Atrial fibrillation and heart failure

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Submitted 25 May 2004; accepted after revision 28 June 2004

KEYWORDS
heart failure; atrial fibrillation; antiarrhythmic drug therapy; overdrive cardiac pacing; cardiac resynchronization;

Atrial fibrillation (AF) and congestive heart failure (CHF) are the new epidemics of the third millennium due to ageing of the population and the success of new therapies for acute cardiac illnesses that, in the past, were fatal. The interactions between AF and CHF are only partially understood, and the effectiveness of drugs as well as that of non-pharmacological interventions remains often disappointing. Furthermore, few studies have been planned with a view to evaluate specifically the combined clinical setting of atrial tachyarrhythmias and CHF.

Antiarrhythmic drugs have been widely used in preparation for cardioversion of AF and maintenance of sinus rhythm, though they have a limited and, usually, temporary efficacy [1]. Furthermore, in patients suffering from CHF, the choice is limited to class III drugs (mainly amiodarone) in view of the adverse cardiovascular effects of class I drugs. Noteworthy new frontiers in the pharmacological treatment of these patients are angiotensin-converting enzyme inhibitors [2] and angiotensin-1 receptor blockers [3], which may prevent AF by unloading the left atrium and by preventing electrical remodelling and interstitial fibrosis via a direct action on atrial myocytes.

Device therapy for atrial fibrillation in congestive heart failure

The limitations of antiarrhythmic drug therapy have prompted the growing use of device therapy...
to treat patients with refractory AF. The antiarhythmic benefits of atrial or dual chamber pacing, as opposed to single chamber ventricular pacing, in reducing the rates of AF recurrences and in slowing the progression to permanent AF have been established in large prospective trials which enroled patients with either sinus node disease or mixed conventional indications for permanent pacing [4–6]. In this respect, the impact of ventricular pacing on haemodynamic function is a major consideration. Physiological pacing by a sequential dual chamber system and an optimised, individually programmed, atrio-ventricular (AV) delay may contribute major improvements in haemodynamic function and clinical outcome, mainly in the presence of CHF [7–9]. On the other hand, asynchronous ventricular activation by right ventricular (RV) apical pacing may be the cause of major inter- and/or intraventricular mechanical dyssynchrony, which may depress haemodynamic function and myocardial metabolism [10]. The prolongation of isovolumic contraction and relaxation times may critically shorten diastolic filling and lower the cardiac output. Furthermore, the delayed activation of the left ventricular (LV) lateral wall may delay its contraction past the closure of the aortic valve, such that it not only fails to contribute to stroke volume, but also interferes with diastolic filling [11]. Programming an AV delay longer than the spontaneous interval may prevent unnecessary ventricular pacing. However, a long AV delay is associated with long device atrial refractory periods and may cause competitive atrial pacing, which may induce AF. Furthermore, despite the programming of a long AV delay, the percentage of ventricular pacing may remain high with dual chamber pacing systems [12]. It was recently reported that the incidence of AF at a mean follow-up of nearly 3 years was significantly lower with AAI (7.4%) than with DDD pacing, even with the programming of a long AV delay (DDD with long AV delay = 17.5%; DDD with short AV delay = 23.5%, \(P = 0.03\) versus AAI) [13]. Algorithms have been introduced to limit ventricular pacing, while preserving back-up pacing in case of AV block, and are currently being refined [14]. The adverse effects of RV pacing could theoretically be prevented by selecting alternative RV pacing sites, which may mitigate the degree of ventricular dyssynchrony compared with apical pacing. Interventricular septum and RV outflow tract pacing have been tested clinically with inconsistent results [15,16]. The role of cardiac resynchronization therapy (CRT) to prevent AF in patients with CHF, standard indications for permanent pacing, and in need of consistent ventricular pacing will be studied in the near future.

Dual chamber defibrillators with atrial antitachycardia functions, including physiological pacing, pacing prevention algorithms, antitachycardia pacing therapies and low energy internal cardioversion have been effective in the management of spontaneous atrial tachyarrhythmias in recipients of devices implanted for life-threatening ventricular arrhythmias [17–19], as well as in patients whose sole indication for device implantation was symptomatic drug refractory atrial tachyarrhythmias [20]. In contrast to a stand-alone atrial defibrillator, which has only been implanted in patients with structurally normal hearts [21], the new devices can be used in patients with CHF since ventricular defibrillation back-up is available to treat life-threatening ventricular tachyarrhythmias. In clinical studies enrolling patients with drug refractory AF, device therapy was associated with a higher quality of life and lower rates of hospitalizations [22]. Furthermore, a long-term reduction in AF burden was observed in patients who were cardioverted soon after the onset of a tachyarrhythmia.

