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Review

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Prevention of atrial fibrillation after surgery[1]

Abstract

Postoperative atrial fibrillation (AF) is the most common arrhythmic complication after cardiac surgery. Despite more than 100 trials dealing with the prevention of postoperative AF and improvements in surgical techniques, questions remain about the optimal approach to prevent postoperative AF. Postoperative AF is associated with increased morbidity, length of hospital stay and costs, and should, therefore, be avoided. Aim of this article is to give an overview of current trends in the prevention of postoperative AF.

Key words: atrial fibrillation; cardiac surgery; postoperative management; risk prediction

Zusammenfassung

Postoperatives Vorhofflimmern (VHF) ist die häufigste arrhythmische Komplikation nach Herzoperationen. Obwohl sich mehr als hundert Studien mit der Prophylaxe von postoperativem Vorhofflimmern auseinander gesetzt und sich die chirurgischen Operationstechniken weiterentwickelt haben, fehlt derzeit immer noch ein klarer Konsens, wie das Auftreten des VHF effizient vermieden werden kann. Da das VHF mit einer erhöhten Morbidität, Verlängerung der Spitalaufenthaltsdauer und vermehrten Kosten verbunden ist, sollte eine effiziente Prophylaxe angestrebt werden. Ziel dieses Artikels ist es, einen Überblick über die derzeitigen Trends in der Prophylaxe von postoperativem VHF zu geben.

Schlüsselwörter: Vorhofflimmern; herzchirurgische Eingriffe; postoperatives Management; Risiko-Stratifikation

How big is the problem?

Atrial fibrillation (AF) after coronary artery bypass grafting (CABG) is a common problem and occurs in 30 to 50% of patients [1, 2]. It is associated with an increased incidence of congestive heart failure (CHF), renal failure, infections and stroke, thereby negatively affecting morbidity, length of hospital stay and costs [3–5].

Despite improvements in anaesthetic and surgical techniques, the incidence of postoperative AF has been reported to increase, and so far, no consistent therapies have been found to avoid it [2, 6]. In a recently published prospective observational study 4657 patients scheduled for CABG were included to identify the most powerful clinical predictors of postoperative AF [4]. Using this data, the authors developed a model that allowed accurate prediction of patients at risk for AF. Risk factors for AF were advanced age, history of prior AF, chronic obstructive pulmonary disease (COPD), valve surgery or postoperative withdrawal from betablocker or angiotensin converting enzyme (ACE) inhibitor therapy. On the other side, postoperative administration of betablockers, ACE inhibitors, potassium supplementation and non-steroidal antiinflammatory drugs (NSAID) reduced the risk of postoperative AF. Based on these predictors, they developed a clinical risk prediction algorithm (table 1), which proved to be highly accurate in identifying patients at very high but also at low risk of postoperative AF in a prospective cohort [4].

This review focuses on short-term strategies to prevent or treat AF in the immediate perioperative setting only. Specifically, we do not address long-term strategies, like angio-

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Table 1
Risk Prediction Score for the estimation of postoperative atrial fibrillation (adapted from [4]).

Age >30 years		+ 6 points for every 10 years of age
History of previous atrial fibrillation		+ 7 points
History of COPD		+ 4 points
Valve surgery		+ 6 points
Withdrawal of betablockers		+ 6 points
Withdrawal of ACE-Inhibitor (ACEI)		+ 5 points
Betablocker treatment (pre- and postoperatively)		– 7 points
Betablocker postoperatively		– 11 points
ACE-Inhibitor pre- and/or postoperatively)		– 5 points
NSAIDs		– 7 points
Total points	**risk of atrial fibrillation**	
<14	low risk	≤10%
14–31	medium risk	11–31%
>31	high risk	32–88%

tensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker use, which develop their preventive effect more over a prolonged period of time, since such treatment is difficult to be established timely once surgery is scheduled [7]. Somewhere in between, there are other substances such as polyunsaturated fatty acids (PUFAs), which at least in one study demonstrated to be effective in the prevention of postoperative AF. In this study PUFAs were given at least five days before elective CABG up to discharge from the hospital. PUFA administration reduced the incidence of AF by 54% and was associated with a shorter hospital stay. However, further studies should be awaited to confirm this favorable results before a general recommendation can be made [8].

What's the mechanism?

