

## CLINICAL STUDY

# Blood pressure prior to cardioversion predicts a conversion to sinus rhythm in patients with atrial fibrillation

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**Abstract:** *Background:* The effect of BP measured prior to the cardioversion has not been studied. *Methods:* Eighty patients (mean age 62±11 yrs, 44 men) with atrial fibrillation (AF), who underwent 92 cardioversions, were included. Non-invasive BP was measured. We performed a retrospective review of clinical data. The variables included into logistic regression analysis were: BP, age, gender, arterial hypertension, coronary artery disease, heart failure, obesity, left atrial diameter, duration of AF, antiarrhythmic and antihypertensive therapy. *Results:* A success rate of cardioversion was 60.9 %. BP was lower in the group of patients with a successful cardioversion (mean BP 97±15 vs 104±10 mmHg,  $p=0.02$ ; systolic BP 130±21 vs 140±18 mmHg,  $p=0.02$ ; diastolic BP 81±14 vs 86±8 mmHg,  $p=0.07$ ). Mean, systolic and diastolic BP cut-off levels with the highest sum of sensitivity and specificity were 103, 138 and 75 mmHg, respectively. *Conclusions:* Subjects with a successful cardioversion had lower BP measured immediately prior to the procedure. BP and concurrent antiarrhythmic treatment were the only predictors of a successful cardioversion (Tab. 1, Ref. 29). Full Text (Free, PDF) [www.bmj.sk](http://www.bmj.sk).  
Key words: direct-current cardioversion, electrical cardioversion, atrial fibrillation, blood pressure, arterial hypertension.

**Abbreviations:** ACE – angiotensin-converting enzyme, AF – atrial fibrillation, ARB – angiotensin receptor blocker, BP – blood pressure, CI – confidence interval, EF – ejection fraction, LA – left atrium, LV – left ventricle, RAAS – renin-angiotensin-aldosterone system, ROC – receiver operator curve.

Atrial fibrillation (AF) is the most common sustained cardiac rhythm disorder and is responsible for substantial morbidity and mortality in the general population (1). Rate-control has been shown to be non-inferior to rhythm-control in large randomized clinical trials (2, 3). Moreover, a pharmacological rhythm control approach may be associated with an increased cardiovascular morbidity and mortality in patients with persistent AF and arterial hypertension, as was shown in the RACE study (4). However, rhythm-control strategy is a reasonable option in many patients, especially in those with first episode of AF, symptomatic arrhythmia and younger age. Conversion to sinus rhythm can be achieved with medical therapy, direct-current electrical cardioversion, or using combination of medications and electrical cardioversion.

The success of electrical cardioversion may be affected by many factors. Higher rates of failed cardioversion were associated with longer arrhythmia duration, history of arterial hypertension, obesity, older age, larger left atrial (LA) diameter, lower mean LA appendage flow velocity, and lower early diastolic deformation of the basal LA wall induced by ventricular motion as measured by tissue Doppler imaging (5–10). Arterial hypertension is one of the most common conditions associated with AF (11). History of arterial hypertension was associated with 1.73 times lower success rate of electrical cardioversion in the study of Berry et al (12). However, the effect of blood pressure (BP) immediately prior to the electrical cardioversion has yet not been studied. The aim of this study was to evaluate the effect of BP immediately prior to the electrical direct-current cardioversion on the successful restoration of sinus rhythm in patients with AF.

## Methods

### Study population

We retrospectively reviewed all medical records of patients hospitalized from January 2002 through December 2006. We included all 80 patients with AF without associated valvular heart disease that underwent a total of 92 non-emergency direct-current electrical cardioversions during the study period. Patients ( $n=6$ ) with associated valvular heart disease were excluded. The only exception was mild mitral regurgitation (subjects with mild mitral regurgitation were included).

