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International Journal of Cardiology 88 (2003) 157–166

International Journal of Cardiology

www.elsevier.com/locate/ijcard

Effectiveness and costs of chemical versus electrical cardioversion of atrial fibrillation

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Received 22 July 2001; received in revised form 4 January 2002; accepted 11 February 2002

Abstract

Background: Atrial fibrillation is the most common sustained cardiac arrhythmia and has an important impact on costs of medical assistance. Traditional interventions to convert atrial fibrillation to sinus rhythm are antiarrhythmic drugs and external electrical cardioversion. However, the best option for starting the cardioversion is not well established. *Methods:* In a multicentre randomised trial of 139 patients with persistent atrial fibrillation lasting less than 6 months, we compared the effectiveness and the cost-effectiveness ratio of initial treatment with chemical or electrical cardioversion. Subjects who did not achieve sinus rhythm with chemical cardioversion were considered to undergo electrical cardioversion and vice-versa. *Results:* The efficacy of the initial attempt for cardioversion was similar with chemical or electrical cardioversion (74 vs. 73%, $P=0.95$). However, the strategy of starting with antiarrhythmic drugs was more effective than with electrical procedure (96 vs. 84%, $P=0.0016$). Initiating with chemical cardioversion was also less expensive than with electrical cardioversion (US$1240 vs. US$1917; $P=0.002$). Life-threatening complications occurred only during chemical cardioversion (5%), all of them in patients with structural heart disease. *Conclusions:* In patients with persistent atrial fibrillation of less than 6 months, initial chemical or electrical cardioversion appear to be similar but the strategy of starting the cardioversion with antiarrhythmic drugs is more effective and less expensive than starting with the electrical procedure. Patients with structural heart disease undergoing chemical cardioversion seem to be more susceptible to severe complications.

Keywords: Atrial fibrillation; Cost-effectiveness; Electrical cardioversion; Antiarrhythmic drug; Cardiac arrhythmia

1. Introduction

Atrial fibrillation affects about 2.2 million people in the United States [1] and is the main cause of hospitalisation for cardiac arrhythmias [2]. These cases represent a total expense of approximately 1 billion dollars a year [3]. The restoration of sinus rhythm alleviates patient's symptoms, prevents ventricular dysfunction and reduces risk of thromboembolism [4]. However, there is no consensus regarding the best treatment for converting atrial fibrillation [5], i.e. starting with chemical or electrical intervention. In the absence of contraindications, both are available and one can be used in the case of failure of the other.

Despite its clinical and economic importance, no prospective randomised study comparing the effectiveness and costs of these strategies for cardioversion of atrial fibrillation has been published. This

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0167-5273/02/$ – see front matter
doi:10.1016/S0167-5273(02)00380-7

multicentre trial compares the effectiveness of electrical versus chemical cardioversion of atrial fibrillation, with the aim of supplying information to manage patients who need this medical intervention, and to help in the decision-making process.

2. Methods

Patients presenting a persistent episode of atrial fibrillation of less than 6 months with indication for restoration of sinus rhythm by either of two methods of cardioversion (chemical or electrical) were considered eligible for the study. The duration of atrial fibrillation was determined by the onset of symptoms or, in the case of asymptomatic or oligosymptomatic patients, it was considered the period since the last electrocardiogram on sinus rhythm. Other inclusion criteria were: hemodynamically stable patients, serum potassium >3.8 mequiv./l, no anaesthetic contraindication and absence of signs of digitalis toxicity.

The following conditions were considered exclusion criteria: a strong belief from the physician or the patient that either of the therapeutic options would have better results based on acquired experience in previous episodes, moderate or severe heart failure, hypertension (diastolic blood pressure >110 mmHg), alcohol or drug abuse, pregnancy or lactation, renal failure, myocardial infarction in the last 30 days, current therapy with antiarrhythmic drugs and left ventricular ejection fraction <0.40. Ethical commissions of all the participating institutions approved the protocol. Each patient gave informed consent.

Each participating centre received sealed opaque envelopes sequentially numbered, with a randomised indication for starting with chemical or electrical cardioversion. Patients were informed in detail about the procedures they could undergo. After a written informed consent was obtained, patients were randomised by opening the envelopes in sequential order.