Generally, postoperative AF is seen in the first two to four days after surgery and is usually self-limited and uncomplicated [9]. Relatively little is known about the detailed onset mechanisms of postoperative AF. Possible contributing factors are pre-existing electric vulnerability of the atria, atrial ischaemia and reperfusion injury, acute atrial stretch, metabolic derangements, pericarditis and elevated sympathetic tone [9].

The onset and maintenance of AF require an initiating event and anatomical substrate, respectively. AF is often initiated by an atrial premature beat (APB) encountering areas of slow conduction with unidirectional functional block [10, 11]. This results in fractioning of the electric wavefront and the initiation of multiple re-entrant circuits propagating through the atria [12]. It has been shown that in most cases the main episode of AF is preceded by short runs of AF or multiple atrial premature beats. In a study by Taylor et al. there was a significantly greater number of APBs seen on days 3 and 4 postoperatively in patients with postoperative AF compared to those without [13].

Recent studies suggested that patients with postoperative AF might have pre-existing electrophysiologic abnormalities [14, 15]. Mariscalco et al. found an association between preprocedural atrial histopathology and postoperative AF [16]. The histologic abnormalities found were interstitial fibrosis, cytoplasmatic vacuolisation and nuclear derangement of myocytes. This supported the hypothesis that in patients with postoperative AF vulnerability to AF (triggers), but also the ability to maintain AF (substrate) are associated with pre-existing degenerative changes.

Other studies have shown that early postoperative AF correlates with an increased inflammatory response after cardiac surgery [17–19]. In an animal study [20] atrial conduction properties were found to be altered by postoperative atrial inflammation, and the degree of inflammation was proportional to the inhomogeneity of atrial conduction. This resulted in an increased incidence and duration of postoperative AF. Inflammation, inhomogeneity of atrial conduction and incidence of postoperative AF were significantly decreased by antiinflammatory treatment with prednisone [20].

With increasing surgical trauma to the atria, there is also an increased incidence of postoperative AF. This explains why patients undergoing valvular surgery have the highest risk of developing postoperative AF [6, 21]. It

has also been shown that less manipulation of the atria decreases atrial inflammation and subsequently atrial fibrillation [22].

Why treating?

Postoperative AF leads to a higher incidence of congestive heart failure (CHF), stroke, prolonged hospital stay and increased costs [6, 21, 23, 24]. In a retrospective cohort study, the Texas Heart Institute Cardiovascular Research database was used to identify patients developing postoperative AF. Atrial fibrillation was diagnosed in 16% (n = 994) of the population (n = 6475). It was associated with greater in-hospital mortality, more strokes and prolonged hospital stays. A case-matched substudy revealed that 5-year-survival was worse in patients with postoperative AF, and the latter was an independent predictor of long-term mortality [25].

In the afore mentioned study by Mathews et al. AF was also associated with a greater incidence of postoperative complications and a higher in-hospital mortality (4.7% *vs* 2.1%; p <0.001) [4]. AF patients had longer intensive care unit (ICU) and hospital stays, mainly due to more neurological, renal and infectious complications [4].

How to deal with?

Non-pharmacological prevention

Numerous studies addressed the issue of AF prevention after surgery. While most studies investigated pharmacological prevention, Melo and colleagues published the results of a randomised trial, in which they studied ventral cardiac denervation as a prophylactic measure against post-CABG (coronary artery bypass grafting) AF [26]. They compared 219 patients undergoing CABG to 207 patients undergoing CABG plus ventral cardiac denervation. The rational of this study was that several previous trials had shown an autonomic nervous imbalance as a potential mediator of postoperative AF [27]. The patients submitted to ventral denervation had fewer and less severe episodes of AF and no patient had AF after discharge. However, in a later study by Alex et al. this method failed to reduce the incidence of postoperative AF [28]. Because of these conflicting results, Cummings et al. investigated the role of vagal innervation of the anterior fat pad of the heart on the incidence of postoperative AF in humans. They demonstrated that preservation of the anterior fat pad during CABG decreases the incidence of postoperative AF [29], suggesting that ventral cardiac denervation is probably of no use for the prevention of postoperative AF. In a recently published meta-analysis, off-pump surgery (OPCAB) was associated with a 30% reduction of atrial fibrillation compared with conventional CABG [30]. Thus, 80 cases of AF could be avoided per 1000 patients undergoing CABG. In several previous studies a reduced inflammatory response after OPCAB was found, which might explain this result in part [31]. However, preservation of the anterior fat pad associated with OPCAB and also patient selection might be other explanations [4].

