Recovered atrial fibrillation mediated cardiomyopathy: pharmacotherapy withdrawal cost-effectiveness

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Background

Atrial fibrillation-mediated cardiomyopathy (AFCM) is a reversible subtype of heart failure where AF is the primary cause of left ventricular (LV) systolic dysfunction.

The WITHDRAW-AF was a multicentre, investigator-initiated, randomised controlled trial conducted across eight Australian centres. Eligible patients had reduced LVEF (<40%) during AF, subsequent LVEF normalisation (>50%) in sustained sinus rhythm for at least 6 months, absence of structural disease on cardiac MRI, and were on ≥HFrEF medications without alternate indications.
Patients were randomised 1:1 to HFrEF therapy continuation or withdrawal. At 6 months, the groups crossed over, allowing paired comparisons. The WITHDRAW-AF trial demonstrated heart failure pharmacotherapy can be safely withdrawn in carefully selected AFCM patients with normalised and stable LVEF following catheter ablation.

We report a cost-effectiveness analysis using WITHDRAW-AF data, exploring cost implications and functional outcomes of withdrawing versus continuing HFrEF pharmacotherapy in this unique population.

Method

- Functional status (VO2 max and 6-minute walk test (6MWT)) and quality-of-life (Minnesota Living with Heart Failure Questionnaire (MLHFQ)) were assessed at baseline, 6 and 12 months. QALYs were calculated by mapping MLHFQ scores to EQ-5D-5L utility values (3). Utility and medication use was calculated based on trial data. As catheter ablation is considered the standard of care for AFCM, the cost of ablation was not included in the analysis. None of the cohort died during the follow-up period, so no adjustments to QALYs were made to account for death.
- A patient-level Markov model simulated costs and outcomes over 5 years, assuming an 8% reinitiation rate in the withdrawal group based on the WITHDRAW-AF trial. Medication costs were based on U.S. Veterans Affairs Federal Supply Schedule data. Monte Carlo simulations (n=2000 iterations) were conducted for probabilistic sensitivity analysis. This research adheres to the Helsinki Declaration as revised in 2013 and was approved by the Alfred Hospital Human Ethics and Research Committee (Melbourne, Australia).

Results

In WITHDRAW-AF, base-case cost savings for withdrawing pharmacotherapy was $1031 per patient/year (withdrawal vs continuation = US $1572.16 vs $2603.74, P<0.001). Utility values were comparable between groups: 6MWT (withdrawal vs continuation = 469m vs 456m, P=0.542), VO2 max (withdrawal vs continuation = 21.0ml/kg/min vs 22.0ml/kg/min, P=0.401), and MLHFQ scores (withdrawal vs continuation = 9 vs 8, P=0.234).

Over 5 years, probabilistic analysis projected cumulative medication costs were US$4437 (95% CI: $4396-$4478) for withdrawal versus US$8438 (95% CI: $8376-$8501) for continuation. Functional outcomes slightly favoured withdrawal: 6MWT distance was higher in 63.9% of simulations (mean difference 15.06m, 95% CI: 12.38-17.73), and VO2 max was higher in 68.2% (mean difference 1.67 ml/kg/min, 95% CI: 1.45-1.88). MLHFQ scores were comparable (mean difference 0.29, 95% CI: -0.41 to 1.0), with no significant difference in QALYs (mean difference -0.002, 95% CI: -0.007 to 0.003), see Figure 1.

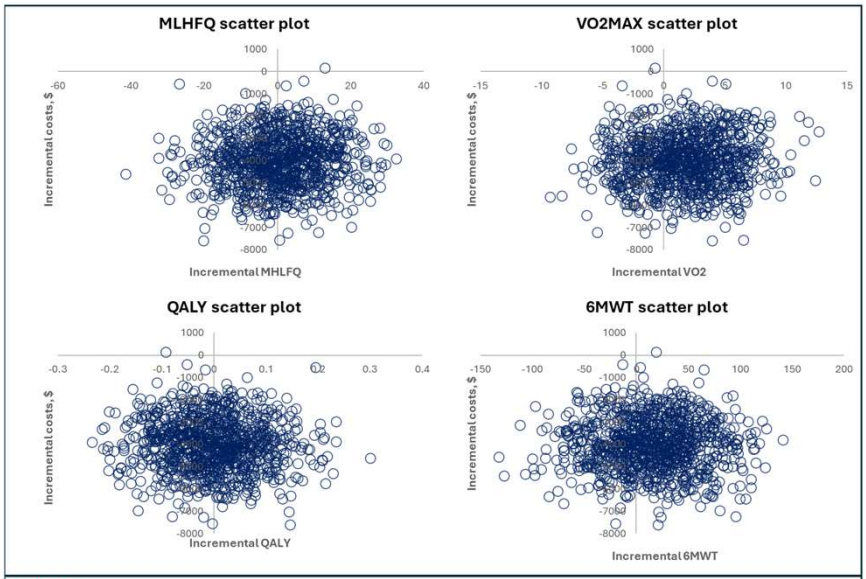

Figure 1: Distribution of 5-year incremental costs and utilities of pharmacotherapy withdrawal versus continuation in patients with recovered AF mediated cardiomyopathy. Scatter plots demonstrate cohort cost saving without cohort detriments in quality of life nor functional status. Abbreviations: 6MWT= 6-minute walk test; MLHFQ=Minnesota living with heart failure questionnaire; QALY= quality adjusted life year; VO2MAX=Volume Oxygen Maximum which is a measure of maximal aerobic capacity

Conclusion

In patients with recovered AFCM, withdrawal of heart failure pharmacotherapy was the dominant strategy, offering significant cost savings without detriment to function or quality of life. As AFCM is an increasingly recognised condition, pharmacotherapy de-escalation may help reduce long-term treatment burden on both patients and healthcare systems.

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