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The efficacy and safety of mechanical hemodynamic support in patients undergoing high-risk percutaneous coronary intervention with or without cardiogenic shock: Bayesian approach network meta-analysis of 13 randomized controlled trials ☆

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ABSTRACT

Background: Studies have reported conflicting results regarding efficacy of mechanical hemodynamic support using intra-aortic balloon pump (IABP) or percutaneous ventricular assisted device (pVAD) in patients undergoing high-risk PCI. We performed a Bayesian network meta-analysis comparing the safety and efficacy of mechanical hemodynamic support devices and medical therapy (MT).

Methods and results: RCTs comparing overall mortality of IABP versus MT or IABP versus pVAD in high-risk PCI populations were included. The primary endpoint was overall mortality, using the longest available follow-up in each study. This analysis included 2843 patients from 13 trials. In network meta-analysis, overall survival benefit was not significant with IABP (RR 0.84, 95% CrI 0.56–1.24) or pVAD (RR 0.95, 95% CrI 0.42–2.06), compared with MT. IABP or pVAD also did not show early survival benefit compared with MT. In terms of bleeding, pVAD was the worst (versus IABP: RR 29.4, 95% CrI 5.99–221.0; versus MT: RR 41.7, 95% CrI 8.19–330.0), which was mainly driven by the higher incidence of bleeding in the ECMO and TandemHeart, while IABP was worse than MT (RR 1.41, 95% CrI 1.01–2.08). The incidence of acute limb ischemia or vascular complication was not different between treatment groups.

Conclusions: In this meta-analysis, routine elective use of IABP or pVAD did not reduce mortality, while it increased bleeding, compared with MT in high-risk PCI population or even in the patients with cardiogenic shock. Thoughtful selection of appropriate patients and balancing the risk and benefit should be the prerequisites to the use of mechanical hemodynamic support devices.

1. Introduction

Although there have been substantial technical advances in coronary intervention, risk of extensive myocardial damage, pump failure and hemodynamic compromise still complicates reperfusion treatments in high-risk population. Adjunctive use of mechanical hemodynamic support devices (MHS) may benefit the outcome of high-risk patients with multi-vessel disease, unprotected left main coronary artery disease, severely depressed left ventricular systolic function, or acute myocardial infarction (AMI) complicated with cardiogenic shock [1].

Since intra-aortic balloon pump (IABP) counterpulsation was introduced in 1968, its physiologic benefits in improving coronary perfusion and reducing afterload were believed to enhance survival in the patients with high-risk PCI or cardiogenic shock [2]. However, the evidences supporting use of IABP in these clinical settings were mainly based on registry data, and there have been conflicting results regarding survival benefit of routine elective use of IABP in high-risk PCI populations or in patients with cardiogenic shock [2,3]. The ACCF/AHA/SCAI guideline downgraded IABP use for high-risk PCI or AMI with cardiogenic shock to a class IIb or IIa, respectively [4–6]. In the recent meta-analysis by Chen et al. [3], the pooled analysis of 10 randomized controlled trials (RCTs) revealed that early mortality rate did not differ between the IABP group and the non-IABP group.

☆ All the 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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Percutaneous ventricular assisted device (pVAD) that provides more powerful support to enhance cardiac output includes percutaneous cardiopulmonary bypass (PCPB), Impella (Impella LP2.5, Abiomed Europe GmbH, Aachen, Germany), or TandemHeart (TandemHeart, Cardiac Assist, Pittsburgh, PA, USA). Although pVADs improved hemodynamic parameters, previous RCTs and meta-analyses consistently showed lack of survival benefit of pVAD compared with IABP [7,8]. The ACCF/AHA/SCAI guideline recommended the use of pVAD in high-risk PCI or AMI with cardiogenic shock as class IIb recommendation, as it does with IABP. Recently, results of two large RCTs comparing IABP to medical therapy (IABP SHOCK II) and IABP to pVAD (PROTECT II) were reported [7,9]. However, comprehensive evidence synthesis encompassing various MHS is still lacking. Since all the clinical trials compared pVAD to IABP, its efficacy compared to medical therapy (MT) is unknown. Here, we report a systematic review and comprehensive frequentist and Bayesian network meta-analysis using all the published RCTs, in order to compare the efficacy and safety between IABP, pVAD and MT in high-risk PCI.

2. Methods

2.1. Data sources and searches

Pertinent published or unpublished studies were independently searched in PubMed, EMBASE, Cochrane Central Register of Controlled Trials, and the United States National Institutes of Health registry of clinical trials (www.clinicaltrials.gov), and relevant websites (www.crtonline.org, www.clinicaltrialresults.com, www.tctmd.com, www.cardiosource.com, and www.pcronline.com) were also searched. Detailed search strategy was presented in the Supplementary Appendix. The electronic search strategy was complemented by manual review of reference lists of included articles. References of recent reviews, editorials, and meta-analyses were also examined. No restrictions were imposed on language, study period, or sample size.

