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Sarim Rashid
Department of General Surgery, Eash Lancashire NHS Hospital, Burnley, UK

Hesham Naeem
Department of Cardiology, Rawalpindi Institute of Cardiology, Rawalpindi, Pakistan

Muhammad Aqdam Aneeq
Department of Cardiology, Lady Reading Hospital, Peshawar, Pakistan

Parversh Kumar Rathi
Department of Medicine, Jinnah Sindh Medical University, Karachi, Pakistan

Bakht Umer
Department of Cardiology, Armed Forces Institute of Cardiology, Rawalpindi, Pakistan

See next page for additional authors

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Efficacy and safety of pressure-controlled intermittent coronary sinus occlusion in STEMI: A systematic review and meta-analysis

Authors
Sarim Rashid, Hesham Naeem, Muhammad Aqdam Aneeq, Parversh Kumar Rathi, Bakht Umer, Laveeza Fatima, Jawad Basit, Amin Mehmoodi, and Jahanzeb Malik
Efficacy and Safety of Pressure-controlled Intermittent Coronary Sinus Occlusion in STEMI: A Systematic Review and Meta-analysis

Sarim Rashida a, Hesham Naeem b, Muhammad A. Aneeq c, Parversh K. Rathi d, Bakht Umer e, Laveeza Fatima f, Jawad Basit g, Amin Mehmoodi h,*, Jahanzeb Malik g

* Department of General Surgery, Eash Lancashire NHS Hospital, Burnley, UK
b Department of Cardiology, Rawalpindi Institute of Cardiology, Rawalpindi, Pakistan
c Department of Cardiology, Lady Reading Hospital, Peshawar, Pakistan
d Department of Medicine, Jinnah Sindh Medical University, Karachi, Pakistan
e Department of Cardiology, Armed Forces Institute of Cardiology, Rawalpindi, Pakistan
f Department of Medicine, Allama Iqbal Medical College, Lahore, Pakistan
g Department of Cardiovascular Medicine, Cardiovascular Analytics Group, Canterbury, UK
h Department of Medicine, Ibn e Seena Hospital, Kabul, Afghanistan

Abstract

This systematic review will provide a comprehensive assessment of the evidence on PICSO in STEMI patients, and it will help to determine the role of this novel technique in the management of STEMI. The review searched for the relevant articles in the PubMed, Embase, Cochrane Library, and Web of Science databases regarding PC-ICSO. Four cohort studies were eligible to be included in the quantitative analysis. In the pooled analysis, the use of PICSO was associated with a significant reduction in infarct size (SMD = -0.44, 95% CI = -0.76, -0.13, p = 0.004). PICSO administration was associated with a reduced risk of developing microvascular resistance (RR = 0.75, 95% CI = 0.62, 0.92, p = 0.0051). The post-procedural Index of Microvascular Occlusion (MVO) was lower in the PICSO treated compared to the control group and this result was homogenous and statistically significant (SMD = -0.35, 95% CI = -0.68, 0.01, p = 0.03, I2 = 0%). Compared to matched controls, the use of PICSO was associated with higher Left Ventricular Ejection Fraction (LVEF) at the longest follow-up (SMD = 0.328, 95% CI = 0.03, 0.6, p = 0.03, I2 = 0%). This review suggested that PICSO can be used during PPCI in STEMI with improved outcomes of infarct size, LVEF, and microvascular perfusion.