The drugs for chemical cardioversion or for sedation, as well as the energy and the number of shocks utilised for electrical cardioversion and the length of hospital stay, were left to investigator's criteria. Also the decision for anticoagulation before cardioversion was left to the investigator, but there was a strong recommendation for its utilisation in patients with high risk of thromboembolic events. Success of cardioversion was defined as maintenance of sinus rhythm 24 h after the successful attempt. Failure of cardioversion was established if a stable sinus rhythm was not achieved immediately after a maximal energy shock (360 J) or 6 h after the maximal planned dose of an antiarrhythmic drug. Early recurrences of atrial fibrillation (until 24 h after cardioversion) were also considered failure of the therapy. In case of failure of the initial procedure (chemical or electrical), it was recommended to the investigator to attempt cardioversion using the other method. After restoration of sinus rhythm, most patients successfully cardioverted to sinus rhythm were treated with sotalol or quinidine according to a protocol published elsewhere [6].

Patients were assigned to the following groups: C (initial chemical cardioversion) or E (initial electrical cardioversion). Success rates were calculated for each group according to the intention-to-treat principle. Once a patient was randomised for a certain type of initial procedure, the patient was considered, in terms of statistical analysis, as belonging to that group until the end of the study, despite whether he or she, later on, underwent the other type of treatment, in the event the first procedure failed. Recent-onset atrial fibrillation was defined as episodes lasting ≤ 48 h and chronic if atrial fibrillation lasted >48 h. The analysis sought, therefore, to evaluate the impact of the initial medical decision from the point of view of effectiveness of the adopted strategy and of the risks for the patient.

We calculated costs from the patient's hospital admission until restoration of sinus rhythm or waiving new attempts. The direct costs related to the hospitalisation, diagnostic tests and cardioversion procedures were computed from the health service payer's point of view and correspond to hospital charges. The following items were computed in the cost analysis: hospital and intensive coronary unit daily expenses, hours of heart monitoring and of oxygen therapy, electrocardiograms, chest radiographies, echocardiograms, defibrillator fees and drugs used. The costs were expressed in dollars (US$) and the effectiveness corresponded to the success rate of each strategy. Cost-effectiveness was determined by dividing the value of mean cost per patient by the correspondent success rate, and expressed in US$/

patient converted to the sinus rhythm [7]. In determining costs in chemical or electrical arm, we also included the costs associated with the alternative cardioversion (costs of electrical cardioversion in the chemical arm and vice-versa).

2.1. Statistical analysis

It was estimated that 140 patients would be needed (70 per group) to detect a 15% absolute difference in the success rates between the two strategies, assuming $\alpha=0.05$ and $\beta=0.20$. Continuous variables with normal distribution were reported as mean±S.D. and compared between the groups by the Student's *t*-test (Gosset), while those with non-parametric distribution were reported as maximum and minimum values and median, and compared using the Wilcoxon–Mann–Whitney test. In the case of costs, mean value was also presented, as is usual in economic calculations. Comparisons of proportions were made by χ^2-test or Fisher's exact test, when appropriate. All tests were two-tailed and $P<0.05$ was considered significant.

3. Results

The trial enrolled 139 patients, 72 were assigned to initial chemical cardioversion (group C) and 67 to initial electrical cardioversion (group E). Baseline characteristics are present in Table 1. No significant differences were detected between the studied groups. The distribution of the patients according to their treatment allocation, cardioversion attempts and outcomes is shown in Fig. 1. The most frequently used drug was quinidine administered orally (62 of 86 patients, 72%) either isolated or following intravenous digitalis. Other intravenous regimens included procainamide (11 patients, 13%) and amiodarone (10 patients, 12%). In three patients (3%), sinus rhythm was restored with digitalis alone, which was administered with the aim of controlling ventricular rate before the administration of a traditional antiarrhythmic drug. Maximal doses were 1600 mg for quinidine, 2 mg/kg of intravenous infusion for procainamide and 600 mg intravenously for amiodarone.

