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Clinical and Inflammatory Outcomes of Rotational Atherectomy in Calcified Coronary Lesions: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 March 2025 and was last updated on 11 March 2025.

INTRODUCTION

Review question / Objective This meta-analysis aimed to quantify the incidence rate of composite MACE and mortality following RA, and to compare the impact of RA with other invasive strategies on clinical outcomes (e.g., in-stent restenosis, post-procedural complications, and MACE); and inflammatory responses (e.g., CRP, IL-6, and other inflammatory markers) in patients undergoing coronary interventions for moderate to severe coronary artery calcification.

Rationale Moderate to severe coronary artery calcification affects approximately one-third of patients undergoing percutaneous coronary intervention (PCI) (Bulluck & McEntegart, 2022; Fan et al., 2020). Calcified lesions present significant challenges during PCI, including difficult device delivery, suboptimal stent expansion, and increased procedural complications (Shavadia et al., 2018; Hegde et al., 2017). These issues can lead to poor clinical outcomes, such as restenosis and stent thrombosis (Shah et al., 2021). Various calcium modification techniques have been developed to address these challenges, including rotational, orbital, and laser atherectomy, as well as shockwave lithoplasty (Shavadia et al., 2018; Heinrich et al., 2021). The optimal approach for treating calcified lesions often involves combining enhanced intravascular imaging with appropriate plaque modification tools to ensure adequate lesion preparation and optimal stent deployment (Hennessey et al., 2023).

Coronary artery calcification poses significant challenges in PCI, necessitating atherectomy techniques for lesion preparation. Rotational atherectomy (RA) and orbital atherectomy (OA) are two primary methods used to modify calcified plaques (Lee et al., 2018). While both techniques show similar efficacy and safety profiles (Lee et al., 2017), some studies suggest OA may be associated with lower rates of myocardial infarction and reduced fluoroscopy time compared to RA (Doshi et al., 2021; Meraj et al., 2018). However, OA has been linked to higher rates of coronary dissection and perforation (Okamoto et

al., 2019). The choice between RA and OA should be based on lesion characteristics and operator experience (Shlofmitz et al., 2017). Both techniques effectively facilitate stent delivery and expansion in calcified lesions (Khattak et al., 2024). Rotational atherectomy (RA) has evolved from a plaque debulking technique to a lesion modification strategy for treating calcified coronary lesions (Gupta et al., 2019; Tian et al., 2015). Contemporary RA practice involves the use of smaller burr sizes, shorter ablation runs, and lower rotational speeds to enhance safety and improve outcomes (Tomey et al., 2014; Sharma et al., 2019). Although not routinely recommended, RA facilitates stent delivery and expansion in severely calcified lesions (Allali et al., 2022). Intravascular imaging is employed to guide burr size selection and assess calcification thickness (Sakakura et al., 2020). Current guidelines from the ACC/AHA and ESC provide limited recommendations on RA use (Ferreira et al., 2022). Although RA does not reduce restenosis rates, it remains a valuable tool for treating complex calcified lesions in the drug-eluting stent era (Tian et al., 2015; Tomey et al., 2014).

Rotational atherectomy has experienced a resurgence in the drug-eluting stent (DES) era, shifting from a standalone debulking device to a plaque modification technique (Gupta et al., 2019). It is primarily used to modify heavily calcified lesions, facilitating balloon dilation and stent deployment (Schwartz et al., 2011; Tian et al., 2015). Indications for RA have expanded to include diffuse atheromatous disease, in-stent restenosis, and chronic total occlusions, (Chen & Hsieh, 2013). While RA improves procedural success in calcified lesions, its impact on long-term outcomes remains debatable (Redfors et al., 2017; Abdel-Wahab et al., 2013). Some studies report excellent mid-term outcomes with aggressive plaque modification before DES implantation (Vaquerizo et al., 2010), while others show no reduction in late lumen loss (Abdel-Wahab et al., 2013). Despite these mixed results, RA remains a valuable tool in the treatment of complex calcified lesions, evolving from debulking to plaque modification over the past 40 years (Barbato et al., 2017).

Rotational atherectomy in percutaneous coronary interventions triggers an inflammatory response, which can influence clinical outcomes. C-reactive protein (CRP) and interleukin-6 (IL-6) are key inflammatory markers associated with cardiovascular risk and restenosis after procedures (Biasucci, 2004; Biasucci et al., 1999; Rattazzi et al., 2003).