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### Blood pressure measurements

BP measurements were obtained per standard institutional protocol at the time of the admission and twice a day in all hospitalized patients. Certified mercury sphygmomanometers were used as a routine method for BP measurement in patients on the Internal Medicine ward. Intensive Care Unit patient monitors (Dash 3000, GE Medical Systems) were used for BP measurements in patients initially admitted to Intensive Care Unit and for BP measurements immediately prior to the cardioversion. Values given by the monitors were based on the Dinamap automated oscillometric method of noninvasive measurement. The following BP measurements were included in the analysis: maximal BP recorded during the hospitalization from the admission date to the date of the cardioversion. BP measured in the morning of the cardioversion day and BP measured immediately prior to the induction of anesthesia for cardioversion.

### Direct-current electrical cardioversion

All external synchronized direct current monophasic cardioversions were performed per standard institutional protocol under a short general intravenous anesthesia (intravenous bolus of sodium thiopental or midazolam). Standard electrode position was antero-lateral, Marquette series 900 defibrillator was used. Energy of the initial and repeated shock was determined for each patient upon the discretion of the attending physician that performed the procedure. Body constitution of the patient was taken into consideration. Success of cardioversion was defined as a sinus rhythm at the electrocardiogram recorded within the first minutes after cardioversion.

### Clinical variables

The following clinical variables were retrospectively collected from the medical records: age, sex, obesity, duration of arrhythmia (from the onset to the cardioversion), past history of AF, arterial hypertension, history of coronary artery disease, history of congestive heart failure, history of hyperlipidaemia, history of thyroid disease, history of alcohol abuse, current smoking. We also recorded all antiarrhythmic and antihypertensive medications at the admission and during the hospitalization prior to the cardioversion.

### Transthoracic echocardiography

Transthoracic echocardiography was performed according to the standard departmental protocol. The measurements included were LA diameter (antero-posterior diameter obtained from left parasternal long axis view), left ventricular (LV) ejection fraction and the presence of LV hypertrophy (defined as interventricular septum thickness >11 mm and/or posterior wall thickness >11 mm).

### Statistical analysis

Continuous data are summarized as mean + standard deviation (normal distribution) or as median and inter quartile range (skewed data). Two-tailed Student's t-test and two-tailed Mann-Whitney test were used for normally and skewed data, respec-

tively. Associations between a cardioversion success and different dichotomous categorical variables were tested by two-tailed Fisher's exact test. The same method was used to test possible interactions between two potential dichotomous covariates of cardioversion success. The nonparametric Spearman's correlation was used to detect interactions between two nominal covariates. Finally, a multifactorial analysis (step-wise logistic regression) was performed to confirm independent relationship between BP and immediate cardioversion success. We accounted for the effects of other covariates identified in previous analysis. Independent effect of dichotomous variable on cardioversion success is expressed as odds ratio with 95% confidence interval (CI). Receiver operator curve (ROC) analysis was performed to determine optimal BP cut-off level with highest sum of sensitivity and specificity. Level of significance was  $p < 0.05$ . Data were analyzed using the SPSS 13.0 statistical software (SPSS Inc., Chicago, IL).

## Results

### Baseline characteristics

Totally, 36 (45.0 %) women and 44 (55.0 %) men were included in the study. The mean age at the time of cardioversion was  $61.8 \pm 10.5$  years (range 31–87 years). Baseline clinical characteristics and medical history are shown in Table 1. More than half of the studied patients (55 %) had history of AF. Arterial hypertension was present in 79 % of subjects. The median LA diameter was 4.1 cm (range 2.6–5.8 cm). Median duration of AF before cardioversion was 30 days (range 1 day–2 years). Twenty eight (30.4 %) cardioversions were performed within the first 48 hours of the AF onset.

