Heart, Lung and Circulation (2015) **24,** 744–752
1443-9506/04/$36.00
http://dx.doi.org/10.1016/j.hlc.2015.02.025

Pulmonary Vein Isolation Compared to Rate Control in Patients with Atrial Fibrillation: A Systematic Review and Meta-analysis

Kaivan Vaidya, MBBS [a], Clare Arnott, MBBS [b], Anne Russell, MECh [c], Philip Masson, MBBS, PhD [a], Raymond W. Sy, MBBS, PhD [b], Sanjay Patel, MBBS, PhD [b,d*]

[a]Sydney School of Public Health, The University of Sydney, Sydney, NSW, Australia
[b]Department of Cardiology, Prince of Wales Hospital, Sydney, NSW, Australia; Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
[c]Department of Cardiology, Prince of Wales Hospital, Sydney, NSW, Australia
[d]Heart Research Institute, Sydney, NSW, Australia

Received 30 December 2014; received in revised form 22 February 2015; accepted 26 February 2015; online published-ahead-of-print 14 March 2015

Background Atrial fibrillation (AF) often coexists with congestive cardiac failure (CCF), with multiple treatment options available.

Methods Systematic review and meta-analysis of randomised control trials (RCT) comparing pulmonary vein isolation (PVI), pharmacological rate control, and atrioventricular junction ablation with pacemaker insertion (AVJAP) for AF, with a subgroup analysis in patients with CCF. We analysed changes in left ventricular ejection fraction (LVEF), Minnesota Living with Heart Failure Questionnaire (MLHFQ) score, six-minute walk distance (6MWD), treadmill exercise time, and treatment complications. Results were expressed as weighted mean differences (WMD) with 95% Confidence-Intervals (95%CI).

Results We included seven RCT (425 participants). PVI was associated with a greater increase in LVEF (WMD+6.5%, 95%CI:+0.6to+12.5) and decrease in MLHFQ score (WMD-11.0, 95%CI:-2.6to-19.4) than pharmacological rate control in patients with CCF. PVI was also associated with a greater increase in LVEF (WMD+9.0%, 95% CI:+6.3to+11.7) and 6MWD (WMD+55.0metres, 95%CI:+34.9to+75.1), and decrease in MLHFQ score (WMD-22.0, 95%CI:-17.0to-27.0), compared to AVJAP in patients with CCF. Irrespective of cardiac function, pharmacological rate control had similar effects to AVJAP on LVEF (WMD+0.6%, 95%CI:-8.3to+9.4) and treadmill exercise time (WMD+0.5 minutes, 95%CI:-0.4to+1.3).

Conclusions Our results support the clinical implementation of PVI over AVJAP or pharmacological rate control in AF patients with CCF, who may or may not have already trialled pharmacological rhythm control.

Keywords Atrial fibrillation • Heart rate control • Catheter ablation • Pulmonary vein isolation • Congestive heart failure • Atrioventricular node

*Corresponding author at: Department of Cardiology, Royal Prince Alfred Hospital, Camperdown, NSW 2050. Tel.: +61427886689,
Email: sanjay.patel@hri.org.au

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, occurring in 1-2% of the general population [1,2] and often coexists with, precipitates and/or exacerbates congestive cardiac failure (CCF) [3–9]. Guidelines [1] recommending whether to use pharmacological rate or rhythm control depend on age, symptoms, haemodynamic instability, the presence of a reversible cause, the duration of AF and concurrent cardiovascular disease. However, several large multi-centre randomised control trials (RCT) have failed to demonstrate a clear superiority of either approach [5–9]. The multi-centre AF-CHF trial [8] compared pharmacological rate and rhythm control specifically in a group of 1376 patients with AF and co-existing CCF (left ventricular ejection fraction (LVEF) $\leq$ 35%), and did not demonstrate a statistically significant difference between the two strategies.