In patients with CHF, automatic antitachycardia pacing and early cardioversion of AF of recent onset may prevent acute cardiac decompensation and alleviate symptoms. Arrhythmia-induced atrial remodelling may be prevented, followed by a secondary decrease in AF recurrences [23]. Controlled studies in this field are to be encouraged.

### Atrial fibrillation in patients with heart failure and ventricular tachyarrhythmias

AF is a highly prevalent arrhythmia, before or after device implantation, in patients with CHF who are also candidates for implantation of a cardioverter defibrillator (ICD) [24]. Overall, >50% of patients are expected to experience AF during the life of an ICD [25]. AF may lead to major adverse events, including inappropriate shocks [26], induction of ventricular tachyarrhythmias [27], haemodynamic impairment, thromboembolic events or acute myocardial infarction. Furthermore, AF is an independent predictor of adverse prognosis in this population [28,29]. In this clinical setting, the benefits expected of dual chamber ICDs equipped with atrial antitachycardia functions include relief of symptoms and limitation of adverse events such as stroke, thromboembolism and recurrent hospitalizations, improvement in haemodynamic function, prevention of ventricular tachycardia or...
fibrillation triggered by atrial tachyarrhythmias, fewer inappropriate shocks, and need for fewer antiarrhythmic drugs.

The value of systematic implantation of ICDs with atrial antitachycardia pacing capability in all patients with CHF and class I device indications and histories of AF, or at risk of atrial tachyarrhythmias, should be examined in prospective studies.

Cardiac resynchronization therapy: perspectives

CRT, though introduced recently, is already playing a prominent role among non-pharmacological therapies of refractory CHF associated with cardiac dyssynchrony. It is noteworthy that all published studies consistently report the immediate relief of oedema, dyspnoea and fatigue, greater general well-being, as well as, in the long-term, a decrease in New York Heart Association (NYHA) functional class, increase in exercise capacity and maximal oxygen uptake, improvement in quality of life, and need for fewer hospitalizations and number of days spent in the hospital. A meta-analysis of published studies and preliminary data from the COMPANION trial (Heart Failure Society of America Scientific Meetings, September 2003 — Late Breaking Trials) suggest a favourable effect of device implantation on survival, a question to be answered by the results of the ongoing CARE-HF trial, which has enrolled >800 patients. Several other issues, however, need to be addressed, including the selection of appropriate candidates to eliminate the “non-responders” phenomenon, the choice of optimal, individual pacing site, and the role of single site versus multisite LV pacing. Furthermore, the expansion of indications to patients in the lower NYHA functional classes to prevent disease progression, or patients with conventional pacing indications and depressed LV function should be studied. Technological improvements facilitating the implantation of CRT systems will probably expand the indications. Finally, prospective studies to evaluate the impact of CRT on the incidence of AF should be strongly encouraged.

Toward a universal device

Combining CRT with ICD is a distinct issue related to cardiac pacing in CHF. One may hypothesise that simultaneous RV and LV pacing could prevent re-entry by reducing the ventricular activation time and eliminate markedly delayed activation of the LV postero-lateral wall. On the other hand, LV epicardial pacing via the coronary venous system could be proarrhythmic by increasing myocardial electrical instability. While this issue remains unsettled, preliminary data suggest a neutral effect of CRT on the development of spontaneous ventricular tachyarrhythmias. Nevertheless, considering the high risk of sudden cardiac death to which patients with CHF are exposed, the liberal use of ICD back-up seems appropriate in CRT. Data from the COMPANION and SCD-HEFT trials, presented recently, strongly support this position. Needless to say, ICD back-up is mandatory in patients with class I or II ICD indications.

The introduction and a broad application of a universal device designed for patients with CHF and AF, which will offer CRT, prevention and termination of atrial tachyarrhythmias, including low energy cardioversion, and ICD therapy, is expected in the next few years. Powerful diagnostic functions will allow the continuous monitoring of arrhythmias and clinical status, facilitating the individual prescription of pharmacological regimens. Drug delivery systems to treat emergencies, such as pulmonary oedema or electrical storms, will be incorporated in implantable devices.

Cost analysis

In this evolving environment, organisational and economical issues will be critical. A strong relationship between heart failure specialists and electrophysiologists will be crucial. Detailed cost—benefit analyses will be needed for each new therapeutic strategy. The increasing costs of treatments and rapidly growing numbers of patients will represent a major challenge for health care providers. The information stored in device memories and automatic delivery of drug or electrical therapies may become the main tools to prevent the acute manifestations of the disease and limit the rates of hospitalization. This, ultimately, may render device therapy cost-effective.

References