Medical management of arterial hypertension included the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) in 57 (62 %), beta-blocker in 61 (66 %), and second-generation calcium channel blockers (e.g. verapamil) in 9 (10 %) patients. Fifty seven (62 %) patients were receiving antiarrhythmic therapy. Amiodarone was used in 34

**Tab. 1. Patients, baseline characteristics.**

	Number of patients (% of total)
Total	80
Left ventricular EF >50%	69 (86.3 %)
History of AF	44 (55.5 %)
Arterial hypertension	63 (78.8 %)
Coronary artery disease	24 (30.0 %)
Congestive heart failure	9 (11.3 %)
Diabetes mellitus	16 (20.0 %)
Hyperlipidaemia	33 (41.3 %)
History of stroke	6 (7.5 %)
History of thyroid disease	13 (16.3 %)
Obesity	30 (37.5 %)
Regular alcohol intake	10 (12.5 %)
Smoking	14 (17.5 %)

AF – atrial fibrillation; EF – ejection fraction

(37 %), propafenone in 24 (26 %), and sotalolol in 4 (4 %) patients. Digoxin was used in 15 (17 %) patients for the acute heart rate control.

#### *Direct-current electrical cardioversion*

Sinus rhythm was recorded in 56 (60.9 %) cardioversions at the electrocardiogram taken within the first minutes after the last discharge. Moreover, short episodes of sinus rhythm were noticed visually on bedside patient monitor totally in 64 (69.6 %) cardioversions. Early, within-minute, recurrences of AF were judged as clinical failure of the procedure. A few sinus beats post discharge with short AF recurrences could not be analyzed reliably from the procedure written notes. Totally, sinus rhythm at discharge from the hospital was recorded in 50 (50.5 %) cases.

Repeated discharge was necessary in 10 finally successful cardioversions (17.9 %). Maximal energy used to restore sinus rhythm was: 360 J in 5 (8.9 %) cardioversions, 300 J in 37 (66.1 %) cardioversions, 200 J in 11 (19.6 %) cardioversions and 100 J in 3 (5.4 %) cardioversions. Maximal energy used in unsuccessful cardioversions was generally higher: 360 J in 5 (13.9 %) cardioversions, 300 J in 28 (77.8 %) cardioversions, 200 J or 100 J together in 3 (8.3 %) cardioversions, repeated discharge was applied in 24 unsuccessful cardioversions (66.7 %). No significant complications of the procedure were recorded.

#### *Blood pressure measurements*

The mean systolic BP recorded immediately prior to the cardioversion was significantly lower in a group of patients with successful cardioversion (systolic BP 130±21 vs. 140±18 mmHg,  $p=0.02$ ; diastolic BP 81±14 vs 86±8 mmHg,  $p=0.07$ ). The difference between BP in these two groups could be demonstrated also for the mean arterial pressure (97±15 mmHg vs 104±10 mmHg,  $p=0.02$ ). Similarly, the morning BP measured at the day of the cardioversion was significantly lower in those with successful cardioversion.

#### *Predictors of the cardioversion success*

Our analysis did not confirm a correlation between an immediate cardioversion success and age, sex, obesity, heart rate measured immediately prior to the cardioversion, LA size, LV hypertrophy, history of AF, history of arterial hypertension, heart failure, diabetes mellitus or regular alcohol intake. Similarly, no association between the use of antihypertensive medications (beta-blockers, ACE inhibitors, ARBs, and calcium channel blockers) and the success of the cardioversion was confirmed. Direct-current cardioversion was more successful in a group of patients that received antiarrhythmic medications (amiodarone, propafenone, or sotalolol) prior to the cardioversion (71.9 % vs 42.9 %,  $p<0.01$ ). The average duration of arrhythmia was shorter in a group of patients successfully converted to sinus rhythm (median 6.0 days with quartiles 2.0 and 60.0 days vs median 52.5 days with quartiles 18.5 and 90.0 days,  $p<0.005$ ).