Non-pharmacological treatments include percutaneous pulmonary vein isolation (PVI) and atrioventricular junction ablation with pacemaker insertion (AVJAP). Current guidelines [1], based on multi-centre RCT comparing PVI to pharmacological rhythm control, recommend PVI in patients with paroxysmal or persistent symptomatic AF refractory to anti-arrhythmic medications. PVI is also recommended as first-line therapy in patients with symptomatic paroxysmal AF who have a low risk of stroke, no structural heart disease, and state a preference for interventional treatment. AVJAP is recommended [1] in patients where pharmacological rate control has been unsuccessful and in patients with symptomatic AF recurrences despite pharmacological rhythm control or prior PVI attempts.

Despite evidence in the literature comparing pharmacological rhythm control to the three alternative treatments (pharmacological rate control, PVI or AVJAP), there are few RCT comparing these three options to each other. Furthermore, patients who have already unsuccessfully trialled or are unsuitable for pharmacological rhythm control will commonly be offered these treatment options. We therefore aimed to compare pharmacological rate control, PVI, and AVJAP, in patients with AF, and determine their effects on LVEF, symptoms, and functional capacity. Specifically, we aimed to determine treatment effects in patients with AF and concomitant CCF or left ventricular (LV) dysfunction.

Methods

Eligibility Criteria and Study Selection

We included RCT where our interventions of interest were compared in patients with atrial fibrillation with a minimum follow-up period of six months. We excluded studies where patients had atrial flutter or other forms of supraventricular tachycardia. Pharmacological rate control was defined based on the medication classes listed in the European Heart Journal's 2010 guidelines for AF management [1], and pharmacological rhythm control was excluded. PVI was defined as application of radiofrequency energy or cryotherapy via a percutaneously-inserted catheter to ablate tissue surrounding the pulmonary veins in the left atrium [10–12]. AVJAP was defined as catheter-mediated radiofrequency ablation of the atrioventricular junction or His bundle, followed by insertion of a permanent implantable pacing device [13–15].

Study Search and Information Sources

Three independent researchers searched the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE (1946 to April 2014), and Embase (1966 to April 2014) using the Medical Subject Headings (MeSH) and free text terms: 'atrial fibrillation', 'catheter ablation', 'radiofrequency ablation', 'pulmonary vein isolation', 'atrioventricular junction ablation', 'atrioventricular node ablation', and 'His bundle ablation'. Ongoing trials were reviewed through the US National Institutes of Health Clinical Trials registry, the Current Controlled Trials database, and grey literature through the Open Grey database. There were no search restrictions based on date of publication or language. Reference lists of relevant trials, systematic reviews, and review articles were subsequently manually searched in an attempt to identify any RCT not identified by electronic searches.

Data Collection and Items

Data were extracted independently and in duplicate from eligible publications [16–22] using a standardised data extraction template. We recorded: author(s), year of publication, RCT inclusion and exclusion criteria, RCT size and duration, and completeness of follow-up. Specifically, we recorded data for the following outcome measures: percentage change in left ventricular ejection fraction (LVEF), change in symptoms of CCF as assessed by the Minnesota Living with Heart Failure Questionnaire (MLHFQ) score (points), change in the distance (metres) a participant could walk in six minutes (6MWD), change in the time (minutes) a participant could exercise on a treadmill, and the number and type of complications. A meta-analysis was conducted for all outcome measures listed except complications.

Risk of Bias in Individual Studies

We assessed methodological quality within studies (Data supplement A) using the Cochrane risk of bias tool [23] which objectively assesses risk of bias in six specific domains. Specifically, sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective outcome reporting are considered.

Summary Measures and Statistical Synthesis of Results

Continuous outcomes were synthesised as weighted mean differences (WMD) with their 95% confidence intervals (CI). For all analyses, a p-value of $\leq$ 0.05 was considered to represent a statistically significant result. The random effects model of analysis was used, as there was expected clinical