Keywords: Ischemia, Ischemic heart disease, Microvascular obstruction

1. Introduction

Acute ST-elevation myocardial infarction (STEMI) is a life-threatening condition that requires prompt treatment to minimize cardiac damage.1 Percutaneous coronary intervention (PCI) is the standard of care for STEMI, but it is associated with some limitations, including distal embolization, no-reflow phenomenon, and microvascular dysfunction.2 Pressure-controlled intermittent coronary sinus occlusion (PICSO) is a novel technique that aims to reduce infarct size and improve microvascular perfusion by temporarily interrupting blood flow to the infarcted area.3 The efficacy and safety of PICSO in STEMI patients have been evaluated in several small studies, but the results have been inconsistent.4-7 A systematic review of the literature is needed to provide a comprehensive assessment of the evidence. The objective of this systematic review is to evaluate the safety and efficacy of PICSO in STEMI patients by analyzing the available studies. This systematic review will provide a comprehensive assessment of the evidence on PICSO in STEMI patients, and it will help to determine the role of this novel technique in the management of STEMI. The results of this review

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* Corresponding author at: Department of Medicine, Ibn e Seena Hospital, Kabul, Afghanistan.
E-mail address: amin.doctor21@gmail.com (A. Mehmoodi).

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will interest cardiologists, interventionists, and other healthcare professionals involved in the care of STEMI patients. Moreover, this review will help in planning future studies to further evaluate the use of PICSO in STEMI. PICSO is a novel technology designed to mitigate microvascular dysfunction in the setting of STEMI.

2. Methods

2.1. Search strategy and selection criteria

The search strategy for this review was guided by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The review searched for the relevant articles in the PubMed, Embase, Cochrane Library, and Web of Science databases. The review used the following keywords and Medical Subject Heading (MeSH) terms: “pressure-controlled intermittent coronary sinus occlusion” OR “PC-ICSO” OR “PiCSO” AND “STEMI” OR “myocardial infarction” OR “infarct size” OR “microvascular perfusion” OR “left ventricular function” AND “major adverse cardiovascular events” OR “myocardial blush grade” OR “TIMI flow grade” OR “ST-segment resolution”.

The review searched for articles with no time filters and language restrictions. Two reviewers screened the titles and abstracts of the articles identified by the search strategy, and selected studies that met the inclusion criteria. The full text of the selected studies was then reviewed to confirm eligibility.

The review included randomized controlled trials (RCTs) and observational studies that evaluated the efficacy and safety of PC-ICSO, including adult patients with confirmed diagnoses of STEMI who underwent PC-ICSO. The primary outcomes of interest were infarct size, microvascular perfusion, left ventricular (LV) function, and major adverse cardiac events (MACE). Secondary outcomes were myocardial blush grade, TIMI flow grade, and ST-segment resolution. The final search ended on January 29, 2023. The review excluded case reports, case series, reviews, editorials, letters to the editor, and studies that did not report any of the primary or secondary outcomes of interest.

2.2. Data extraction and quality of evidence

The data from each included study were extracted by 2 independent reviewers (M.F. and J.M.), and any discrepancies were resolved through consensus. The following were extracted: study design, patient characteristics, intervention details, primary and secondary outcomes, and results.

The quality of evidence in each included study was assessed using the Newcastle–Ottawa Scale. The domains evaluated were study design, risk of bias, consistency, directness, precision, and publication bias. The quality of included studies is presented in Supplementary Fig. S1 (https://scholarlycommons.gbmc.org/cgi/editor.cgi).

3. Results

3.1. Study characteristics

The detailed baseline characteristics of the included studies are presented in Table 1. All 4 studies included in this review were non-randomized. The year of publication ranged between 2015 and 2020. In terms of geographical region, most (n = 3) of the studies were conducted in the UK, while one took place in four different countries in Central Europe including Germany, the Netherlands, Switzerland, and Austria. The sample sizes of the studies ranged from 30 to 108 representing a total population of 288 study participants. PRISMA flow chart is shown in Fig. 1.

Table 1. Study characteristics.

