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Review

Short and long-term safety and efficacy of polymer-free vs. durable polymer drug-eluting stents. A comprehensive meta-analysis of randomized trials including 6178 patients

Eliano P. Navarese [a,m,*], Mariusz Kowalewski [b,m], Bernardo Cortese [c], David Kandzari [d], Sofia Dias [e], Wojtek Wojakowski [f], Antonino Buffon [g], Alexandra Lansky [h], Paolo Angelini [i], Rebecca Torguson [j], Jacek Kubica [k,m], Malte Kelm [l], Menko-Jan de Boer [a], Ron Waksman [j], Harry Suryapranata [a]

[a] Department of Cardiology, Radboud University Medical Center, Nijmegen, The Netherlands
[b] 10th Military Research Hospital and Polyclinic, Bydgoszcz, Poland
[c] Interventional Cardiology Unit, Ospedale Fatebenefratelli, Milan, Italy
[d] Department of Cardiology, Piedmont Heart Institute, Atlanta, GA, USA
[e] University of Bristol, School of Social and Community Medicine, Bristol, UK
[f] Department of Cardiology, Medical University of Silesia, Katowice, Poland
[g] Department of Cardiovascular Sciences, Catholic University of the Sacred Heart, Rome, Italy
[h] Department of Cardiology, Yale Medical School, New Haven, CT, USA
[i] Department of Cardiology, Texas Heart Institute of St. Luke's Episcopal Hospital, Houston, TX, USA
[j] Department of Cardiology, MedStar Washington Hospital Center, Washington, DC, USA
[k] Department of Cardiology and Internal Medicine, Ludwik Rydygier Collegium Medicum, Nicolaus Copenicus University, Bydgoszcz, Poland
[l] Department of Internal Medicine, Division of Cardiology, Pulmonology and Vascular Medicine, Heinrich-Heine-University, Düsseldorf, Germany
[m] Systematic Investigation and Research on Interventions and Outcomes (SIRIO) MEDICINE Research Network

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ABSTRACT

Background: The efficacy and safety of polymer-free drug-eluting stents (DESs) in clinical practice is currently subject of debate; randomized trials (RCTs) conducted so far provided conflicting results or were underpowered to definitively address this question; we aimed to investigate the efficacy and safety profile of polymer-free vs. durable polymer DES by a comprehensive meta-analysis of RCTs.
Methods: MEDLINE, Google Scholar, EMBASE and Cochrane databases were searched for RCTs comparing polymer-free to durable polymer DES. Safety endpoints at short-term (≤1 year) and long-term follow-up (>1-year) were: death, myocardial infarction (MI) and stent thrombosis (ST); main efficacy endpoints were: target lesion revascularization (TLR) and target vessel revascularization (TVR).
Results: Eight RCTs including 6178 patients were included. No significant differences in mortality were observed between polymer-free and durable polymer DESs at both short- and long-follow up (OR [95% CI] = 0.79 [0.58−1.08], $p = 0.14$; and 0.80 [0.58−1.10], $p = 0.17$ respectively); polymer free and durable polymer DESs provided comparable short and long-term MI rates; at short-term: OR [95% CI] = 1.13 [0.83 −1.54], $p = 0.44$ and at long-term: OR [95% CI] = 1.27 [0.87−1.85], $p = 0.22$. Similarly, these two different devices proved equally effective in regards to ST, TLR and TVR over the short and long follow-up period.
Conclusions: Polymer-free DESs are as safe and effective as durable polymer DES; however, there is no evidence of any additional benefits provided by this new technology.

* Corresponding author. Department of Cardiology, Radboud University Medical Center, Geert Grooteplein 10, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands.
E-mail address: eliano.navarese@alice.it (E.P. Navarese).

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Contents

1. Introduction

Coronary angioplasty with drug-eluting stent (DES) implantation is currently the most common stent procedure worldwide. However, several concerns emerged with first-generation DES which have been associated with higher rates of late stent thrombosis (ST), mainly attributed to delayed healing and delayed re-endothelization, due to the presence of the durable polymer coating [1,2]; indeed, the long-term direct contact between the polymer and the arterial wall remains an important issue, since several sources of evidence point toward this contact as a cause of vascular toxicity with chronic inflammation. Polymer-free stents are emerging technology which has been designed to offer an attractive prospect of controlled drug-release without the potential of late polymer-associated adverse effects; on the other hand, randomized controlled trials (RCTs) conducted so far provided conflicting results or were underpowered to address the question of their efficacy and safety [3]. While in numerous trials polymer-free DES proved non-inferior in regards to angiographic outcomes, in other studies they failed to reach the non-inferiority margin for safety. In light of these conflicting results, we aimed to perform a comprehensive meta-analytic overview of RCTs of polymer-free stents vs. durable polymer DES.

2. Methods

2.1. Selection criteria and study endpoints

Prespecified safety endpoints included overall mortality, myocardial infarction (MI) and definite-or-probable stent thrombosis (ST) according to the definition criteria of the Academic Research Consortium [4]. Efficacy endpoints were target lesion revascularization (TLR) and target vessel revascularization (TVR). Data for short- and long-term follow-up ($\leq$1 year and $>$1 year, respectively) were chosen for abstraction. Angiographic outcomes analyses comprised in-stent late lumen loss (LLL) and in-stent diameter stenosis (DS).

Citations were screened at title/abstract level and retrieved as full reports. Inclusion criteria were: 1. human studies; 2. randomized controlled studies (RCTs); 3. studies comparing safety AND/OR efficacy of polymer-free vs. durable polymer DES; 4. additional longer follow-up data available. Exclusion criteria were: a) review articles; b) animal studies; c) bare metal (BMS) or biodegradable polymer stents as a control group; d) same stent design: polymer-free vs. polymer-free stents studies; e) first-in-man trials with polymer-free DES without comparator. A list of the excluded trials is displayed in Supplementary Table 1. Internal validity was appraised by two unblinded investigators (MK and EPN) according to proper allocation sequence/concealment, patient blinding, investigator blinding and complete outcome data/full reporting.

2.2. Statistical analysis

Data were analyzed according to the intention-to-treat principle. Odds ratios (ORs) and 95% CIs were used as summary statistics. Heterogeneity was assessed by the Cochran Q test. Statistical heterogeneity was summarized by the I^2 statistic, which quantifies the percentage of variation in study results that is due to heterogeneity rather than chance [5]. Pooled ORs were calculated using a Fixed effect model with the Mantel–Haenszel method. The DerSimonian and Laird random effects model was used in case of significant heterogeneity and/or moderate or significant inconsistency ($>$50%) across studies [6]. In addition, as sensitivity analysis, the influence of each study was assessed by testing whether, deleting each in turn, would have significantly changed the pooled results of the meta-analysis; separate prespecified analyses were also performed in patients treated with sirolimus or paclitaxel eluting stents and a p value for interaction was calculated to formally explore any statistical difference between the two first-generation DES. Potential publication bias for the subgroups was examined by constructing a