

Are there sex differences following treatment of left ventricular outflow tract obstruction in adults with hypertrophic cardiomyopathy?

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Hypertrophic obstructive cardiomyopathy (HOCM) is the most common inherited cardiomyopathy, affecting approximately 1 in 500 individuals. The male predominance of the condition varies from 51% to 91%, suggesting other factors (i.e. environment, sex hormones, and epigenetics) affect the phenotype.¹ Women with HOCM tend to be more symptomatic, present later in life, are more likely to have left ventricular outflow tract obstruction, and have greater mortality when < 50 years of age.² Because the selection of treatment is based on symptom presentation, it is unclear if there is a sex bias in applying the criteria and/or outcomes independent of selection bias, and whether females' benefit more from a particular therapy. Thus, an *a priori* protocol to determine if there were sex differences in selection of treatment and outcomes for HOCM was created for a systematic review to predefine population criteria, description of interventions, and comparisons of the outcomes of interest of three treatments for HOCM: surgical myectomy (SM), alcohol septal ablation (ASA), and dual chamber pacing (DDD) according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).³ Electronic databases (MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, and Scopus) were searched for studies of a minimum of 5 adults who underwent SM, ASA, or DDD as a primary procedure from inception in 1946 to 30 December 2015. The detailed search strategy, list of studies included and discussion are reported in the Supplementary material online.

Sixty-three studies were included (Figure 1) reporting on 4586 patients: 1852 (40.4%) were male, 1780 (38.8%) were female, 954 (20.4%) were unidentifiable by sex. Of the total number of patients, 2212 (48.2%) underwent ASA, 1920 (41.9%) underwent SM and 454 (9.8%) underwent DDD. Of the 63 studies, 11 articles did not report sex in basic demographics, or grouped all treatments together, such that

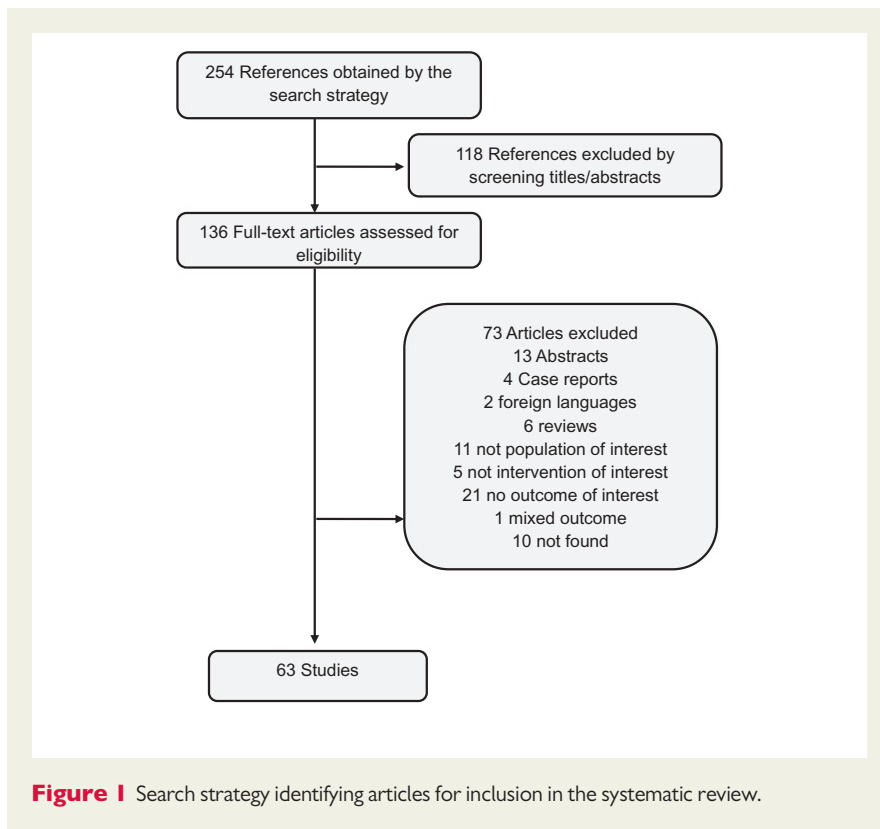


Figure 1 Search strategy identifying articles for inclusion in the systematic review.

numbers of each sex by treatment could not be determined. Where sex was reported, females made up 847 (49.6%) of patients in ASA studies, 770 (48.5%) of patients in SM, and 163 (48.0%) of patients in DDD studies.

Only 1 case series of 18 patients (9 males) treated by DDD reported outcomes by sex.⁴ In that study, there was no difference in mean gradient reduction following DDD pacing: males -58.5 (25.5) mmHg vs. females -55.7 (19.3) mmHg ($P=0.82$). Similarly, reduction in New York Heart Association functional class did not differ by sex. None of the other studies stratified any of the baseline characteristics of patients by sex and there were minimal outcome data stratified by other confounders such as age and disease severity. Therefore, subgroup analyses based on sex and other patient characteristics that are prognostic effect modifiers were not possible.

A patient's sex, age, stage of disease, and other comorbidities will influence choice of treatment and outcomes. Therefore, critical to

evaluations of outcomes in treatment modalities is the accurate reporting of these characteristics. Sex is a basic biological variable that should be included in reporting of clinical outcomes even if the study is not powered to show a sex difference. In the USA, the 1993 Revitalization Act required inclusion of women in clinical studies but not in the reporting of data by sex. As medicine embraces a precision, personalized approach, reporting and analysis of data by sex and other important patient characteristics will inform the practice so that treatment approaches maximize patient outcomes. Requiring such reporting in future studies would accelerate the knowledge base to better inform patient selection and treatment strategies.⁵

Supplementary material

Supplementary material is available at *European Heart Journal—Quality of Care and Clinical Outcomes* online.

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