Anticoagulation was not used in the 83 patients with recent-onset arrhythmia. All 38 patients with atrial fibrillation lasting more than 7 days and five of

Table 1
Baseline characteristics

	Group C	Group E
Age (years)	56±13	56±13
Sex		
Male	37 (51%)	37 (55%)
Female	35 (49%)	30 (45%)
Height (cm)	165±9	164±10
Weight (kg)	73±14	71±13
Duration of atrial fibrillation episode (h)		
Mean±S.D.	18±41	23±44
Median	24	48
Recent-onset atrial fibrillation (≤48 h)	47 (65%)	36 (54%)
Chronic atrial fibrillation (>48 h)	25 (35%)	31 (46%)
Number of previous episodes		
≤5	65 (90%)	61 (91%)
>5	7 (10%)	6 (9%)
Congestive heart failure (New York Heart Association)		
Class I	64 (89%)	60 (90%)
Class II	8 (11%)	7 (10%)
Left atrial diameter (cm)	3.9±0.6	4.1±0.7
Lone atrial fibrillation	30 (42%)	26 (39%)
Systemic hypertension	30 (42%)	29 (43%)
Ischaemic heart disease	4 (6%)	3 (4%)
Valvular heart disease	15 (21%)	11 (16%)
Idiopathic dilated cardiomyopathy	8 (11%)	7 (10%)
Operated atrial septal defect	0 (0%)	1 (1%)

C, chemical; E, electrical.

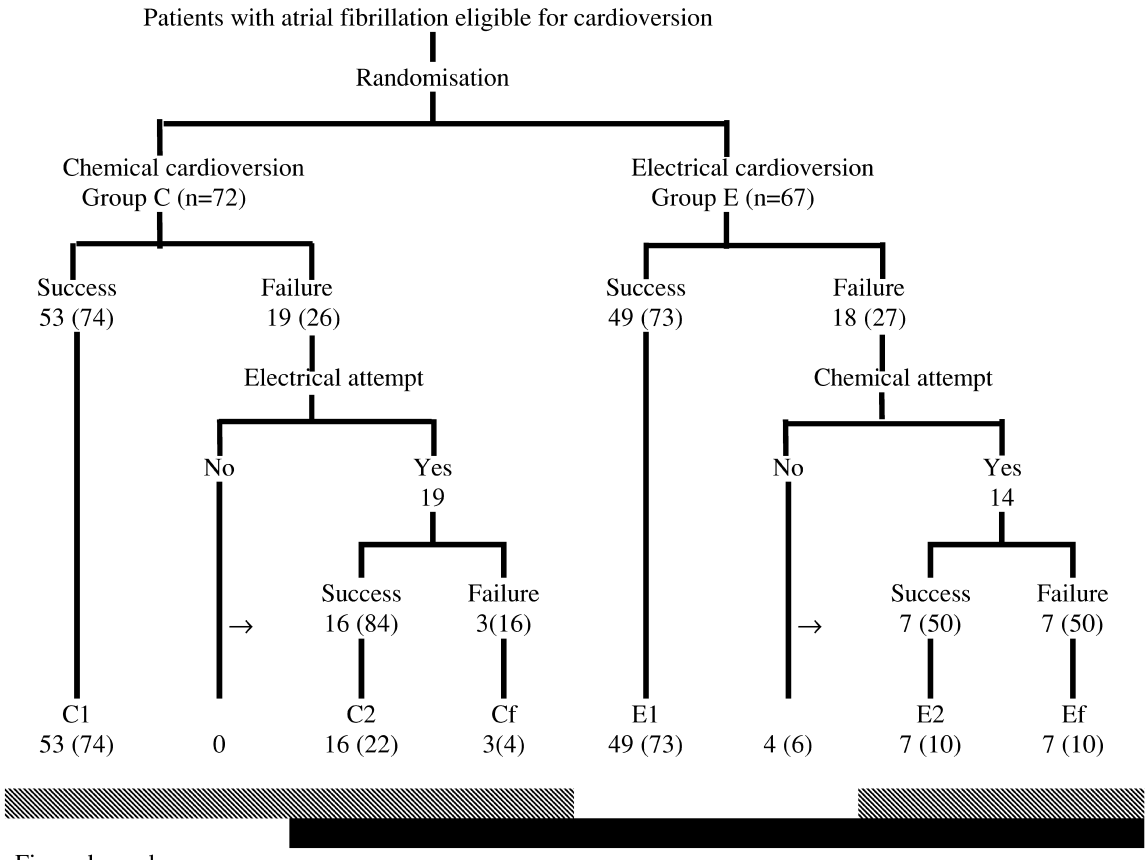

Figure legends

Total of chemical cardioversions

Total of electrical cardioversions

Abbreviations:

C1 Primary success with chemical cardioversion

C2 Primary failure with chemical cardioversion followed by success at electrical attempt

Cf Failure with both chemical and electrical attempts

E1 Primary success with electrical cardioversion

E2 Primary failure with electrical cardioversion followed by success at chemical attempt

Ef Failure with both electrical and chemical attempts

Values are shown as n (%). Percentages indicated by arrows (→) are related to the total of patients submitted to a second attempt of cardioversion in each group.

