Effects of topical medications on radial artery spasm in patients undergoing transradial coronary procedures: a systematic review protocol

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Review objective: The objective is to identify the effectiveness of topical medications in reducing radial artery spasm in patients undergoing transradial coronary procedures.

Keywords Angioplasty; coronary angiogram; radial artery; spasm; transradial

Background

Percutaneous coronary procedures are the current gold standard utilized internationally for the diagnosis and/or treatment of coronary artery disease. 1,2 Percutaneous coronary procedures, traditionally carried out via the femoral artery, are now increasingly being performed via the brachial and radial arteries. 3,4 Initially, the femoral artery was the preferred option as it provided a large access point; however, this requires the patient to remain lying flat for an extended period of time during and after the procedure to restore hemostasis. 4,5 The anatomical location of the femoral artery can result in severe complications when removing the sheath and applying pressure to restore hemostasis, while the extended period of recovery time lying flat can often lead to lower back pain for the patient. 4,5 The transfemoral approach has also been associated with a number of complications including bleeding (particularly retroperitoneal hemorrhage), hematoma, pseudoaneurysm, nerve damage, arteriovenous fistulae, stroke and death. 6 In a meta-analysis of radial versus femoral catheterization for primary angioplasty where antiplatelet and thrombolytics are routinely used, the radial approach was associated with a significant (P < 0.001) reduction in mortality (5.2 versus 10.3%, OR (odds ratio) 0.42, 95% confidence interval [95% CI] 0.37, 0.48) and major bleeding complications (1.9 versus 4.7%, OR 0.38, 95% CI 0.31, 0.47, P < 0.0001). 6 Over the last 20 years, there has been a global increase in the number of proceduralists performing percutaneous coronary procedures via the transradial approach. This increase can be attributed to the lower amount of complications in comparison to the femoral approach. 7 Campeau 8 initially recommended the radial approach for undertaking percutaneous diagnostic procedures due to its anatomic location and absence from major veins or nerves, resulting in the potential to reduce the rate of complications such as nerve damage and arteriovenous fistulae. Since then, the radial approach has also been documented as an option for undertaking percutaneous interventional procedures. 9-11

Despite the significant reduction in severe complications and the increase in popularity of the radial approach for percutaneous coronary procedures, concerns remain regarding the rates of procedural success. Procedural failure commonly occurs as a result of inability to cannulate the radial artery due to radial artery spasm (RAS), 12 causing severe limitations in the ability of the operator to manipulate the guide wires and catheters along the tortuous pathways of the arteries. 6,13 As a result, the operator may be required to cross over to an alternate access site to gain vascular access, which can, potentially, increase time and radiation exposure in the cardiac catheter laboratory. The radial artery is a type III limb artery and, as a result, is more easily prone to spasm in comparison to larger arteries. 14 The decreased diameter of the radial artery also presents a challenge...
in relation to the size of the catheter that can be used. The literature suggests that catheter size and number of attempts at gaining access can have an impact on the level of trauma to the artery, leading to radial artery occlusion, hemorrhage, radial artery dissection, vasospasm, pseudoaneurysm, pain and thrombosis of the vessel. The incidence of RAS has also been associated with an increase in the patient’s experience of pain during cannulation of the radial artery. A study that aimed to identify variables associated with RAS during transradial percutaneous coronary procedures found that 90% of patients who experienced severe pain during radial artery catheterization also experienced RAS during the procedure.

Various intra-arterial, intravenous and topical medications have been used to reduce the occurrence of vasospasm. Although the need for a prophylaxis to reduce the occurrence of RAS has previously been agreed upon by experts, a specific medication or spasmolytic cocktail and method of administration has yet to be agreed upon. Intravenous or intra-arterial medications commonly utilized include calcium channel blockers and nitrates. The use of topical nitroglycerine and lidocaine has been suggested in the literature to have an impact on the reduction in RAS incidents by causing vasodilation and increasing the radial artery diameter. However, the evidence from the literature remains contradictory. Two studies assessing the effectiveness of topical nitroglycerine and lidocaine reported a statistical significant (\(P < 0.0001\) and \(P = 0.005\)) increase in the diameter of the radial artery but no statistical significant decrease in the incidence of RAS, with RAS occurring in 25% of patients in both the placebo and treatment groups. In contrast, other studies have reported a reduction in RAS incidents in patients receiving topical medications.

Given the controversy that surrounds the use of topical medications, a systematic review will be conducted to identify the effectiveness of topical medications on the incidence of RAS in patients having transradial coronary procedures. Kristic and Lukenda carried out a review of trials assessing the effect of premedications on RAS. However, this did not include topical medications. Currently, there are no systematic reviews of randomized and quasi-randomized controlled trials addressing the effect of topical medications on RAS during percutaneous coronary procedures.

