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Meta-analysis on the impact of percutaneous coronary intervention of chronic total occlusions on left ventricular function and clinical outcome ☆

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ABSTRACT

Background: Percutaneous coronary intervention (PCI) of chronic total occlusions (CTOs) may have a beneficial effect on survival through a better-preserved or improved LVEF. Current literature consists of small observational studies therefore we performed a weighted meta-analysis on the impact of revascularization of CTOs on left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume (LVEDV) and long-term mortality.
Methods: We conducted a meta-analysis evaluating LVEF before and after CTO PCI and long-term mortality. No language or time restrictions were applied. References from the identified articles and reviews were examined to find additional relevant manuscripts.
Results: Of the 812 citations, 34 studies performed between 1987–2014 in 2243 patients were eligible for LVEF and 27 studies performed between 1990–2013 in 11,085 patients with success and 4347 patients that failed CTO PCI were eligible for long-term mortality. After successful CTO PCI, LVEF increased with 4.44% (95% CI: 3.52–5.35, $p < 0.01$) compared to baseline. In a small cohort of ~70 patients, no significant difference in LVEF was observed after non-successful CTO PCI or reocclusion. Additionally, 8 studies reported the change in left ventricular end-diastolic volume (LVEDV) in a total of 412 patients. LVEDV decreased with 6.14 ml/m^2 (95% CI: −9.31 to −2.97, $p < 0.01$). Successful CTO PCI was also associated with reduced mortality in comparison with failed CTO PCI (OR: 0.52, 95% CI: 0.43–0.62, p-value < 0.01).
Conclusions: The current meta-analysis revealed that successful recanalization of a CTO resulted in an overall improvement of 4.44% absolute LVEF points, reduced adverse remodeling and an improvement of survival (OR: 0.52).

1. Introduction

On coronary angiography, a chronic total occlusion (CTO) is observed in approximately 16% of patients with significant coronary artery disease [1,2]. Of these patients, the majority will be treated medically (64%) or are referred for CABG surgery (26%) whereas only 10% will be referred for percutaneous CTO revascularization [1]. The overall conservative approach is somewhat concerning as observational data has shown a possible beneficial effect on clinical outcome after percutaneous coronary intervention (PCI). Numerous beneficial effects have been reported e.g. improvement of angina and quality of life, improvement of electrical myocardial stability, reduced need for CABG surgery, but above all, improved survival [3–5]. It has been hypothesized that the underlying mechanism primarily accountable for this effect is an improved or better preserved left ventricular function (LVF) [6]. Current literature contains several reports addressing the effect of CTO PCI on left ventricular ejection fraction (LVEF) though they are mostly small observational studies which could under- or over-estimate the true effect. For this reason, we decided to perform a meta-analysis of the literature describing the impact of CTO PCI on LVEF that has never been reported before (references reported in Appendix 1). Furthermore, we will update the most recent meta-analyses on long-term survival (references reported in Appendix 1) [7].

2. Methods

2.1. Literature search and study selection

This meta-analysis was conducted and reported according to the proposal for conducting and reporting Meta-analyses of Observational

☆ These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Studies in Epidemiology (MOOSE) [8]. A literature search was performed using major databases, including PubMed, the Cochrane Library, and ClinicalTrials.gov website for randomized controlled trials until January 20th 2014 evaluating the impact of successful chronic total occlusion (CTO) percutaneous coronary intervention (PCI) on left ventricular function and comparing long-term mortality after successful versus failed CTO PCI. The initial key words were: "chronic total occlusion(s)," "chronic total coronary occlusion(s)", "chronic", "occlusion(s)", "percutaneous coronary intervention", "angioplasty", "recanalization", "revascularization", "ventricular function," "ventricular contraction", "ejection fraction", and "successful". No language or time restrictions were applied. References from the initially identified articles and reviews were examined to find additional relevant manuscripts. The titles and abstracts of relevant studies were identified through the data search and reviewed independently by 2 investigators (LPH, BEC) to determine whether they met the eligibility criteria for inclusion. Discrepancies regarding whether to include or exclude a study were resolved by consensus with the other co-authors. To be included for the meta-analysis on left ventricular function, studies had to include patients with a chronic occlusion who received successful revascularization by percutaneous intervention only and the left ventricular function needed to be assessed before revascularization and after at least 1 month of follow-up. For the meta-analysis on long-term mortality, studies had to include patients with a chronic occlusion who were compared according to the successfulness of the percutaneous intervention and reported on all-cause mortality or when absent, cardiac mortality, at $\geq$1 year after the index procedure. To prevent patient overlap, only the latter study was included in the final analysis in case multiple separate studies reported on the same patient data and outcomes from a single center. Fig. 1 shows the complete search strategy with inclusion and exclusion criteria.

