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Effects of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on left ventricular mass index and ejection fraction in hemodialysis patients: A meta-analysis with trial sequential analysis of randomized controlled trials

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ABSTRACT

Background: Angiotensin-converting enzyme inhibitor (ACEI) and angiotensin receptor blocker (ARB) are effective therapies for left ventricular hypertrophy and heart failure. We aimed to assess the efficacy of ACEI and ARB in hemodialysis patients.
Methods: The MEDLINE, EMBASE, and Cochrane Library databases were searched to identify studies published before December 2015 that investigated the use of ACEI or ARB compared with controls to determine the effect on the left ventricular mass index (LVMI) and ejection fraction (EF) in hemodialysis patients, and trial sequential analysis was also performed for outcomes.
Results: A total of 357 cases of patients involved in 8 clinical trials (nine comparisons) were included. Compared with controls, ACEI/ARB treatment resulted in more effective improvement of LVMI in hemodialysis patients (weighted mean difference (WMD) −14.42, 95% confidence interval (CI) −20.89 to −7.95), and the cumulative z curve crossed the trial sequential monitoring boundary for benefit in trial sequential analysis. Although ACEI/ARB and controls did not show significant differences with regards to EF (WMD: −0.84, 95% CI: −2.91 to 1.24).
Conclusions: The comparison between ACEI/ARB and controls showed that the former type of drug causes a greater reduction in LVMI with hemodialysis patients, although they have no significant impact on the EF. Compared with other antihypertensive drugs or placebo, ACEI/ARB is recommended as a better choice in hemodialysis patients.

1. Introduction

Cardiovascular disease (CVD) is the most important cause of death in patients with end-stage renal disease (ESRD) on chronic dialysis, with mortality rates 10 to 30 times higher than in the general population [1,2], approximately 45% of reported deaths of hemodialysis patients in the United States are relevant to CVD [3]. For maintenance hemodialysis patients, cardiac diseases were common at baseline of renal replacement therapy. Approximately 80% of 1846 maintenance hemodialysis patients enrolled in HAEMO study had some form of heart disease, 59% had left ventricular hypertrophy (LVH) and 40% had congestive heart failure (CHF) [3]. LVH is a strong and independent predictor of cardiovascular morbidity and mortality [4] and CHF is the most common types of cardiac death, behind ischemic heart disease only [3].

In addition to its role in regulating blood pressure, ACEI and ARB has been proved with the greatest relative and absolute benefits in patients with left ventricular dysfunction, signs or symptoms of heart failure, or both [5,6]. An early meta-analysis focus on LVMI with hemodialysis patients has been published in 2010 [7] though with a relative small sample size. After five years, we have more evidences. Therefore, we undertook a meta-analysis of the latest, most convincing evidence to evaluate the effects of ACEI and ARB on LVMI and EF in randomized controlled trial (RCTs) with hemodialysis patients, trial sequential analysis (TSA) was also performed to determine whether the available evidence was sufficient and conclusive.

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2. Methods

The current meta-analysis was performed according to the recommendations of the Cochrane handbook for systematic reviews of interventions [8] and was reported in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines [9]. Protocol and registration information were available on http://www.crd.york.ac.uk/PROSPERO/ (CRD42015026276).

2.1. Search strategy

We performed a systematic electronic search in PubMed, Embase, and the Cochrane Library from inception through December 2015. We conducted electronic searches using exploded Medical Subject Headings (MeSH) terms and corresponding key words. The search terms used were (MeSH exp. "renal dialysis", "kidney failure," and key words "hemodialysis", "haemodialysis," and "dialysis"), and (MeSH exp. "Angiotensin-Converting Enzyme Inhibitors" and key words "ace inhibit*"), and (MeSH exp. "Angiotensin Receptor Antagonists" and key words "angiotensin receptor block*"). The searches were performed in English. After completing the electronic database search, a manual search for professional journals was performed.