Fig. 1. Flow chart of study patients according to the strategies and outcomes. Patients with atrial fibrillation eligible for cardioversion.

18 (27%) of patients with duration between 48 h and 7 days were anticoagulated. No thromboembolic events occurred.

3.1. Overall efficacy

Analysis of only the efficacy of the initial procedure did not reveal a difference in the success rates between chemical (74%, 53 patients) and electrical (73%, 49 patients) cardioversion ($P=0.95$). However, the strategy of beginning with chemical cardioversion was effective in 96% (69 patients) of the cases, compared with 84% (56 patients) beginning with electrical cardioversion ($P=0.016$).

3.2. Analysis of subgroups

Of the 83 patients with recent-onset atrial fibrillation, 47 were of the group C and 36 of the group E. Primary success rates were the same in group C (81%, 38 patients) and group E (81%, 29 patients) ($P=0.97$). In these patients, the conversion rates also did not differ between the strategy of beginning with antiarrhythmic drugs (96%, 45 patients) or with electrical procedure (86%, 31 patients) ($P=0.35$). Of the 56 patients with chronic atrial fibrillation, 25 were of group C and 31 of group E. Primary success rates were similar in group C (60%, 25 patients) and in group E (65%, 20 patients) ($P=0.73$). In these cases, the conversion rates also did not differ between the strategy of beginning with drugs (96%, 24 patients) or with electrical procedure (81%, 25 patients) ($P=0.20$).

Of the 83 patients with structural heart disease, 42 were of group C and 41 of group E. Primary success rates did not differ significantly between group C (64%, 27 patients) and group E (73%, 30 patients) ($P=0.38$). In these patients, the conversion rates were also equivalent between the strategy of beginning with antiarrhythmic drugs (93%, 39 patients) or with electrical procedure (88%, 36 patients) ($P=0.48$). Of the 56 patients with lone atrial fibrillation, 30 were of group C and 26 of group E. In these cases, the difference in primary success rates did not reach statistical significance between group C (87%, 26 patients) and group E (73%, 19 patients) ($P=0.20$). However, all 30 patients with lone atrial fibrillation that started with chemical therapy were cardioverted to sinus rhythm versus only 77% (20 patients) of the cases beginning with electrical procedure ($P=0.007$).

Table 2
Length of stay and cost-effectiveness of cardioversion of atrial fibrillation according to treatment strategy

	Group C	Group E	*P*-value
Length of stay (days)			
Mean±S.D.	1±2	2±2	0.65
Median	1	2	
Range	0–11	0–16	
Mean cost per patient (US$)	1188	1603	0.0002
Range (US$)	185–6605	720–6734	
Effectiveness	0.958	0.836	0.016
Cost-effectiveness[a]	1240	1917	0.002

Group C, starting with chemical cardioversion. Group E, starting with electrical cardioversion.

[a] Costs (US$) for a successful cardioversion.

3.3. Cost-effectiveness

Sedation for electrical cardioversion was performed by cardiologists in all procedures, with no anaesthesiologist costs. The length of stay did not differ between the groups (Table 2). Costs analysis favoured beginning treatment with a chemical regimen. The main factors responsible for the increased cost of electrical cardioversion were the heart monitoring and the use of drugs and oxygen (Table 3). Other costs such as diagnostic tests were not different. Strategy C was not only more effective, but

Table 3
Items related to the increased costs observed in group E in comparison to group C

Item	Group C	Group E	*P*-value
Heart monitoring			0.05
Number of patients	51 (81%)	67 (100%)	
Median (US$)	30	30	
Range (US$)	0–1140	5–810	
Oxygen			0.00001
Number of patients	14 (19%)	39 (58%)	
Median (US$)	0	45	
Range (US$)	0–270	0–495	
Drugs[a]			0.00001
Median (US$)	15	39	
Range (US$)	1–104	17–227	

All other costs did not differ between the studied groups. Group C, starting with chemical cardioversion. Group E, starting with electrical cardioversion.

[a] Include antiarrhythmic agents and drugs used for anaesthesia during electrical cardioversion.