2.2. Data extraction and data analysis

The primary endpoint was the change in left ventricular ejection fraction (LVEF) from baseline to follow-up after successful CTO PCI and long-term mortality after successful versus failed CTO PCI. Initially, all studies reporting on a "chronic occlusion" were included in the analysis, regardless of the CTO definition. To prevent distortion of the results by the inclusion of acute or sub-acute 100% occlusions, a subgroup analysis was performed on only those studies that included patients with a CTO of at least 3 months. Furthermore, in this $\geq$3 months occlusion duration subgroup for the outcome LVEF, studies with a follow-up duration < 4 months were excluded as recovery of LV function in chronically ischemic viable hibernating or stunned myocardium starts within 1 to 4 weeks after revascularization and is usually complete within 3 months [9,10]. When several methods were used for LVEF assessment magnetic resonance (MRI) data were preferentially included in the analysis, followed by nuclear imaging, echocardiography, and left ventricular (LV) angiography.

The secondary outcomes were change of LVEF after CTO PCI failure, change of LVEF after reocclusion during follow-up and change in left ventricular end-diastolic volume (LVEDV) reported as ml/m^2 to assess the effect on left ventricular remodeling.

For LVEF and LVEDV measurements, we used the reported mean and standard deviation at baseline and follow-up. For mortality, absolute numbers of mortality events were primarily used but when absent they were calculated from the Kaplan–Meier estimates or extracted from the survival curves. When reported or published data were incomplete, we requested additional details by correspondence or calculated or estimated the missing data using the method of the Cochrane handbook [11]. In case of an intervention or experimental study, only the control group was included.

2.3. Statistical analysis

For the outcomes LVEF and LVEDV, summary results were presented as weighted mean difference with 95% CI. For the outcome long-term mortality, summary results were presented as odds ratios (OR) with 95% CI. We examined heterogeneity across studies by calculating an I^2-value for every outcome. A standard fixed-effects model (Mantel–Haenszel method) was used in the absence of heterogeneity among studies (I^2 value less than 25%). In the presence of heterogeneity, the DerSimonian and Laird random effects model was used.

Potential publication bias was assessed by visual assessment of constructed funnel plots (Appendix 2). Tests were two-tailed and a p-value of 0.05 was considered statistically significant. All analyses were performed using Review Manager 5.2.

3. Results

Of the 812 citations 666 were initially excluded after screening at the title and abstract level (Fig. 1). Of the remaining 146 studies, a total of 34 were eligible for inclusion in the meta-analysis on left ventricular

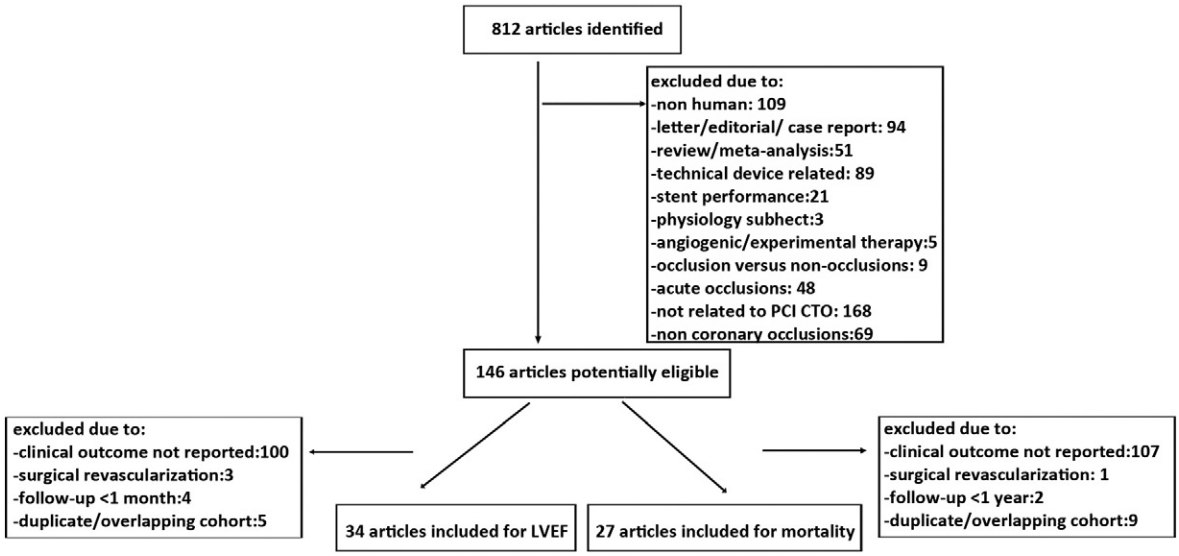

Fig. 1. Flow diagram of studies included in the meta-analysis.