2.2. Inclusion and exclusion criteria

This investigation required studies to meet the following inclusion criteria: (1) patients with maintenance hemodialysis; (2) administration of ACEI or ARB and the observation of medication use longer than

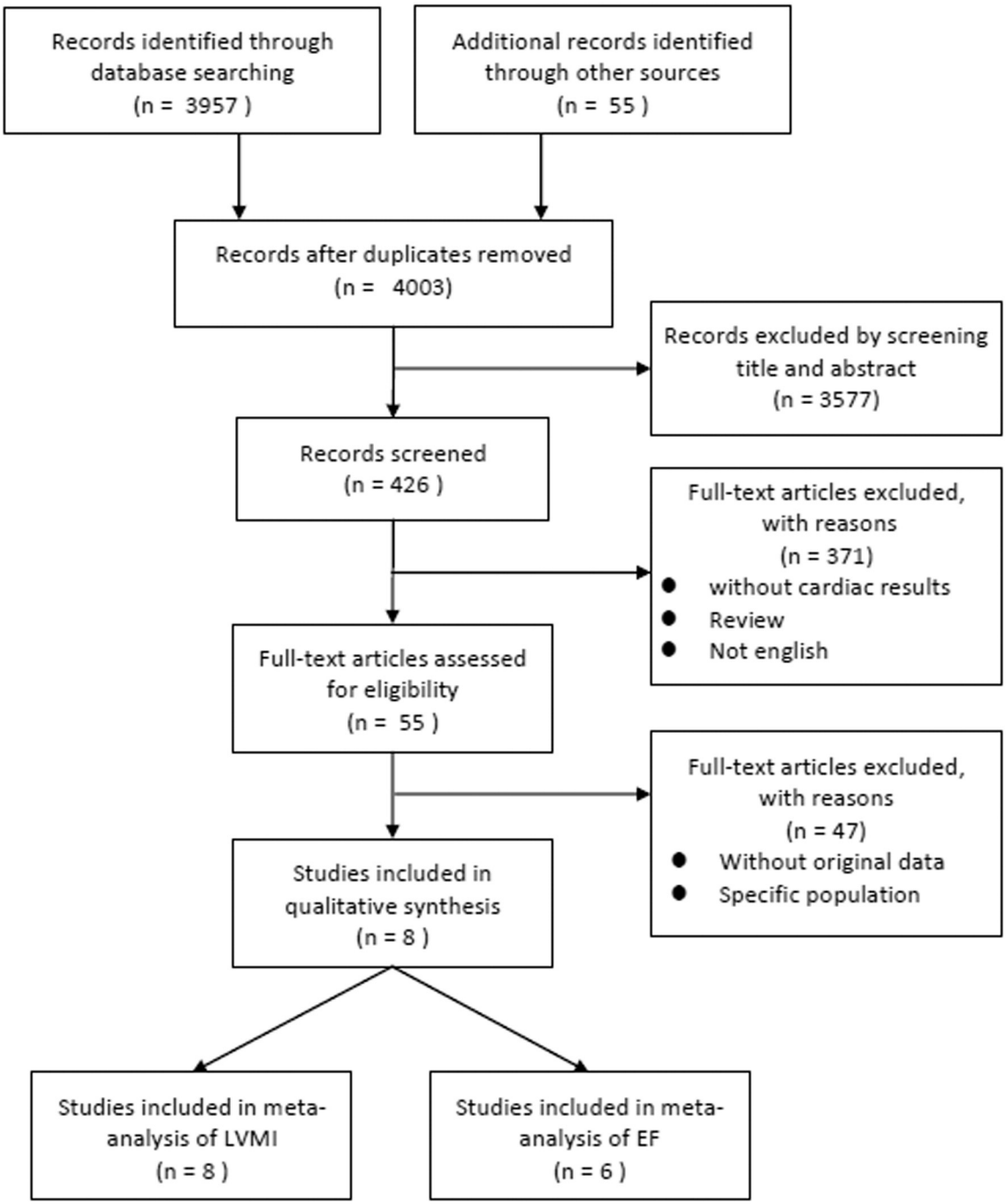

Fig. 1. Flow diagram of study identification, inclusion and exclusion.