Table 4
Costs and effectiveness of strategies for converting atrial fibrillation according to underlying heart disease

	Lone atrial fibrillation		Structural heart disease	
	Group C	Group E	Group C	Group E
Mean cost per patient (US$)	965	1554	1135	1593
Effectiveness	1.0	0.769	0.928	0.878
Cost-effectiveness[a]	965	2021	1223	1814

Group C, starting with chemical cardioversion. Group E, starting with electrical cardioversion.
[a] Costs (US$) for a successful cardioversion.

incurred a lower mean cost per case reverted ($1240 vs. $1917) ($P=0.002$). According to the underlying heart disease, the best cost-effectiveness ratio was obtained with strategy C in cases of lone atrial fibrillation ($965) (Table 4).

3.4. Complications

Clinical complications of cardioversion were classified as severe (life-threatening) or mild. Minor side-effects such as nausea, vomiting, hyper- or hypotension, benign arrhythmias, agitation, sweating and apnoea not requiring intubation due to drugs used for chemical cardioversion or sedation before electrical cardioversion were considered mild complications.

Mild complications were present in 43 patients (50%) who underwent electrical cardioversion versus only 10 patients (12%) undergoing chemical cardioversion ($P<0.001$). In group E, they were related to sedation (apnoea 13 cases, 15%; nausea/vomiting 11 cases, 13%) and were easily managed by the attending physicians. Diarrhoea (six cases, 7%) and nausea (three cases, 3%) were the more frequent side effects of group C.

There were four cases (5%) of severe complications associated with antiarrhythmic drug therapy, all of them with structural heart disease (Table 5). Of these, three had been initially allocated to chemical and one to electrical cardioversion. No severe complication was observed with electrical procedures. There were no deaths.

4. Discussion

The success rate of pharmacological cardioversion varies widely depending on the characteristics of the patients, doses, administration route and kind of drug and observation time. In our study, the primary success rate was 74% and quinidine was the most frequently used drug (in 72% of the cases). Previous studies demonstrated conversion rates with oral quinidine of 11–88% [8–10]. By the time that this trial was carried out, there was no clear evidence that one drug was superior to another [11]. A recent meta-analysis of randomised controlled trials showed that flecainide, ibutilide and dofetilide seem to be the most efficient drugs to convert atrial fibrillation [12]. All of them were not used in our trial but we think that this restriction did not influence results in the main because, if these drugs had been used, the superiority of chemical cardioversion over electrical procedure would probably be strengthened.

We obtained initial success with electrical cardioversion in 73% of the cases. It is possible to speculate that the cardioversion rate with the electrical procedure was inferior to that expected based on

Table 5
Severe complications in four of the 86 patients who underwent chemical cardioversion

Heart disease	Drug	Complication
Mitral valve disease	Procainamide 1 g intravenous	High ventricular response atrial fibrillation+acute pulmonary oedema
Ischaemic heart disease	Digitalis+quinidine 1400 mg	Sustained ventricular tachycardia
Mitral valve disease	Digitalis+quinidine 600 mg	Bradycardia+cardiogenic shock
Idiopathic dilated cardiomyopathy	Digitalis+quinidine 600 mg	Long QT+sustained ventricular tachycardia+ventricular fibrillation

the literature date and it may have influenced our results. Previous studies reported cardioversion rates between 70 and 94% [13–18]. However, these results are difficult to compare because of the variety of patients' characteristics among the studies.

4.1. Effectiveness of cardioversion strategies

Since primary success rates of electrical and chemical cardioversion were similar, the best result obtained by strategy C was due to the differences observed in the success rates of the subsequent procedure. About 84% of the patients who underwent electrical cardioversion after an unsuccessful chemical attempt were converted to sinus rhythm, representing an increment of 22% in the overall success rate in group C. However, only 50% of the patients who underwent chemical cardioversion after an unsuccessful electrical attempt achieved success.

Recent studies demonstrated that a premedication with antiarrhythmic drugs can increase the efficacy of direct current shock or, at least, prevent early recurrences of atrial fibrillation [19–22]. Despite the lack of evidence from randomised trials, some reports suggested that quinidine also increases the efficacy of the electrical cardioversion [23,24]. Probably, an increased efficacy of electrical cardioversion in patients previously treated with antiarrhythmic drugs may have influenced the higher conversion rate of group C.