2.2. Study selection

We included RCTs that met the following criteria. First, all studies enrolled adult patients undergoing PCI. Second, adjunctive mechanical hemodynamic support devices were used and compared with MT or other type of device. Mechanical hemodynamic support devices were IABP or pVAD which included percutaneous cardiopulmonary bypass (extracorporeal membrane oxygenator, emergency bypass system), Impella (Impella LP2.5, Abiomed Europe GmbH, Aachen, Germany), or TandemHeart (TandemHeart, Cardiac Assist, Pittsburgh, PA, USA). Third, studies focused on high-risk PCI regardless of its definition or primary PCI in AMI with or without cardiogenic shock. However, studies that focused on treatment of cardiogenic shock itself without PCI were excluded. Finally, all-cause mortality was reported in included studies, regardless of the timing of data collection. We excluded RCTs conducted on pediatric patients (including neonates and preterm infants) and RCTs that assigned patients to both mechanical hemodynamic support device and MT.

2.3. Data extraction and quality assessment

Summary data as reported in the published manuscripts were used in the analysis. A standardized form was used to extract characteristics of trials, study design (including randomization sequence generation, allocation concealment, crossover between assigned groups, number of post-randomization withdrawals or loss to follow-up), number of study patients, age, eligibility criteria of each trials, definition of high-risk PCI in each trials, type of coronary intervention (percutaneous balloon angioplasty only or PCI with stent implantation), duration of mechanical support, length of follow-up, and mortality and adverse events data reported on an intention-to-treat basis. The mortality data were separately collected according to the pre-specified criteria, as follows; early mortality included up to 30 days, late mortality included at least 3 months after the index procedure. Since previously published trials or meta-analyses have showed the hemodynamic benefits of improvement in diastolic coronary blood flow, systemic blood flow, mean arterial pressure, pulmonary arterial pressure, or pulmonary capillary wedge pressure with IABP or pVAD, we primarily focused our analysis on the effect of mechanical support on both overall mortality and adverse events associated with the mechanical support during PCI. The quality of eligible RCTs was assessed using the Cochrane Collaboration's tool for assessing the risk of bias for RCTs (Supplementary Table 1). We also provided the Jadad score for quantitative comparison of quality of each trial, as well as the Cochran Collaboration's tool, for each RCT [10]. Two investigators (JML and JP) independently performed screening of titles and abstracts, identified duplicates, reviewed full articles, and determined their eligibility. Disagreements were resolved by discussions. The last search was performed in February 2014.

2.4. Outcomes and definitions

The primary outcome was all-cause mortality at the longest available follow-up. Secondary outcomes included early and late mortality, and early mortality stratified according to the presence of cardiogenic shock, adverse events associated with the mechanical hemodynamic supports (moderate to severe bleeding, recurrent ischemia or infarction, hemorrhagic or ischemic stroke, vascular complications in the access site, acute limb ischemia, and infection including sepsis, aortic dissection or perforation). Early mortality was defined as those that occurred within 30 days after enrollment, while late mortality was those that occurred at 3 month follow-up at least. All of the patients and outcomes were analyzed according to the originally assigned group.

2.5. Data synthesis and analysis

The primary outcome was analyzed by both traditional head-to-head frequentist meta-analysis, comparing IABP versus MT and IABP versus pVAD, and Bayesian network meta-analysis, comparing the three treatment groups (IABP, pVAD, and MT). The secondary outcomes (early and late mortality, adverse events) were analyzed by Bayesian network meta-analysis, comparing the three treatment groups (IABP, pVAD, and MT). The κ statistic was used to assess agreement between investigators for study selection. The present study was performed in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the review protocol has not been registered (Supplementary Table 2).

2.6. Traditional frequentist meta-analysis

The traditional head-to-head frequentist meta-analytic approach regarding primary outcome involved both a random effects model and a fixed effects model. Relative risks (RRs) with 95% confidence interval (CI) were presented as summary statistics. The pooled RR was calculated with the DerSimonian and Laird method for random effects, as well as the Mantel–Haenszel method for fixed effects. Statistical heterogeneity was assessed by Cochran's Q via a χ^2 test and was quantified with the I^2 test [11]. Publication bias was assessed by funnel plot asymmetry, along with Egger's and Begg's test. Results were considered statistically significant at 2-sided $p < 0.05$. Statistical analysis was performed with the use of STATA/SE 12.1 (Stata Corp LP, College Station, Texas, USA).

2.7. Bayesian network meta-analysis

A Bayesian random effects model for multiple treatment comparisons was constructed to compare primary and secondary outcomes among the three treatment groups (IABP, pVAD, or MT). We used Bayesian extension of the hierarchical random-effects model proposed