A Randomised-Controlled Pilot Trial of The Feasibility And Safety Of Therapy Withdrawal In Asymptomatic Patients With A Prior Diagnosis Of Dilated Cardiomyopathy & Recovered Cardiac Function

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Background: Around 1/3 of patients with DCM undergo left ventricular (LV) reverse remodelling following appropriate medical therapy leading to recovery of cardiac function and remission of symptoms. Studies demonstrate that such patients have an excellent long-term prognosis. However, it is not clear whether these patients still require ongoing life-long treatment. Current practice varies amongst clinicians and guidelines do not make recommendations. There is an unmet need to address this question.

Project Design**:** With support from a **BHF grant**, we aim to pilot an initial safety and **feasibility randomised-controlled trial of treatment withdrawal** in patients with a previous diagnosis of DCM and recovered cardiac function. The Research Ethics Committee has the given the study a favourable opinion.

Inclusion criteria: We aim to recruit: **50 patients** with a previous diagnosis of **DCM** who:
1) have previously had a **LVEF<40%,** that has **recovered to >50%** with **normal LV size**
2) have **no symptoms of heart failure**
3) have an **NT-pro-BNP <250ng/ml (or a BNP <100pg/ml)** and
4) are still taking at least **one heart failure medication** (ACEi/ARB, beta-blocker, MRA or loop diuretic).

Exclusion criteria: Uncontrolled hypertension (BP>160/100mmHg); poorly controlled atrial or ventricular arrhythmia; renal impairment (eGFR <30mls/min); pregnancy; angina; more than moderate valve disease.

Project protocol: We will randomise patients to either continue their medications or stop them in a structured, supervised fashion (starting with loop diuretics). Patients assigned to the withdrawal arm will have their medications stopped gradually over a period of 4-16 weeks (see flow diagram below) with changes every 2 weeks.

Before each change is made, patients will be reviewed in clinic or via telephone. Plasma NT-pro-BNP will be measured every 4 weeks. Therapy will be re-established if there are early signs of recurring heart-failure.

All patients will be assessed at baseline, 16 weeks and 6 months with **NT-pro-BNP, CMR and CPET**, performed at the Royal Brompton Hospital (RBH). At baseline genetic analysis for common DCM mutations will be performed and biomarkers of collagen metabolism and inflammation will be measured.

Those patients with a **contraindication to CMR will undergo echocardiography**.

Primary end-point: The primary end-point will be a relapse of heart failure (defined by a reduction in LVEF >10%, an increase in LV volumes by 10% or a two-fold rise in NT-pro-BNP and to >400ng/ml).

If this study demonstrates the safety and feasibility of treatment withdrawal, a multi-centre trial powered to clinical end-points will be planned.

Patient implications: Patients in the **withdrawal arm** will typically have **4-5 visits** to the RBH over **6 months**. Reasonable travel expenses will be provided. Patients in the **control arm** will be given the opportunity to undergo **treatment withdrawal after 6 months** so that all patients have the chance to do so. Normal and routine care will remain under the usual Consultants.

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Study protocol