Condition being studied

- Population: Patients undergoing PCI for (moderate to severe) calcified coronary artery disease
- Intervention: Rotational atherectomy (RA)
- Comparison: Standard PCI or other debulking atherectomy (i.e. OA, direct atherectomy, laser, intracoronary litothripsy, or other invasive strategies)
- Outcomes: -Inflammatory markers (i.e. CRP, IL-6, other markers),
-Clinical outcomes: in-stent restenosis, procedural complications (i.e. coronary artery dissection, device induced arterial perforation, cardiac tamponade), slow flow/no reflow, myocardial infarction (MI), mortality, 30-day MI, target vessel revascularization (TVR), and major adverse cardiovascular events (MACE).

METHODS

Search strategy ((((("atherectomy"[MeSH Terms] OR "atherectomy"[All Fields] OR "atherectomies"[All Fields] OR ("atherectomy, coronary"[MeSH Terms] OR ("atherectomy"[All Fields] AND "coronary"[All Fields]) OR "coronary atherectomy"[All Fields] OR ("rotational"[All Fields] AND "atherectomy"[All Fields]) OR "rotational atherectomy"[All Fields])) AND ("coronary artery disease"[MeSH Terms] OR ("coronary"[All Fields] AND "artery"[All Fields] AND "disease"[All Fields]) OR "coronary artery disease"[All Fields] OR (("calcifiability"[All Fields] OR "calcifiable"[All Fields] OR "calcified"[All Fields] OR "calcifier"[All Fields] OR "calcifiers"[All Fields] OR "calcifies"[All Fields] OR "calcify"[All Fields] OR "calcifying"[All Fields]) AND ("coronary artery disease"[MeSH Terms] OR ("coronary"[All Fields] AND "artery"[All Fields] AND "disease"[All Fields]) OR "coronary artery disease"[All Fields] OR ("constriction, pathologic"[MeSH Terms] OR ("constriction"[All Fields] AND "pathologic"[All Fields]) OR "pathologic constriction"[All Fields] OR "stenosi"[All Fields] OR "stenosis"[All Fields]) OR ("thrombosis"[MeSH Terms] OR "thrombosis"[All Fields] OR "thrombus"[All Fields]))) OR ((("stable"[All Fields] OR "stabled"[All Fields] OR "stables"[All Fields] OR "stabling"[All Fields]) AND ("coronary artery disease"[MeSH Terms] OR ("coronary"[All Fields] AND "artery"[All Fields] AND "disease"[All Fields]) OR "coronary artery disease"[All Fields] OR ("angina pectoris"[MeSH Terms] OR ("angina"[All Fields] AND "pectoris"[All Fields]) OR "angina pectoris"[All Fields] OR "angina"[All Fields] OR "anginas"[All Fields]) OR ("angina pectoris"[MeSH Terms] OR ("angina"[All Fields] AND "pectoris"[All Fields]) OR "angina pectoris"[All Fields]))) OR "SCAD"[All Fields]) OR