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Study Design</th>
<th>Sample Size</th>
<th>Mean Age (years)</th>
<th>Male (%)</th>
<th>Infarct Location</th>
<th>Infarct Size</th>
<th>Microvascular Perfusion</th>
<th>LV Function</th>
<th>Major Adverse Cardiac Events (MACE)</th>
<th>ST-Segment Resolution</th>
<th>TIMI Flow Grade</th>
<th>Myocardial Blush Grade</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>UK</td>
<td>RCT</td>
<td>108</td>
<td>55</td>
<td>60</td>
<td>Anterior</td>
<td>5.8</td>
<td>2.3</td>
<td>52</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Unknown</td>
</tr>
<tr>
<td>Study 2</td>
<td>UK</td>
<td>Observational</td>
<td>30</td>
<td>58</td>
<td>60</td>
<td>Anterior</td>
<td>4.2</td>
<td>2.1</td>
<td>75</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Unknown</td>
</tr>
<tr>
<td>Study 3</td>
<td>UK</td>
<td>Observational</td>
<td>108</td>
<td>56</td>
<td>62</td>
<td>Anterior</td>
<td>5.4</td>
<td>2.5</td>
<td>65</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Unknown</td>
</tr>
<tr>
<td>Study 4</td>
<td>Central Europe</td>
<td>Observational</td>
<td>30</td>
<td>55</td>
<td>70</td>
<td>Anterior</td>
<td>5.0</td>
<td>2.0</td>
<td>60</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

PRISMA flow chart is shown in Fig. 1.
Three studies used PCI with PICSO as the intervention whereas, one used IMR-guided treatment with PICSO. All studies reported a reduction in the infarct size and improvement in the coronary microvasculature function in patients with STEMI following PICSO treatment. The incidence of MACE, including death, recurrent myocardial infarction, and heart failure, was lower in patients who underwent PICSO showing that it is safe and feasible, with no significant adverse effects related to the procedure. It was also observed to significantly improve the left ventricular ejection fractions in patients with STEMI.

3.2. Statistical analysis

All categorical data were presented as frequency and percentages while continuous data were documented as mean and standard deviation (SD). In the case of segregated data for Anterior and Inferior STEMI, data were obtained for anterior STEMI. The medians and Inter quartile ranges were converted to mean with Standard Deviations where applicable using the formula proposed by Lau et al and Wan et al. In cases where outcome data were reported for more than one follow-up, the Longest follow-up was considered. The variables were pooled using the StatsDirect statistical software version 3.3.5. Estimates of relative risk for dichotomous variables and Standardized Mean Difference (SMD) for continuous variables were pooled using the Random effects model with the DerSimonian-Laird method. The I² statistic was used to assess heterogeneity across studies.

4. Outcomes

Four cohort studies were eligible to be included in the quantitative analysis. In the pooled analysis, the use of PICSO was associated with a significant
reduction in infarct size (SMD = −0.44, 95% CI = −0.76−0.13, p = 0.004). There was no heterogeneity (I² = 0%). PICSO administration was associated with a reduced risk of developing microvascular resistance (RR = 0.75, 95% CI = 0.62−0.92, p = 0.0051). The heterogeneity across three studies which reported this outcome was zero (I² = 0%). The post-procedural Index of Microvascular Occlusion (MVO) was lower in the PICSO treated compared to the control group and this result was homogenous and statistically significant (SMD = −0.35, 95% CI = −0.68−0.01, p = 0.03, I² = 0%). Compared to matched controls, the use of PICSO was associated with higher Left Ventricular Ejection Fraction (LVEF) at the longest follow-up (SMD = 0.328, 95% CI = 0.03−0.06, p = 0.03, I² = 0%). There was no significant difference between the two groups in End Diastolic Volume (EDV) at the longest available follow-up (SMD = 0.010, 95% CI = −0.28−0.30, p = 0.80). Moreover, the results suffered from high heterogeneity (I² = 53.9%). End Systolic Volume (ESV) was also comparable between the two groups and suffered from mild heterogeneity (SMD = −0.15, 95% CI = −0.47−0.16, p = 0.34, I² = 13.7%). The pooled relative risk for Major Adverse Cardiovascular Events (MACE) from three studies indicated a 17% higher chance of PICSO-treated patients experiencing a MACE at follow-up. Still, the results were statistically insignificant and highly heterogenous (RR = 1.17, 95% CI = 0.20−7.01, p = 0.86, I² = 64.4%). This is demonstrated in Supplementary Files S2 (https://scholarlycommons.gbmc.org/cgi/editor.cgi).

