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RESEARCH ARTICLE

Atrio-ventricular nodal ablation with biventricular pacing in atrial fibrillation with narrow QRS – a novel strategy to reduce mortality independent of underlying left ventricular function.

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ABSTRACT

Historically, clinical studies have demonstrated conflicting results for rate-control versus rhythm-control strategy in patients with permanent atrial fibrillation (AF) in terms of long-term mortality and morbidity. The concept of atrioventricular (AV) nodal ablation coupled with permanent biventricular pacing has recently been advocated as the closest approach to obtain a physiological reset especially in AF patients having underlying ventricular dysfunction. Herein, we present a critical analysis and detailed review based on prior and currently available evidence based on the ablation in permanent atrial fibrillation – cardiac resynchronization therapy (APAF-CRT) mortality trial.

Background

Previous studies have demonstrated potential harm of biventricular pacing in patients having narrow QRS.¹ Due to loss of atrio-ventricular (AV) synchrony in atrial fibrillation, usefulness of cardiac resynchronization therapy (CRT) has been questioned for long.² However, in symptomatic permanent AF patients who had failed or are unsuitable for AF ablation having poorly controlled ventricular rate by pharmacological therapy, biventricular pacing along with AV junction (AVJ) ablation has been shown to reduce heart failure related hospitalization and improve QoL outcomes (APAF-CRT trial).³ Our aim is to unravel the effect of nodal ablation along with CRT on long-term clinical outcomes including mortality which has not been evaluated previously in this subset of patient population by expository dissection of a recently published study in this regard.

Methodology and results

This was an extended phase of APAF-CRT trial⁴ primarily focussed on assessing mortality outcomes. This investigator-initiated, multicentric, prospective, open-label, blinded-outcomes, parallel-arm RCT enrolled severely symptomatic permanent AF (>6 months) patients in which AF ablation was unsuccessful or was contraindicated and having narrow QRS (≤ 110 msec) with at least one heart failure related hospitalization in the past one year. 133 patients were randomized in 1:1 fashion to AVJ ablation plus CRT arm (n=63) and drug treatment alone arm (n=70). Trial population comprised of elderly patients (median age=73 years), male-females sex ratio of 1:1, with mild LV dysfunction [mean LV ejection fraction (LVEF) = 41%]. One-third patients had LVEF <35% with 60% of patients in drug treatment arm taking digoxin. Notable exclusions involved patients having hypotension, New York Heart Association (NYHA) class IV, recent acute coronary syndrome (ACS) and prior cardiac implantable electronic device (CIED) implant with $\geq 5\%$ pacing demands. The trial was stopped for efficacy at the interim analysis after a median follow-up of 29 months per patient.

AVJ ablation plus CRT arm showed significant reduction of all-cause mortality in primary outcome analysis (11% vs 29; HR 0.26, 95% CI:0.10-0.65; $p=0.004$) with majority reduction in cardiovascular mortality. The estimated death rates at four years were 14% and 41% in the AVJ ablation plus CRT and drug arms, respectively. At four years, the relative and absolute risk reductions were 74% and

27%, respectively with number needed-to-treat (NNT) being 3.7 for ablate-and-pace strategy. AVJ ablation and CRT reduced the secondary endpoint of the combined risks of death from any cause or hospitalization for heart failure by 60% (95% CI 0.22–0.73; $p=0.002$).

Discussion

The observed benefit was due to the combination of the strict rate control and rate regularization achieved by AV junction ablation, together with biventricular pacing which counteracted the adverse effects of right ventricular pacing. Trial population in addition to being relatively smaller in size, also had higher baseline ventricular rate which might have created an extra scope for interventional therapies to contribute towards stricter rate control which in turn could have resulted in improved clinical outcomes. Whether this strategy would be as effective in patients with better baseline rate control or even in slowly conducting AF is still unclear. This being an open-label trial, there was a high unidirectional cross-over rate (n=18) from pharmacological arm to interventional arm. Also, some bias could have been introduced due to the lack of sham-procedure provisions in pharmacological arm. Although, the hazard ratios of primary endpoint while stratifying based on LVEF were similar in patients having LVEF >35% or $\leq 35\%$, yet the confidence limits in patients having LVEF $\leq 35\%$ crossed unity thereby rendering an insignificant p-value (HR 0.34, 95% CI:0.06-1.92; $p=0.22$) in contrast to patients having LVEF >35% (HR 0.27, 95% CI:0.08-0.84; $p=0.02$). The trial is also unclear on analysis of patients having near-normal or preserved ejection fraction thereby not clarifying the alleged advantage of CRT over right ventricular pacing regarding this patient sub-set. Clinical practice guidelines still maintain that for patients who are undergoing AV nodal ablation and have normal ejection fractions, right ventricular (RV) apical pacing is recommended.⁵ While the results of this trial are intriguing, ultimately CRT with AV node ablation is such an overly invasive strategy that the patient comorbidities and overall risks for an individual need to be weighed carefully.

Conclusion

In selected patients, the 'ablate and pace' strategy involving biventricular pacing is superior to pharmacological treatment alone in reducing mortality, death due to heart failure and recurrent hospitalizations in addition to improving quality of life indicators in symptomatic permanent AF

patients with heart failure having narrow QRS, irrespective of basal LV ejection fraction.

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