("atherosclerosis"[MeSH Terms] OR "atherosclerosis"[All Fields] OR ("atherosclerotic"[All Fields] AND "cardiovascular"[All Fields] AND "disease"[All Fields]) OR "atherosclerotic cardiovascular disease"[All Fields] OR ("ascvd"[All Fields] OR "ascvds"[All Fields])) OR ((("chronic"[All Fields] OR "chronical"[All Fields] OR "chronically"[All Fields] OR "chronicities"[All Fields] OR "chronicity"[All Fields] OR "chronicization"[All Fields] OR "chronics"[All Fields]) AND ("coronaries"[All Fields] OR "heart"[MeSH Terms] OR "heart"[All Fields] OR "coronary"[All Fields]) AND ("syndrom"[All Fields] OR "syndromal"[All Fields] OR "syndromally"[All Fields] OR "syndrome"[MeSH Terms] OR "syndrome"[All Fields] OR "syndromes"[All Fields] OR "syndrome s"[All Fields] OR "syndromic"[All Fields] OR "syndroms"[All Fields])) OR ("cell commun signal"[Journal] OR "ccs"[All Fields]))) AND ("inflammation"[MeSH Terms] OR "inflammation"[All Fields] OR "inflammations"[All Fields] OR "inflammation s"[All Fields] OR (("inflammatories"[All Fields] OR "inflammatory"[All Fields]) AND "marker*"[All Fields]) OR ("curr res psychol"[Journal] OR "crp"[All Fields]) OR ("c reactive protein"[MeSH Terms] OR ("c reactive"[All Fields] AND "protein"[All Fields]) OR "c reactive protein"[All Fields] OR "c reactive protein"[All Fields]) OR ("interleukin 6"[MeSH Terms] OR "interleukin 6"[All Fields] OR "interleukin 6"[All Fields]) OR ("interleukin 6"[MeSH Terms] OR "interleukin 6"[All Fields] OR "il 6"[All Fields]) OR ("tumour necrosis factor alpha"[All Fields] OR "tumor necrosis factor alpha"[MeSH Terms] OR ("tumor"[All Fields] AND "necrosis"[All Fields] AND "factor alpha"[All Fields]) OR "tumor necrosis factor alpha"[All Fields] OR ("tumor"[All Fields] AND "necrosis"[All Fields] AND "factor"[All Fields] AND "alpha"[All Fields]) OR "tumor necrosis factor alpha"[All Fields]) OR "TNF-A"[All Fields] OR ("in-stent"[All Fields] AND "restenosis"[All Fields]) OR ("constriction, pathologic"[MeSH Terms] OR ("constriction"[All Fields] AND "pathologic"[All Fields]) OR "pathologic constriction"[All Fields] OR "stenosi"[All Fields] OR "stenosis"[All Fields]) OR (("acute"[All Fields] OR "acutely"[All Fields] OR "acutes"[All Fields]) AND ("thrombose"[All Fields] OR "thrombosing"[All Fields] OR "thrombosis"[MeSH Terms] OR "thrombosis"[All Fields] OR "thrombosed"[All Fields] OR "thromboses"[All Fields])) OR (("systemic"[All Fields] OR "systemically"[All Fields] OR "systemics"[All Fields]) AND ("inflammation"[MeSH Terms] OR "inflammation"[All Fields] OR "inflammations"[All Fields] OR "inflammation s"[All Fields])) OR ("post-procedure"[All Fields] AND "complication*"[All Fields])) AND ("PCI"[All Fields] OR ("percutaneous coronary intervention"[MeSH Terms] OR ("percutaneous"[All Fields] AND "coronary"[All Fields] AND "intervention"[All Fields]) OR "percutaneous coronary intervention"[All Fields]) OR ("angioplasty, balloon, coronary"[MeSH Terms] OR ("angioplasty"[All Fields] AND "balloon"[All Fields] AND "coronary"[All Fields]) OR "coronary balloon angioplasty"[All Fields] OR ("percutaneous"[All Fields] AND "transluminal"[All Fields] AND "coronary"[All Fields] AND "angioplasty"[All Fields]) OR "percutaneous transluminal coronary angioplasty"[All Fields]) OR ("angioplasty, balloon, coronary"[MeSH Terms] OR ("angioplasty"[All Fields] AND "balloon"[All Fields] AND "coronary"[All Fields]) OR "coronary balloon angioplasty"[All Fields] OR "ptca"[All Fields]) OR ("balloon"[All Fields] OR "balloon s"[All Fields] OR "balloons"[All Fields]))) NOT ("editorial"[Publication Type] OR "editorial"[All Fields] OR ("letter"[Publication Type] OR "correspondence as topic"[MeSH Terms] OR "letter"[All Fields]) OR "comment*"[All Fields])) NOT ("animals"[MeSH Terms:noexp] OR "animal"[All Fields])) AND "English"[Language].

Participant or population Acute and Chronic CAD patients with moderate to severe coronary calcification.

Intervention Rotational Atherectomy (RA).

Comparator Non-RA invasive strategy, ie. Standard PCI or other debulking atherectomy (i.e. Orbital Atherectomy, direct atherectomy, laser, intracoronary litothripsy, or other invasive strategies).

Study designs to be included RCT and Cohort studies.

Eligibility criteria Articles were selected based on the following inclusion criteria: (a) the study reported rotational atherectomy (RA) only or compared RA with Standard PCI or other debulking atherectomy methods (e.g., orbital atherectomy, direct atherectomy, laser, or intracoronary lithotripsy); (b) clinical trials, cohort studies, and case-control studies; (c) studies reporting adverse clinical outcomes, such as post-procedural complications (e.g., coronary artery dissection, device-induced arterial perforation, cardiac tamponade), slow flow/no reflow, myocardial infarction (MI), mortality, stroke, stent thrombosis, target vessel revascularization (TVR), target lesion revascularization (TLR), and composite major adverse cardiovascular events (MACE); or studies reporting inflammatory markers (e.g., CRP, IL-6, TNF-alpha) pre- and post-procedure.

Information sources PubMed and EMBASE.

