of 9 mmHg. Propafenone (1-2 mg/kg over 10 min followed by an infusion of 420 mg in 24 h) was compared to amiodarone (2.5-5 mg/kg over 10 min followed by an infusion of 900 mg in 24 h) in 40 patients following coronary artery bypass grafting or aortic valve replacement [62]. No beta blocking agents, calcium channel blockers, or other antiarrhythmics were given concurrently. There was no significant difference between the two groups in terms of conversion rates or hemodynamic performance. Propafenone seemed to act slightly faster than amiodarone.

Flecainide

By comparison with digitalis (0.5 mg i.v. followed by 0.25 mg after 6 and 12 h) [63] flecainide (1 mg/kg over 10 min followed by an infusion of 1.5 mg/kg per h for 1 h, then 0.25 mg/kg per h for 24 h) led to conversion to sinus rhythm significantly more often. No patient in the digitalis group converted to sinus rhythm. No serious side effects were observed in either group. Flecainide (2 mg/kg i.v. over 20 min followed by an infusion of 0.2 mg/kg per h for 12 h) compared to a combination of digitalis (0.75 mg i.v.) followed by disopyramide 2 h later (2 mg/kg and an infusion of 0.4 mg/kg per h for 10 h) showed almost identical conversion rates, but flecainide

acted significantly faster (80 vs 220 min) [64]. Considering the prolonged time for conversion using digitalis, this group of patients may have experienced spontaneous conversion. One fatality in the flecainide group was due to intractable ventricular fibrillation.

Cibenzoline

Cibenzoline (1.2 mg/kg over 2 min i.v.) has been compared to placebo in a double-blinded trial, in which no other antiarrhythmics were given concurrently [65]. Significantly more patients of the active group converted to sinus rhythm (30 vs 6.9%), and the ventricular rate was significantly lower. No side effects were noted in this study population, which had an average ejection fraction of approximately 60%.

Beta blockers

No prospective randomized studies comparing the therapeutic use of beta blockers with other drugs or placebo have been performed.

Amiodarone

Amiodarone (5 mg/kg up to 400 mg over 30 min, then 25 mg/h and a possible rise to 40 mg/h) has been compared to digitalis (1 mg over 9 h i.v. followed by oral maintenance) [10] and showed comparable conversion rates to sinus rhythm within 24 h. The ventricular rate during atrial fibrillation, blood pressure, and side effects were also comparable. Amiodarone (5 mg/kg over 20 min i.v.) was compared to Quinidine (2×400 mg per os in 4 h) in a randomized crossover study [42]. Significantly more patients converted under quinidine as with the first drug (64 vs 41 %), the difference being no more significantly more patients receiving quinidine first, some of which were severe (e.g., torsades de pointes, severe nausea and vomiting).

Sotalol

Sotalol (1 mg/kg bolus, plus 0.2 mg/kg over 12 h) has been compared to a combination of digitalis plus disopyramide (digitalis 0.75 mg i.v. followed 2 h later by disopyramide 2 mg/kg bolus and 0.4 mg/kg per h for 10 h) [66]. Conversion rates were equal in both groups, but those in the sotalol group converted significantly faster (58 vs 187 min) and had fewer relapses. The most frequent side effect attributable to sotalol was hypotension, leading to a drop in blood pressure of at least 20 mmHg, or to below 90 mmHg in over 75% of patients. Disopyramide had to be stopped in several cases due to anticholinergic side effects.

Dofetilide

Dofetilide, a class III antiarrhythmic agent without negative inotropic effects, has been compared in a doubleblinded manner in two dosages (4 µg/kg and 8 µg/kg over 15 min) to placebo [67]. Within 3 h of drug administration, conversion rates were 24 and 44 % for placebo and 8 µg/kg dofetilide respectively, a nonsignificant difference. Dofetilide was well tolerated and had no negative inotropic effect.

Verapamil

Verapamil (0.075 mg/kg followed by 0.15 mg/kg later) has been compared to placebo in two double-blinded crossover studies [58, 68]. The ventricular heart rate during atrial fibrillation was significantly reduced, although the effect wore off rapidly after discontinuing the drug. Verapamil was not superior to placebo in conversion into sinus rhythm, but led to a significant reduction in diastolic blood pressure [58].