Betablockers

Betablocker therapy is certainly the mainstone of AF prevention and should be routinely used in every patient [32, 33]. However, it should also be realised that even in modern large trials, where this strategy was widely applied, the incidence of postoperative AF remains up to 60% in selected patients [4]. This clearly emphasises the need of further preventive strategies on top of betablockade.

Class I drugs

There are only a few small randomised studies on the use of class IA drugs for treatment of postoperative AF, and because of their toxicity, virtually none on their preventive use in this setting. In two small studies, procainamide was not more effective than digoxine for the conversion of AF [34, 35]. Although effective in prevention and treating postoperative AF, procainamide may cause hypotension and should not be used in the presence of renal failure. For quinidine and disopyramide, there is even more limited evidence for their use in the literature [36, 37]. Most importantly, however, is the fact that neither procainamide, quinidine nor dysopyramide are on the market anymore. The only remaining class IC agents flecainide and propafenone have been tested in a few small randomised trials. The studies had important limitations and the administration of IC antiarrhythmic drugs is generally no longer recommended for the prevention or conversion to sinus rhythm in the perioperative setting [38].

Class III drugs

Sotalol has also been shown to be effective for the prevention of postoperative AF, either compared against placebo [39], but also compared against betablocker therapy with the scope to

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elucidate it's pure class III action [40, 41]. However, its side effects (hypotension, bradycardia), and in particular, its proarrhythmic effects limit its use in todays perioperative management.

For pharamcological prevention on top of routine betablockade, a short perioperative course of oral amiodarone is probably the most promising approach. This therapy was associated with a 50% reduction of postoperative atrial tachyarrhythmias in patients having CABG and/or valve replacement/repair. The number needed to treat in the largest prospective trial, the PAPABEAR trial, was only 7.5 overall to prevent one patient from postoperative AF [42]. A meta-analysis including 19 trials comparing amiodarone with placebo for the prevention of postoperative AF revealed that the results of the large PAPABEAR trial were consistent with the pooled results of these trials [43]. In these 19 trials amiodarone reduced atrial fibrillation by 50 % (95% CI: 0.43 to 0.59, p <0.0001). It also significantly reduced ventricular tachyarrhythmias, strokes and hospital stay. Furthermore, amiodarone-treated patients had a significantly lower heart rate during AF-episodes, one of the main determinants of AF related morbidity. The authors came to the conclusion that prophylactic amiodarone should be implemented as routine therapy for high risk patients undergoing cardiac surgery [43]. The prophylactic effect of amiodarone seems to be independent of the route of administration (oral, intravenous, or combined). In the PAPABEAR trial oral amiodarone was administered six days before and after surgery at a dosage of 10 mg/kg daily, divided into two doses per day. Given the potential risk of side effects of amiodarone (*eg*, bradycardia, AV-block and others), it seems advisable to use amiodarone particularly in patients at high risk of posteroperative AF. Thereby, an easy clinical algorithm (table 1) may serve to select patients appropriately.

New class III drugs

The new class III drug ibutilide is very effective in the conversion of postoperative atrial fibrillation [44]. However, since ibutilide can cause potentially fatal arrhythmias, particularly torsade de pointes tachycardias, it should be administered only in a setting of continous ECG monitoring. The drug dofetilide is not available in Switzerland.

Corticosteroids

If one supposes that atrial fibrillation is induced not only by a local atrial inflammation, but also by a systemic inflammatory reaction to surgery and extracorporeal circulation, corticosteroid treatment should reduce the incidence of postoperative AF. In a recently published trial by Halonen and colleagues the effect of intravenous corticosteroid administration after cardiac surgery was tested [45]. The incidence of AF was significantly reduced in the hydrocortisone group compared to the placebo group. Patients receiving corticosteroids did not have higher rates of infections or other major complications. The authors concluded that hydrocortisone treatment was very effective in preventing postoperative AF and was well tolerated [45].

