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Phenotypic Characteristics of PRKAG2 Cardiomyopathy: Systematic Review

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ADMINISTRATIVE INFORMATION

Support - N/A.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202460104

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 June 2024 and was last updated on 25 June 2024.

INTRODUCTION

Review question / Objective Hypertrophic Cardiomyopathy is the most frequently inherited cardiac disease, with a clinical spectrum spanning from an asymptomatic state to considerable risks for morbidity and mortality. Mutations in the PRKAG2 gene may result in a progressive cardiomyopathy associated with significant phenotypic variability. In spite of a recent surge in the quantum of literature on PRKAG2 cardiomyopathy, the precise prevalence of PRKAG2 cardiomyopathy is still unknown and the full clinical spectrum of this disease is just emerging. Therefore, this systematic review aims to consolidate, and summarise the morphological expression, clinical course and outcomes of PRKAG2 cardiomyopathy in comparison to sarcomeric hypertrophic cardiomyopathy.

Rationale Recent advancements in contemporary gene sequencing techniques have identified non-sarcomeric hypertrophic cardiomyopathy (HCM) phenocopies that manifest several of the phenotypic characteristics of HCM, including left ventricular hypertrophy. PRAKG2 (Protein Kinase Adenosine monophosphate-activated Gamma 2 non-catalytic subunit 2) cardiomyopathy is a rare autosomal dominant, non-lysosomal glycogen storage disease characterised by LV hypertrophy, ventricular pre-excitation, and conduction defects amongst several other cardiovascular features.

Condition being studied PRKAG2 Cardiomyopathy.

METHODS

Search strategy Databases:
PubMed, EMBASE, MEDLINE, CINAHL, EBSCO, Cochrane and Scopus
Restrictions:
- Language - Only articles written in english will be included
There will be no restrictions on publication date.

Participant or population
Inclusion criteria:
a) Studies involving adult patients with confirmed PRKAG2 Cardiomyopathy
B) Includes outcomes of interest – minimum of one primary or secondary outcome
Exclusion criteria:
a) Review articles; clinical studies in non-human subjects; simulation studies; studies with no outcome measures of interest; case series/reports
b) Studies will be screened for duplication and duplicates will be excluded.
c) Less than 5 patients in the group of interest
Population:
A) Patients with PRKAG2 Cardiomyopathy
B) Any age group.

Intervention
Intervention:
- Pharmacological agents - rate control agents - beta-blockers, arrhythmic
- Surgical Intervention - Cardiac transplantation, alcohol septal ablation, septal myectomy
- Cardiac Implantable Electronic Device (CIED) insertion.

Comparator Sarcomeric HCM.

Study designs to be included Inclusion:- Randomised controlled trials- Non-randomised control trials- Cohort studies- Case control- Cross-sectional studies- Retrospective studiesExclusion:- Case reports- Case series.

Eligibility criteria Inclusion criteria:
a) Studies involving adult patients with confirmed PRKAG2 Cardiomyopathy
B) Includes outcomes of interest – minimum of one primary or secondary outcome
Exclusion criteria:
a) Review articles; clinical studies in non-human subjects; simulation studies; studies with no outcome measures of interest; case series/reports
b) Studies will be screened for duplication and duplicates will be excluded.
c) Less than 5 patients in the group of interest
Population:
A) Patients with PRKAG2 Cardiomyopathy
B) Any age group.

Information sources Databases: PubMed, EMBASE, MEDLINE, CINAHL, EBSCO, Cochrane and Scopus.

Main outcome(s)
Primary outcome:
- Prevalence of Pre-excitation - determined via ECG/ EP studies
- Prevalence of Left ventricular outflow tract obstruction - determined via echocardiography
- All-cause mortality
- Sudden cardiac death.

Additional outcome(s)
Secondary outcomes:
- Prevalence of atrial fibrillation
- Prevalence of AV block
- Prevalence of ventricular tachycardia
- Prevalence of LV impairment
- Prevalence of CIED implantation.

Data management A standardised data collection tool that conformed to the Cochrane Collaboration guidelines for systematic review will be developed and used to extract the following details from each study: Title, authors, year of publication, country of publication, study methodology, sample size, population demographics, clinical presentation, diagnostic findings, and clinical outcomes. Diagnostic modalities included ECG, echocardiogram, Holter, cardiac exercise stress test, cardiac magnetic resonance imaging, coronary angiography, electrophysiology studies, histological assessment, and genetic testing. Clinical course and outcomes described surgical intervention, cardiac device implantation, major adverse cardiovascular events, all-cause mortality, and sudden cardiac death.

Quality assessment / Risk of bias analysis The Cochrane's risk of bias tool will be used for RCTs and ROBINS-I by Cochrane will be used for non-RCT comparative studies. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach will be utilised for assessment of the methodological quality of the studies. An assessment of heterogeneity will be performed using Stata (Statacorp LLC).

Strategy of data synthesis A quantitative assessment will be undertaken based on the response to therapy derived from primary outcomes and secondary outcomes. The total number of patients will be collected for the outcome parameters. Heterogeneity among studies will be assessed by a Chi–square test and the I^2 statistic. Random-effects models will be used to combine the statistical data. For dichotomous variables, the inverse variance risk ratio (RR) will be calculated with corresponding 95% confidence intervals (CIs) to evaluate the effects of the intervention. For single populations, an analysis of proportions will be carried out.

Subgroup analysis No subgroup analysis planned.

Sensitivity analysis None planned.

Language restriction English.

Country(ies) involved United Kingdom.

Keywords PRKAG2 Cardiomyopathy, hypertrophic cardiomyopathy, sarcomeric hypertrophic cardiomyopathy.

Dissemination plans Peer-reviewed Publication.

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