Digitalis

Digitalis has long been considered the drug of choice for supraventricular arrhythmia [10], although it has no intrinsic antiarrhythmic effect [69]. No prospective randomized studies have been done comparing digitalis to placebo. Digitalis alone or in combination with disopyramide was compared to procainamide, flecainide, cibenzoline, amiodarone, and sotalol, as summarized in Table 2, but in no case was digitalis better than the comparative drug. In addition, in the nonoperative setting digitalis does not convert atrial fibrillation faster or better than placebo [70]. It may have an indirect beneficial effect mediated via improvement of hemodynamic status [69] and lowering of heart rate.

Anticoagulation

Left atrial thrombus began to form in 14% of 143 patients with acute atrial fibrillation within 3 days, as detected by transesophageal echocardiography (TEE) [71]. However, among patients presenting with atrial fibrillation that was clinically estimated to have lasted less than 48 h, the likelihood of cardioversion – related clinical thromboembolism was very low [72]. The use of TEE to identify atrial thrombus and decide on its severity is controversial [73, 74]. A meta-analysis of three randomized trials has suggested a small positive effect of aspirin in preventing stroke [75]. Anticoagulation with warfarin is more effective and significantly reduces the incidence of embolism [76–78]. But all studies mentioned have been performed in a nonpostoperative setting. Therefore, no therapeutic guidelines exist for pati-

ents after cardiac surgery. The risk of thromboembolism must be weighed against the possible hazard of anticoagulation, especially when administered shortly after major surgery. A reasonable approach at present is that if atrial fibrillation persists for 24 h or more, anticoagulation should be started.

A practical approach

As in the management of any other medical problem, all patients have to be evaluated on an individual basis, considering factors such as type of operation, age, preoperative medication, and hemodynamic status.

Prophylaxis

Older patients, with a history of atrial fibrillation undergoing heart valve operations are at an increased risk and benefit from pharmacological prophylaxis. As the peak incidence of atrial tachyarrhythmia is during the second to third postoperative day, prophylaxis should be started as early as possible. Beta blockers are the most widely investigated drugs for the prophylaxis of postoperative atrial tachyarrhythmias and are considered by many to be the drug of choice. In established preoperative beta blockade, they should be continued during the whole postoperative period. Combined therapy with digitalis may be considered in patients with depressed left ventricular function. Sotalol has been used with good results and may even be superior to other beta blockers. In the case of intolerance to beta blockers, amiodarone and propafenone has been shown to be effective. Presently none of the data justify the prophylactic use of digitalis alone, nor calcium antagonists. In recurrent atrial tachyarrhythmia, amiodarone or sotalol may be used as prophylaxis, even if controlled studies are lacking. No data exist concerning the duration of prophylactic medication.

Therapy

In patients with hemodynamically poorly tolerated atrial tachyarrhythmia, DC cardioversion is imperative. In the case of hemodynamic stability, the goal of therapy is to control ventricular rate and convert to sinus rhythm. If ventricular function is normal, rate control may be achieved using careful titration of beta blockers. Digitalis may be considered in patients with congestive heart failure.

If conversion to sinus rhythm does not occur spontaneously, procainamide, propafenone, or flecainide is effective and safe for pharmacologic cardioversion. No controlled studies indicate that the use of beta blockers or calcium antagonists is justified in cardioversion. Although used by many, no convincing data exist either for the use of amiodarone or digitalis. We do not recommend prolonged use of flecainide due to its possible proarrhythmic effect. If atrial fibrillation is recurrent or lasts more than 24 h, intravenous anticoagulation with heparin, followed by oral anticoagulation, is recommended. Two to four weeks of anticoagulation is prudent before elective DC cardioversion.

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Note added in proof

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Appendix. A professional search was performed by the documentation service of the Swiss Academy of Medical Sciences using Medline databank. The English language literature from 1982 until May 1997 was considered. The mesh headings "atrial fibrillation, atrial flutter" and "tachycardia, supraventricular" were combined with the mesh headings "heart" and "surgery" using subheadings "coronary artery bypass, heart bypass, heart valve, internal mammary artery anastomosis, arrhythmias, etiology" and others, respectively. Furthermore, the Current Contents databank was searched using the same keywords. Additional material was found using the reference lists of all the above retrieved articles.