Electrical cardioversion

Since postoperative AF is mostly self-limiting, electrical cardioversion is usually not necessary. When cardioversion is applied, the same precautions regarding anticoagulation as in nonsurgical cases should be used. After the return to sinus rhythm anticoagulation therapy is recommended for 30 days [46].

Taking all this evidence into account, there still remains the question of the optimal approach of AF prevention. A large meta-analysis by Burgess et al. comparing the different approaches analysed 94 trials of post-operative AF prevention [47]. In summary, this meta-analysis confirmed the recommendation that betablockers are effective and should not be withdrawn in the post-operative period. Overall, betablockers significantly reduced postoperative AF. However, there is a great heterogeneity between trials with regard to their effectiveness, which partly is explained by the withdrawal of non-study betablockers in the control groups of early trials, thereby overestimating the beneficial effects of betablockers. Compared to betablockers, sotalol significantly reduced the rate of postoperative AF, but increased the rate of complications. Magnesium therapy offered no additional benefit and was not recommended by the authors. For amiodarone they found sufficient evidence to advise its use in combination with betablocker therapy. Digoxine and calcium channel blockers were not effective in the prevention of AF. In contrast bi-atrial pacing showed a significant reduction in AF and was the only therapy that was applied exclusively postoperatively without negative inotropic or chronotropic effects. There were some trials excluded from this meta-analysis investigating the use of IA and IC antiarrhythmic drugs, N-3 fatty acids or off-pump coronary bypass

surgery because they had significant heterogeneity [47].

Conclusions

Firstly, the risk for postoperative AF of patients undergoing cardiac surgery should be assessed on an individual basis. Main risk factors for postoperative AF are advanced age, valve surgery, history of previous episodes of AF, history of COPD, and betablocker or ACE-inhibitor withdrawal. Secondly, betablockers should be given pre- and postoperatively in any patient without contraindication. Thirdly, perioperative amiodarone treatment in addition to betablockers may be considered for patients at high risk according to preoperative risk stratification. Fourthly, bi-atrial pacing should be used, if possible at higher than intrinsic rates in order to avoid the competition between sinus and atrial paced rhythm. Finally, there is no additional benefit from the use of magnesium, calcium-blockers, digoxine, dofetilide or flecainide, and of course, any measure should be taken to minimise surgical trauma and post-operative inflammatory response.