Atrial fibrillation duration varies largely in clinical trials testing antiarrhythmic drugs and a cut-off of 48 h, 1 week or 6 months have been the most frequently used. Antiarrhythmic drugs are more effective to convert recent-onset atrial fibrillation but high conversion rates have been observed even when duration up to 6 months was considered the inclusion criteria [25–27]. In our study, no difference was encountered with the initial attempt or with the strategy of starting with chemical or electrical cardioversion in the subgroup analysis of patients with recent-onset and chronic atrial fibrillation.

It is difficult to determine how many patients would follow with spontaneous conversion in our trial. After randomisation, no patient had atrial fibrillation converted to sinus rhythm before the institution of the specific antiarrhythmic therapy. We believe that, since the studied groups were randomised and well matched, this variable did not influence the observed results. In the chemical arm, an observation time of 6 h until the performance of the electrical cardioversion could be considered short for antiarrhythmic drugs such as quinidine, our preferred drug. This decision was made to reduce a possible influence of spontaneous conversion if a long observation time was used.

4.2. Effectiveness in subgroups

In the subgroups with recent-onset and chronic atrial fibrillation, the success rates of chemical and electrical cardioversion did not differ significantly. In patients with lone atrial fibrillation, the strategy of beginning with chemical cardioversion was significantly superior to the strategy of initiating with electrical cardioversion while in patients with structural heart disease this was not evident. All patients with lone atrial fibrillation who were not converted to sinus rhythm with drugs, were successfully converted in the subsequent electrical cardioversion, suggesting that this is the subgroup that most benefits from that strategy.

4.3. Cost-effectiveness

We observed that the mean cost of the chemical cardioversion was US$1240 per patient versus US$1917 with the electrical strategy, a reduction of $677 initiating with chemical intervention. This was especially favourable in cases with lone atrial fibrillation. Sedation and electrical cardioversion involve the use of specific technical apparatus and, frequently, the use of oxygen, contributing to greater costs.

Two studies compared the costs of ibutilide versus a projected first-line electrical cardioversion and demonstrated that the strategy of starting with the antiarrhythmic drug reduced the costs per patient from $260 ($1621 vs. $1881 with the electrical procure) [28] to $324 ($718 vs. $1042 with direct current shock) [29]. In a retrospective study, Dell'Orfano et al. [30] reported a reduction of $4211 with chemical cardioversion ($5681 vs. $9892 with electrical cardioversion). Costs of the procedures vary largely among different studies, but there was always a reduction in costs with an initial chemical intervention. Our costs are equivalent to those two studies

[28,29] but they are very inferior to that reported by Dell'Orfano et al. [30]. However, in this investigation, the hospital length of stay was superior to ours: 3 days for chemical and 5 days for electrical cardioversion versus 1 and 2 days, respectively, in our trial. Thus, the difference between these studies is smaller if we consider costs per day: $1959 with chemical and $1866 with electrical in the North American study versus $1033 and $1065, respectively, in our trial.

Recently, Oral et al. [31] compared the costs of electrical cardioversion of atrial fibrillation with and without ibutilide pre-treatment and observed that, in the presence of an anaesthesiologist, the mean cost of cardioversion was determined by the success rates of chemical and electrical cardioversion and that, in the absence of an anaesthesiologist, ibutilide pre-treatment increased the cost of cardioversion. In our trial, the anaesthesiologist was not required for electrical cardioversion, thus, if he was involved in all electrical procedures, certainly the advantage of chemical cardioversion would be strengthened.

4.4. Complications during cardioversion

The risk of dangerous pro-arrhythmias during chemical cardioversion of atrial fibrillation includes ventricular arrhythmias, severe bradycardia or high degree AV block at the moment of the conversion or acceleration of ventricular response [32–37]. We had a relatively high rate of life-threatening complications (5%), all of which occurred during attempts at chemical cardioversion. To avoid serious pro-arrhythmic complications, it has been considered good practice to monitor patients 24–48 h after antiarrhythmic drug administration. By study design, the length of hospital stay after antiarrhythmic drug administration was left to each investigator. Despite the fact that not all patients had received this caution, all pro-arrhythmic complications occurred during the in-hospital period, reflecting that high-risk patients were carefully treated.

In addition to minor problems directly related to the sedation, possible complications with electrical cardioversion such as ventricular arrhythmias [35], severe bradycardia [38] and coronary spasm [39] were not observed.