Inclusion criteria

Types of participants

The current review will consider studies that include participants aged 18 years and over undergoing non-emergent transradial coronary procedures.

Types of intervention(s)/phenomena of interest

The current review will consider studies that use topical medications prior to commencing transradial coronary approaches to reduce RAS. Specific comparisons will be made between:

- Topical medication compared to no treatment
- Topical medication compared to placebo
- Topical medications compared to other medications.

Outcomes

The current review will consider studies that include the following outcomes: RAS as assessed by angiography, ultrasound to visualize RAS or resistance felt by the operator while manipulating the catheter. Secondary outcomes will include a change in radial artery diameter measured by angiography or ultrasound and side effects of medications.

Types of studies

The current review will consider randomized and quasi-randomized controlled trials.

Search strategy

The search strategy aims to find both published and unpublished studies. A three-step search strategy will be utilized in this review. An initial limited search of MEDLINE, EMBASE and Scopus will be undertaken followed by an analysis of the text words contained in the title and abstract, and of the index terms used to describe an article. A second search using all identified keywords and index terms will then be undertaken across all included databases. The key terms used will be transradial coronary procedures, coronary angiography, premedication, lidocaine, nitroglycerine, Eutectic Mixture of Local Anesthetics, topical, artery spasm, radial. Third, the reference list of all identified reports and articles will be searched for additional studies. Studies published in English between 1989 to present will be considered for inclusion in this review. This date was selected as, prior to 1989, no studies on transradial percutaneous coronary procedures had been published.
The databases to be searched include: MEDLINE, EMBASE, Scopus, Cochrane Central Register of Controlled Trial and clinicaltrials.gov.

The search for unpublished studies will include: dissertation abstracts international, ProQuest dissertations & theses and MedNar.

Assessment of methodological quality

Papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix I). Any disagreements that arise between the reviewers will be resolved through discussion or with a third reviewer.

Data extraction

Quantitative data will be extracted from papers included in the review using the standardized data extraction tool from JBI-MAStARI (Appendix II). The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives. Data extraction will be carried out by one of the authors and checked by a second. In the event of missing information, the corresponding author will be contacted and clarification will be attempted.

Data synthesis

Quantitative data will, where possible, be pooled in statistical meta-analysis using JBI-MAStARI. All results will be subject to double data entry. Effect sizes expressed as odds ratio (for categorical data) and weighted mean differences (WMDs) (for continuous data), and their 95% CIs will be calculated for analysis.

Clinical heterogeneity will be assessed by considering the populations, interventions and outcomes between the studies. Statistical heterogeneity will be investigated by calculating the $I^2$ statistic, and if this indicates a high level of heterogeneity (75-100%) among the trials included in an analysis, a random effects meta-analysis will be preferred for the overall summary. Fixed effects meta-analysis will be used for combining study data if the trials are judged to be sufficiently similar. Analysis of continuous data will be undertaken using the mean and standard deviation values to derive WMDs and their 95% CIs. Where synthesis is inappropriate, a narrative overview will be undertaken.

References

12. Majure D, Hallaux M, Yeghiazarians Y, Boyle A. Topical nitroglycerin and lidocaine locally vasodilate the radial
Appendix I: Appraisal instrument

MAStARI appraisal instrument

**JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial**

<table>
<thead>
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<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>Not Applicable</th>
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<td>1. Was the assignment to treatment groups truly random?</td>
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<td>2. Were participants blinded to treatment allocation?</td>
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<td>3. Was allocation to treatment groups concealed from the allocator?</td>
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<td>4. Were the outcomes of people who withdrew described and included in the analysis?</td>
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<td>5. Were those assessing outcomes blind to the treatment allocation?</td>
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<td>6. Were the control and treatment groups comparable at entry?</td>
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<td>7. Were groups treated identically other than for the named interventions</td>
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<td>8. Were outcomes measured in the same way for all groups?</td>
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<td>9. Were outcomes measured in a reliable way?</td>
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<td>10. Was appropriate statistical analysis used?</td>
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Overall appraisal: [ ] Include [ ] Exclude [ ] Seek further info. [ ]

Comments (Including reason for exclusion)

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Appendix II: Data extraction instrument

MAStARI data extraction instrument

**JBI Data Extraction Form for Experimental / Observational Studies**

Reviewer __________________________ Date __________________________

Author __________________________ Year __________________________

Journal __________________________ Record Number __________________________

**Study Method**

- RCT ☐
- Quasi-RCT ☐
- Longitudinal ☐
- Retrospective ☐
- Observational ☐
- Other ☐

**Participants**

Setting __________________________

Population __________________________

**Sample size**

Group A __________________________ Group B __________________________

**Interventions**

Intervention A __________________________

Intervention B __________________________

**Authors Conclusions:**

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**Reviewers Conclusions:**

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**Study results**

**Dichotomous data**

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**Continuous data**

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