References

1 Amar D, Shi W, Hogue CW, Jr., et al. Clinical prediction rule for atrial fibrillation after coronary artery bypass grafting. J Am Coll Cardiol. 2004;44(6):1248–53.
2 Auer J, Weber T, Berent R, Ng CK, Lamm G, Eber B. Risk factors of postoperative atrial fibrillation after cardiac surgery. J Card Surg. 2005;20(5):425–31.
3 Hravnak M, Hoffman LA, Saul MI, Zullo TG, Whitman GR, Griffith BP. Predictors and impact of atrial fibrillation after isolated coronary artery bypass grafting. Crit Care Med. 2002;30(2):330–7.
4 Mathew JP, Fontes ML, Tudor IC, et al. A multicenter risk index for atrial fibrillation after cardiac surgery. JAMA. 2004;291(14):1720–9.
5 Borzak S, Tisdale JE, Amin NB, et al. Atrial fibrillation after bypass surgery: does the arrhythmia or the characteristics of the patients prolong hospital stay? Chest. 1998;113(6): 1489–91.
6 Creswell LL, Schuessler RB, Rosenbloom M, Cox JL. Hazards of postoperative atrial arrhythmias. Ann Thorac Surg. 1993;56(3):539–49.
7 White CM, Kluger J, Lertsburapa K, Faheem O, Coleman CI. Effect of preoperative angiotensin converting enzyme inhibitor or angiotensin receptor blocker use on the frequency of atrial fibrillation after cardiac surgery: a cohort study from the atrial fibrillation suppression trials II and III. Eur J Cardiothorac Surg. 2007;31(5):818–21.
8 Calo L, Bianconi L, Colivicchi F, et al. N-3 fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a randomized, controlled trial. J Am Coll Cardiol. 2005;45(10):1723–8.
9 Steinberg JS. Postoperative atrial fibrillation: a billion-dollar problem. J Am Coll Cardiol. 2004;43(6):1001–3.
10 Jalife J, Berenfeld O, Skanes A, Mandapati R. Mechanisms of atrial fibrillation: mother rotors or multiple daughter wavelets, or both? J Cardiovasc Electrophysiol. 1998;9 (8 Suppl):S2–12.
11 Papageorgiou P, Monahan K, Boyle NG, et al. Site-dependent intra-atrial conduction delay. Relationship to initiation of atrial fibrillation. Circulation. 1996;94(3):384–9.
12 Moe GK, Abildskov JA. Atrial fibrillation as a self-sustaining arrhythmia independent of focal discharge. Am Heart J. 1959;58(1):59–70.
13 Taylor AD, Groen JG, Thorn SL, Lewis CT, Marshall AJ. New insights into onset mechanisms of atrial fibrillation and flutter after coronary artery bypass graft surgery. Heart. 2002;88(5):499–504.
14 Ad N, Snir E, Vidne BA, Golomb E. Potential preoperative markers for the risk of developing atrial fibrillation after cardiac surgery. Semin Thorac Cardiovasc Surg. 1999;11(4): 308–13.
15 Ak K, Akgun S, Tecimer T, et al. Determination of histopathologic risk factors for postoperative atrial fibrillation in cardiac surgery. Ann Thorac Surg. 2005;79(6):1970–5.
16 Mariscalco G, Engstrom KG, Ferrarese S, et al. Relationship between atrial histopathology and atrial fibrillation after coronary bypass surgery. J Thorac Cardiovasc Surg. 2006;131(6):1364–72.
17 Bruins P, te Velthuis H, Yazdanbakhsh AP, et al. Activation of the complement system during and after cardiopulmonary bypass surgery: postsurgery activation involves C-reactive protein and is associated with postoperative arrhythmia. Circulation. 1997;96(10):3542–8.
18 Chung MK, Martin DO, Sprecher D, et al. C-reactive protein elevation in patients with atrial arrhythmias: inflammatory mechanisms and persistence of atrial fibrillation. Circulation. 2001;104(24):2886–91.
19 Aviles RJ, Martin DO, Apperson-Hansen C, et al. Inflammation as a risk factor for atrial fibrillation. Circulation. 2003; 108(24):3006–10.
20 Ishii Y, Schuessler RB, Gaynor SL, et al. Inflammation of atrium after cardiac surgery is associated with inhomogeneity of atrial conduction and atrial fibrillation. Circulation. 2005;111(22):2881–8.
21 Almassi GH, Schowalter T, Nicolosi AC, et al. Atrial fibrillation after cardiac surgery: a major morbid event? Ann Surg. 1997;226(4):501–11; discussion 11–3.
22 Stamou SC, Dangas G, Hill PC, et al. Atrial fibrillation after beating heart surgery. Am J Cardiol. 2000;86(1):64–7.
23 Abreu JE, Reilly J, Salzano RP, Khachane VB, Jekel JF, Clyne CA. Comparison of frequencies of atrial fibrillation after coronary artery bypass grafting with and without the use of cardiopulmonary bypass. Am J Cardiol. 1999;83(5):775–6, A9.
24 Weintraub WS, Jones EL, Craver J, Guyton R, Cohen C. Determinants of prolonged length of hospital stay after coronary bypass surgery. Circulation. 1989;80(2):276–84.
25 Villareal RP, Hariharan R, Liu BC, et al. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. J Am Coll Cardiol. 2004;43(5):742–8.
26 Melo J, Voigt P, Sonmez B, et al. Ventral cardiac denervation reduces the incidence of atrial fibrillation after coronary artery bypass grafting. J Thorac Cardiovasc Surg. 2004;127 (2):511–6.
27 Kalman JM, Munawar M, Howes LG, et al. Atrial fibrillation after coronary artery bypass grafting is associated with sympathetic activation. Ann Thorac Surg. 1995;60(6):1709–15.
28 Creswell LL, Alexander JC, Jr., Ferguson TB, Jr., Lisbon A, Fleisher LA. Intraoperative interventions: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. Chest. 2005;128(2 Suppl):S28–35.
29 Cummings JE, Gill I, Akhrass R, Dery M, Biblo LA, Quan KJ. Preservation of the anterior fat pad paradoxically decreases the incidence of postoperative atrial fibrillation in humans. J Am Coll Cardiol. 2004;43(6):994–1000.