The bivariate analysis showed no significant interaction between the arterial pressure measured immediately prior to the cardioversion and antiarrhythmic treatment, ACE inhibitors or

ARBs treatment, age, sex, obesity, heart rate measured immediately prior to the cardioversion, LA size or LV hypertrophy. The mean BP measured immediately prior to the cardioversion was higher in the group of patients with the history of arterial hypertension (systolic BP 137±20 mmHg vs 122±20 mmHg,  $p<0.05$ ; diastolic BP 85±13 mmHg vs 78±11 mmHg,  $p<0.05$ ; mean arterial pressure 102±13 mmHg vs 93±14 mmHg,  $p<0.01$ ). A weak positive correlation between duration of arrhythmia and BP measured immediately prior to the cardioversion (Spearman's rho for mean arterial pressure 0.38,  $p<0.001$ ) was spurious, and disappeared when only patients with arrhythmia lasting more than 48 hours before cardioversion were included in the analysis.

#### *Logistic regression analysis*

BP measured immediately prior to the cardioversion ( $p<0.05$ ) and concurrent treatment with antiarrhythmics (adjusted OR 3.3, 95 % CI 1.3–8.0,  $p<0.01$ ) were the only variables that predicted successful cardioversion in logistic regression analysis. BP cut-off levels with highest sum of sensitivity and specificity was chosen in the ROC analysis as 138 mmHg for systolic BP, 75 mmHg for diastolic BP, and 103 mmHg for mean arterial pressure. The cardioversion was more likely to be successful, if BP at the time of cardioversion was lower than cut-off values (adjusted odds ratios for mean arterial BP 3.2, 95 % CI 1.2–8.2,  $p=0.02$ ; systolic BP 3.1, 95 % CI 1.2–7.6,  $p=0.02$ ; diastolic BP 5.8, 95 % CI 1.2–28.3,  $p=0.03$ ). Similarly, BP immediately prior to the cardioversion was identified as an independent predictor of sinus rhythm at discharge from hospital (odds ratio for mean arterial BP 2.6, 95 % CI 1.1–6.7,  $p=0.04$ ).

## **Discussion**

The results of our study suggest that BP immediately prior to the cardioversion influence the success of the procedure. Subjects with a successful cardioversion had BP prior to the procedure closer to normal BP 120/80 mmHg. BP and concurrent treatment with antiarrhythmics were the only predictors of successful cardioversion in the logistic regression analysis.

Higher than normal BP in patients that failed to restore sinus rhythm with the electrical cardioversion may reflect a higher activation of renin-angiotensin-aldosterone system (RAAS) or higher sympathetic activity. Indeed, RAAS-dependent mechanisms were suggested as an important factor in the development of the structural and electrophysiologic substrate for AF (13). ACE inhibitors and ARBs appear to be effective in the prevention of AF and the use of these drugs following cardioversion appears promising as concluded in large meta-analysis (14). Autonomic nervous system plays an important role in all phases of AF, including its onset, maintenance, and termination (15). Conversely, AF itself may be responsible for sympathetic system activation (16). Beta-blockers have been shown to protect against early AF recurrences, particularly in subjects with arterial hypertension (17). The power of our study was not strong enough to confirm benefit of ACE inhibitors, ARBs or betablockers treatment on cardioversion success.

Higher than normal BP at the time of cardioversion could also be a marker of pre-hypertensive state in some patients with already developed incipient micromorphologic or electrophysiologic LA changes. Katritsis et al documented 45.6 times higher risk of arterial hypertension during 3 years follow-up of patients with lone AF that did not respond to antiarrhythmic therapy (18). Mechanisms by which sustained arterial hypertension predispose to AF include an increased afterload with compensatory LV hypertrophy and decreased LV compliance leading to anatomic and functional changes in the LA (e.g. stretch, hypertrophy, and alterations in atrial electrophysiology). Increased BP at the time of the electrical cardioversion may lead to the elevation of intra-atrial pressure or other electrophysiologic changes that decrease the success rate of the procedure.