There were no thromboembolic complications. During our study, only 27% of the patients atrial fibrillation with duration between 48 h and 7 days were anticoagulated. Despite the lack of strong evidence regarding the exact duration of atrial fibrillation that determines the anticoagulation before the cardioversion of atrial fibrillation [37], current guidelines recommend that all cases with arrhythmia of more than 48 h must be anticoagulated [11,40,41].

4.5. Study limitations

The protocol for cardioversion and for sedation, as well as the length of hospital stay, was not previously determined. This decision was based on a previous observation that there was a surprisingly personal and institutional heterogeneity regarding the management of atrial fibrillation among major experts of the SOCESP [42], which was also observed in other countries [43]. Our objective was to include a large number of cardiologic centres in order to reflect the current practice on treatment of atrial fibrillation in Brazil. Furthermore, because a blinded trial with these two strategies was not feasible, we decided for an open-label protocol.

Our patients were not homogeneous in terms of duration of atrial fibrillation, including patients with recent-onset and chronic atrial fibrillation. Furthermore, by our study protocol, patients were submitted only once to the alternative procedure. This means that cases with initial failure with electrical cardioversion and a further failure with chemical procedure were not submitted to another electrical procedure.

We did not perform a long-term follow-up to assess the efficacy of the initial challenge of antiarrhythmic therapy. For instance, it is quite possible that patients who required the alternative method to restore sinus rhythm would resort earlier into atrial fibrillation. This idea was not tested between chemical or electrical cardioversion but was already demonstrated for other cardioversion techniques, such as external versus internal electrical cardioversion; in this situation, the increased cardioversion rate obtained with internal procedure did not remain over the follow-up [44].

Finally, costs of cardiovascular care vary widely and the results of our economic evaluation may have limited applicability in other countries.

5. Conclusion

In summary, in this study population, the efficacy of the initial attempt of cardioversion was similar for chemical or electrical cardioversion but the strategy of starting treatment using chemical cardioversion was more effective and less expensive than starting with electrical cardioversion, and it is especially adequate when applied in patients with atrial fibrillation without underlying heart disease. In patients with structural heart disease, the risks of complications with chemical cardioversion must be carefully evaluated and this factor may influence the choice of the initial strategy to be used.

Acknowledgements

This study was supported by Bristol-Myers Squibb S.A., São Paulo, Brazil.

Appendix A

The Cardiology Society of São Paulo (Sociedade de Cardiologia do Estado de São Paulo, SOCESP) Investigators: Angelo A.V. de Paola, MD, Edilberto Figueiredo, MD, Henrique H. Veloso, MD, Luis A. Renjel Prudencio, MD (Federal University of São Paulo/Paulista School of Medicine); Giovanni M.V. Bellotti, MD, Luiz A.M. César, MD, João F.M. Ferreira, MD, David Pamplona, MD (University of São Paulo/Heart Institute); Rodolfo P. de Albuquerque, MD, Ariovaldo Marques, MD (University of São Paulo/University Hospital); Roberto Franken, MD, Valdir Golin, MD, Afonso Celso, MD (Santa Casa de Misericórdia, São Paulo); Júlio C. Gizzi, MD, Dalmo R. Moreira, MD (Dante Pazzanese Heart Institute, São Paulo); João Pimenta, MD, Ney Valente, MD (Hospital do Servidor Público Estadual, São Paulo); Ricardo F. Salvadori, MD, Antonio C. Nogueira, MD (Unicor, São Paulo); Hermes T. Xavier, MD, Luiz F.G. Silva, MD (Santos); Otávio R. Coelho, MD, Cláudio Pinho, MD (Campinas); Hudson H. França, MD, José R. Maiello, MD (Sorocaba); Wilson Salgado Fo., MD, Eduardo Costa, MD, José R. Tavares, MD (Sao José dos Campos); José A. Marin Neto, MD, Marcelo G. Leal, MD (University of São Paulo/Medical School of Ribeirão Preto); Adalberto M. Lorga, MD, Ricardo Sanches, MD, Sílvio R.B. Alessi, MD (São José do Rio Preto); João C.F. Braga, MD, Benito Garbelini Jr., MD (Marília); Cláudio L.P. da Cunha, MD, Murilo Bittencourt, MD (Curitiba); José E. Siqueira, MD, Edgard Santos Jr., MD (Londrina); Mauro R. Wanderley, MD, Aston M. da Silva Jr., MD (Campo Grande); Cídio Halperin, MD, Moacir Zeni, MD (Porto Alegre).

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