30 Sedrakyan A, Wu AW, Parashar A, Bass EB, Treasure T. Off-pump surgery is associated with reduced occurrence of stroke and other morbidity as compared with traditional coronary artery bypass grafting: a meta-analysis of systematically reviewed trials. Stroke. 2006;37(11):2759–69.
31 Ascione R, Caputo M, Calori G, Lloyd CT, Underwood MJ, Angelini GD. Predictors of atrial fibrillation after conventional and beating heart coronary surgery: a prospective, randomized study. Circulation. 2000;102(13):1530–5.
32 Lamb RK, Prabhakar G, Thorpe JA, Smith S, Norton R, Dyde JA. The use of atenolol in the prevention of supraventricular arrhythmias following coronary artery surgery. Eur Heart J. 1988;9(1):32–6.
33 Matangi MF, Strickland J, Garbe GJ, et al. Atenolol for the prevention of arrhythmias following coronary artery bypass grafting. Can J Cardiol. 1989;5(4):229–34.
34 Geelen P, O'Hara GE, Roy N, et al. Comparison of propafenone *vs* procainamide for the acute treatment of atrial fibrillation after cardiac surgery. Am J Cardiol. 1999;84(3): 345–7, A8–9.
35 Hjelms E. Procainamide conversion of acute atrial fibrillation after open-heart surgery compared with digoxin treatment. Scand J Thorac Cardiovasc Surg. 1992;26(3):193–6.
36 Campbell TJ, Gavaghan TP, Morgan JJ. Intravenous sotalol for the treatment of atrial fibrillation and flutter after cardiopulmonary bypass. Comparison with disopyramide and digoxin in a randomised trial. Br Heart J. 1985;54(1): 86–90.
37 Gavaghan TP, Koegh AM, Kelly RP, Campbell TJ, Thorburn C, Morgan JJ. Flecainide compared with a combination of digoxin and disopyramide for acute atrial arrhythmias after cardiopulmonary bypass. Br Heart J. 1988;60(6):497–501.
38 Martinez EA, Bass EB, Zimetbaum P. Pharmacologic control of rhythm: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. Chest. 2005;128 (2 Suppl):S48–55.
39 Pfisterer ME, Kloter-Weber UC, Huber M, et al. Prevention of supraventricular tachyarrhythmias after open heart operation by low-dose sotalol: a prospective, double-blind, randomized, placebo-controlled study. Ann Thorac Surg. 1997; 64(4):1113–9.
40 Sanjuan R, Blasco M, Carbonell N, et al. Preoperative use of sotalol *vs* atenolol for atrial fibrillation after cardiac surgery. Ann Thorac Surg. 2004;77(3):838–43.
41 Parikka H, Toivonen L, Heikkila L, Virtanen K, Jarvinen A. Comparison of sotalol and metoprolol in the prevention of atrial fibrillation after coronary artery bypass surgery. J Cardiovasc Pharmacol. 1998;31(1):67–73.
42 Mitchell LB, Exner DV, Wyse DG, et al. Prophylactic oral amiodarone for the prevention of arrhythmias that begin early after revascularization, valve replacement, or repair (PAPABEAR): a randomized controlled trial. JAMA. 2005; 294(24):3093–100.
43 Bagshaw SM, Galbraith PD, Mitchell LB, Sauve R, Exner DV, Ghali WA. Prophylactic amiodarone for prevention of atrial fibrillation after cardiac surgery: a meta-analysis. Ann Thorac Surg. 2006;82(5):1927–37.
44 VanderLugt JT, Mattioni T, Denker S, et al. Efficacy and safety of ibutilide fumarate for the conversion of atrial arrhythmias after cardiac surgery. Circulation. 1999;100(4): 369–75.
45 Halonen J, Halonen P, Jarvinen O, et al. Corticosteroids for the prevention of atrial fibrillation after cardiac surgery: a randomized controlled trial. JAMA. 2007;297(14):1562–7.
46 Epstein AE, Alexander JC, Gutterman DD, Maisel W, Wharton JM. Anticoagulation: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. Chest. 2005;128(2 Suppl):S24–7.
47 Burgess DC, Kilborn MJ, Keech AC. Interventions for prevention of post-operative atrial fibrillation and its complications after cardiac surgery: a meta-analysis. Eur Heart J. 2006;27(23):2846–57.