We demonstrated that patients treated with antiarrhythmic therapy had a better chance for a successful electrical cardioversion. These findings are in accordance with previous studies. Amiodarone was shown to increase the efficacy of direct-current cardioversion (19). Oral pretreatment with sotalolol resulted in a higher rate of sinus rhythm restoration in patients with persistent AF refractory to cardioversion (20). Propafenone, given before the electrical cardioversion in chronic AF, did not show the relation to the rate of conversion, but decreased the recurrence of AF early after the shock, thus allow more patients to be discharged from the hospital with sinus rhythm (21).

We failed to show an association between previously reported predictors such as history of arterial hypertension or LA diameter and the immediate success of electrical cardioversion. This may be due to a small sample size (total number of cardioversions remarkably declined within past years) or as in the case of arterial hypertension also due to high prevalence of arterial hypertension in the study population. Also, previous studies were inconsistent in the determination of the successful cardioversion prediction according to LA size. Patients with larger LA diameter had lower chance to successful cardioversion in studies by Tebbe et al, Palinkas et al or Wand et al (6, 10, 22). Conversely, larger LA diameter did not predict cardioversion failure in study by Elhendy et al or Blich et al (9, 23). The time of LA diameter measurement may be important for the predictive value of this parameter. Reversible LA dilatation caused by loss of atrial contractility during first days of AF and LA size normalization after sinus rhythm restoration was documented by Schotten et al (24). LA size in the absence of mitral valve disease or AF may reflect the chronicity and duration of LA hypertension (25).

Current guidelines recommend a non-emergency direct current cardioversion after considering antiarrhythmic drug therapy in the case of newly diagnosed persistent AF (26). Guidelines recommend also an initiation of drug therapy before electrical cardioversion for recurrent persistent AF to reduce the likelihood of early recurrences of AF. Pretreatment with antiarrhythmics can be useful to enhance the success of direct-current cardioversion.

The results of our study suggest that a good BP control prior to the cardioversion will improve the success rate of the procedure. As the RASS and sympathetic nervous system play impor-

tant role in the development and maintenance of AF, a pre-treatment with beta-blockers, ACE inhibitors and ARBs would be optimal.

### Limitations

We performed a retrospective study. Therefore, our analysis was limited to recorded clinical data and measurements. Slower and more irregular heart rate could interact with BP measurements. We did not find significant difference in heart rate between the patient subgroups at the time of BP measurement, what should exclude the effect of heart rate on BP measurement and on the results.

A rather low success rate of cardioversions in our study, particularly in the firsts minutes after the procedure, could be explained by a significant group of patients, who underwent cardioversions without antiarrhythmics treatment before the procedure. Moreover, traditionally we used monophasic waveform defibrillator with antero-lateral electrode position at the study period, and there were significant number of the procedures with maximal energy applied lower than 360 J. The acute AF recurrences also lowered the success rate evaluated according to the rhythm on the first electrocardiogram after the procedure. Cardioversions success rate was documented in a broad range 70–100 % in previous studies (5, 6, 9, 12, 22, 27). First shock success rate reached only 42 % for 200 J and 68 % for 360 J discharge applied in anteroapical electrode position compared to second shock success rate 86 % for 360 J discharge applied in anteroposterior electrode position in study by Boodhoo et al (28). In study by Neumann et al a cardioversion success rate reached 100 % for the biphasic compared to 74 % for the monophasic waveform discharge (27). Early AF recurrences after the cardioversion were noted in 26 % patients in the study performed by Yu et al (29). A lower success rate of cardioversions in our study may increase sensitivity of our statistical analysis. However, reliability of the conclusions should not be significantly affected by the success rate of the procedures. Due to a sample size and retrospective design of the study, the effect of BP on immediate success or within-seconds early AF recurrences could not be analyzed separately.

### Conclusions

In our study we demonstrated that subjects with a successful cardioversion had BP immediately prior to the procedure closer to normal BP than patients with a cardioversion failure. BP and concurrent antiarrhythmic treatment were the predictors of a successful cardioversion.

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