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Systematic Review/Meta-analysis

A Systematic Review and Meta-analysis of the Association Between Implantable Cardioverter-Defibrillator Shocks and Long-term Mortality

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ABSTRACT

Background: It is unknown whether implantable cardioverter-defibrillator (ICD) discharges actively contribute to a worse prognosis independent of the underlying arrhythmia. There is considerable variability in the reported risk of mortality after appropriate and inappropriate ICD shocks. The aim of our systematic review was to provide a reliable effect size of the association between ICD shock and mortality

RÉSUMÉ

Introduction : On ignore si les décharges électriques des défibrillateurs cardioverteurs implantables (DCI) contribuent activement à un plus mauvais pronostic indépendamment de l'arythmie sous-jacente. On note une forte variabilité du risque de mortalité rapporté après des décharges électriques appropriées et inappropriées des DCI. Le but de notre revue systématique était d'offrir une amplitude fiable de l'effet

Randomized trials have validated implantable cardioverter-defibrillator (ICD) therapy as being effective for the prevention of sudden cardiac death in high-risk patients.[1-6] Subsequent analyses of the same trials raised concerns about a worse long-term prognosis after ICD discharges.[7-9] Indeed, several studies reported an increased risk for cardiac mortality after appropriate and inappropriate ICD shocks.[7-16] Experimental models have documented well the biophysical injury on the myocardium by the energy delivered by ICD shock.[17-20] Clinically, a causative link between ICD shocks and clinical outcomes remains to be demonstrated. Consequently, whether shocks contribute to the progression of the disease or constitute a marker of progressively worsening myocardial disease or disease severity remains unclear. There is a high degree of variability in the reported hazard ratios (HRs) for mortality after ICD shock.[7-15,21,22] The current clinical approach focuses on prevention of the shock event and on an accurate clinical re-evaluation after the first shock.[23]

The aims of our systematic review are to (1) review the literature regarding this issue, (2) perform a quality assessment of the studies published, (3) evaluate the heterogeneity present among the studies, (4) provide a reliable effect size of the association between ICD shock and mortality, and (5) assess the difference between appropriate and inappropriate ICD shocks.

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for both types of therapies.

Methods: On the basis of a systematic literature search, 10 studies were considered eligible for inclusion in the analysis, and data on the hazard ratio (HR) of mortality after ICD shock were extracted from each study.

Results: On pooled analysis, a substantial difference was detected in the risk for subsequent mortality between appropriate and inappropriate shocks. Among patients receiving an appropriate ICD shock, the HR for cardiac death was 2.95 (95% confidence interval [CI], 2.12-4.11; $P < 0.001$) compared with an HR of 1.71 (95% CI, 1.45-2.02) for those receiving an inappropriate shock. Clinical variables like ejection fraction, New York Heart Association class, and length of follow-up did not affect the HRs in our meta-regression models.

Conclusions: Our analysis showed a significant association between appropriate and inappropriate ICD shocks and mortality, with a stronger association for appropriate shocks. Previous trials of ICD therapy reduction programming have shown a significant reduction of inappropriate shocks. The management of appropriate shocks is more challenging and may be optimized by the assessment and treatment of the underlying ventricular arrhythmias. The role of therapies aimed at modifying the arrhythmic substrate and the potential impact on ICD shocks and mortality requires further investigation.

de l'association entre la décharge électrique du DCI et la mortalité pour les deux types de traitements.

Méthodes : En s'appuyant sur une recherche documentaire systématique, 10 études considérées comme étant admissibles à l'analyse ont fourni des données sur le rapport de risque (RR) de mortalité après la décharge électrique du DCI.

Résultats : À l'analyse des données groupées, une différence substantielle dans le risque de mortalité subséquente était détectée entre les décharges électriques appropriées et inappropriées. Chez les patients recevant une décharge électrique appropriée du DCI, le RR de mort cardiaque était de 2,95 (intervalle de confiance [IC] à 95 %, 2,12-4,11; $P < 0,001$) comparativement à un rapport de risque de 1,71 (IC à 95 %, 1,45-2,02) chez ceux recevant une décharge inappropriée. Dans nos modèles de méta-régression, les variables cliniques comme la fraction d'éjection, la classification de la New York Heart Association et la durée du suivi n'affectaient pas les RR.

Conclusions : Malgré une importante association entre les décharges électriques appropriées et inappropriées des DCI et la mortalité, notre analyse montrait toutefois une plus grande association avec les décharges électriques appropriées. Les essais précédents sur la programmation de la réduction du traitement par DCI ont montré une réduction significative des décharges électriques inappropriées. La prise en charge des décharges électriques appropriées est plus difficile et peut être optimisée par l'évaluation et le traitement des arythmies ventriculaires sous-jacentes. D'autres études sur le rôle des traitements visant la modification du substrat arythmique, les effets potentiels des décharges électriques des DCI et la mortalité sont nécessaires.

Methods

Search strategy

Studies were identified by searching electronic databases (MEDLINE through OvidSP, EMBASE through OvidSP, MEDLINE through PubMed, BIOSIS Previews through OvidSP, Web of Science, and Scopus) from inception to November 14, 2014. The literature search used text words and relevant indexing to capture data on mortality associated with ICD shock therapy. The search strategy adopted was the same for all databases and was developed using the following key words: defibrillators, implantable, ICD shock, ICD therapy, death, mortality, and morbidity. No restriction on study type or language was applied.

Study selection

Randomized controlled studies or cohort studies were included if they met all 3 of the following criteria: (1) inclusion of patients with ICDs (with or without concomitant resynchronization therapy), (2) long-term follow-up on survival after ICD shock, and (3) reported results of at least 1 relevant outcome, including HR of mortality after ICD shock.

Data extraction

Data was extracted from each included trial regarding (1) characteristics of trial participants (age and sex) and country where the study was performed and (2) survival after ICD shock, including HR of mortality for appropriate shock vs no shocks, HR of mortality for inappropriate shocks vs no shock, HR of mortality for both type of shocks vs no shock, and HR of mortality for any shocks vs no shocks.

Two authors (RP and MD) independently extracted data from studies and entered them into the data extraction form. Disagreements were resolved by discussion; if no accord was reached, it was planned that a third author (CL) would decide.

The clinical characteristics of each study were also extracted for inclusion in meta-regression models. The 4 variables of clinical interest were the mean ejection fraction (EF) of the study population, the percentage of patients in the study with New York Heart Association (NYHA) class III or higher, the type of cardiomyopathy (whether ischemic or nonischemic), and the length of follow-up for the study.

Quality assessment

We performed quality assessment using methods described by Hayden et al.[24] for evaluation of prognosis studies in systematic reviews. Specifically, the risk of bias was assessed in the following domains:

- Study participation, including the selection and description of the study population
- Study attrition, including percentages of losses to follow-up in the trial and methods applied for dealing with attrition
- Prognostic factors measurement, including definition and description of prognostic factor provided
- Outcome measurement, based on the description and assessment of the outcome of interest