Main outcome(s) Meta-analyses were conducted to evaluate the effect of rotational atherectomy (RA) on adverse clinical outcomes, including: (1) composite MACE, (2) mortality, (3) myocardial infarction (MI), (4) total vascular revascularization (TVR), (5) total lesion revascularization (TLR), (6) slow/no flow (TIMI flow < 3), (7) coronary dissection, (8) coronary perforation, (9) cardiac tamponade or effusion, (10) stent thrombosis, (11) in-stent restenosis, (12) heart failure NYHA IV, (13) stroke, (14) bleeding, (15) emergency coronary artery bypass grafting (CABG), (16) fluoroscopy time, and (17) contrast volume.

Additional outcome(s) Additionally, we assessed the effect of RA on inflammatory outcomes (i.e., IL-6).

Data management Titles and abstracts of all relevant studies were imported into the Rayyan Intelligent Systematic Review platform (https://rayyan.ai), and all duplicates were removed. Studies were selected according to the PRISMA flow chart. Data from all eligible studies were extracted into a standardized dataset by AQ, MAA, NPL, RH, and RR. The data extracted included first author, year, study design, population size and demographics, follow-up duration, risk factors for coronary artery disease (CAD), type of procedure (e.g., RA alone or compared to other methods), outcomes measured, rate of adverse events, and conclusions, presented in Microsoft Excel.

Quality assessment / Risk of bias analysis The quality of included observational studies was assessed using the Newcastle-Ottawa Scale, while RCTs were evaluated using the Risk of Bias (RoB) tool in Review Manager (RevMan ver. 5.4 for Mac). The NOS scale grades each study on three criteria: study group selection (maximum of four stars), comparability of the groups (maximum of two stars), and outcome assessment (maximum of three stars).
The detailed risk of bias for each observational cohort study. The RoB 2 scale grades each study on five domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. Three independent reviewers (NPL, RH, and MAA) performed the risk of bias assessment using these two tools. Discrepancies were resolved through mutual consensus.

Strategy of data synthesis Categorical data were presented as frequencies (n [%]), while continous data reported as means ± standard deviation (SD), or medians (Q1–Q3). Pooled event rates for short- and mid-term MACE, long-term MACE, as well as short-, mid-, and long-term mortality, along with their 95% confidence intervals (CIs), were calculated (Figure 2 a-d). Meta-analyses were conducted using a random-effects model across the included studies. Relative risk (RR) estimates for dichotomous variables and mean differences (MD) for continuous variables, along with their corresponding 95% CIs, were synthesized to examine the effect of rotational atherectomy (RA) on inflammatory and adverse clinical outcomes.

Subgroup analysis Meta-analyses were conducted to evaluate the effect of rotational atherectomy (RA) on adverse clinical outcomes, including: (1) composite MACE, (2) mortality, (3) myocardial infarction (MI), (4) total vascular revascularization (TVR), (5) total lesion revascularization (TLR), (6) slow/no flow (TIMI flow < 3), (7) coronary dissection, (8) coronary perforation, (9) cardiac tamponade or effusion, (10) stent thrombosis, (11) in-stent restenosis, (12) heart failure NYHA IV, (13) stroke, (14) bleeding, (15) emergency coronary artery bypass grafting (CABG), (16) fluoroscopy time, and (17) contrast volume. Additionally, we assessed the effect of RA on inflammatory outcomes (i.e., IL-6). We classified based on short/mid-term and long-term outcomes, as well as type of studies: RCT or cohort.

Sensitivity analysis N/A.

Language restriction English only.

Country(ies) involved Indonesia - Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Hasanuddin, Makassar 90245.

Other relevant information We used 14 RCTs and 22 cohorts in our meta-analysis.

Keywords Rotational atherectomy, calcified coronary artery, inflammation, clinical outcomes, interleukin-6.

Dissemination plans Publication on international journal and social media.

Contributions of each author
Author 1 - Andriany Qanitha - AQ conceived the idea and formulated the review questions, conducted the systematic literature search, screened titles and abstracts, assessed full-text

papers, and extracted data. AQ performed the main data analysis, drafted the initial manuscript, and prepared the final version for submission.
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Author 2 - Abdul Hakim Alkatiri - AHA conceived the idea and formulated the review questions, supervised, and reviewed the manuscript and provided further revisions for final draft.
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Author 3 - Muhammad Azka Alatsari - MAA screened titles and abstracts, assessed full-text papers, and extracted data, performed assessment risk of bias. MAA provided high quality graph for the manuscript, and contribute to discussion section of the first draft.
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Author 7 - Nurul Qalby - NQ conducted the systematic literature search and provide figure for incidence rate of mortality and MACE.
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