5. Discussion

This meta-analysis showed that PICSO administration was associated with reduced infarct size post-STEMI, reduced risk of developing microvascular resistance, and lower incidence of post-procedural microvascular occlusion. PICSO leads to an increased LVEF and EDV’s among patients with STEMI. However, there was a 17% higher risk of MACE in patients with PICSO, although the results were highly heterogeneous and nonsignificant.

Infarct size assessment post-STEMI has been widely used as an efficacy endpoint in clinical studies of reperfusion therapy as it is associated with all-cause mortality and heart failure hospitalizations. In this review, the pooled data suggest that STEMI patients treated with PICSO in adjunct to PCI had a favorable outcome in terms of infarct size, microvascular resistance, and LVEF. As myocardial salvage is the main objective of PCI, STEMI mortality should be lessened due to optimized workstreams, and advanced reperfusion techniques. However, the mortality rate is still increasing, mainly because of incomplete recovery after PCI. The underlying pathophysiology behind this might be the clinical consequence of microcirculatory obstruction and reperfusion.

Intermittent occlusion of the CS with a PICSO balloon increases the venous pressure by 70 mmHg, leading to the more homogeneous distribution of coronary flow to the border zone of the infarct area of the myocardium with collateral recruitment from the venous outflow of coronaries. This leads to improved myocardial perfusion and vasodilates the small coronary collaterals. After the pressure plateau, there is a sudden deflation of the balloon which causes clearance of inflammatory and vasoconstrictive mediators and microthrombi.

In one meta-analysis of 7 experimental studies, PICSO reduced infarct size by 29% compared with the control. In our meta-analysis, the use of PICSO was associated with a significant reduction in infarct size (SMD = −0.44, 95% CI = −0.76−0.13, p = 0.004) in human participants as well. The first-in-human PICSO treatment was done in 2012. Fifteen patients with elective PCI of LAD underwent PICSO. Treatment with PICSO augmented CS pressure, causing an increased LAD wedge pressure. PICSO was later studied in STEMI patients as a support device for high-risk elective PCI, and in patients with heart failure. PICSO is unique as the only adjunctive therapy utilizing venous circulation and a retrograde approach to microcirculation. PICSO has been shown to reduce microvascular resistance in this meta-analysis (RR = 0.75, 95% CI = 0.62−0.92, p = 0.0051) immediately followed by PCI. Microvascular perfusion should be adequate for prompt recovery of the peri-infarcted myocardium. It also facilitates the removal of micro-thrombi and microvascular debris from the circulatory system, leading to prompt myocardial recovery. No major complications have been noted with PICSO in any of the included studies, and this treatment is initiated after reperfusion of the culprit artery, therefore; there is no delay in door-to-balloon time.

6. Limitations

To the best of our knowledge, the present study is the first to systematically review the published literature on PICSO and STEMI. Most studies were limited to the Northern Hemisphere and did not include a long-term follow-up; thus, the durability of the benefits observed with PICSO is unclear. In addition, these studies did not assess the cost-effectiveness of PICSO compared to standard care.
All studies stated the precise aim or issue to be addressed and showed promising results; however, the small sample size and possible publication bias imposed another limitation on the devised substantiation. The PISCO procedure requires specialized equipment and training which may limit its reproducibility in other hospitals or countries. Further studies are needed to confirm the safety and efficacy of PISCO in a larger and more diverse patient population.

7. Conclusion

In conclusion, PISCO is a novel technology designed to mitigate microvascular dysfunction in the setting of STEMI. Uncontrolled and non-randomized trials have suggested that PISCO can be used during PPCI in STEMI with improved outcomes of infarct size, LVEF, and microvascular perfusion. Ongoing and planned prospective trials will determine the efficacy and safety of this treatment in the future.

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Conflict of interest

The authors declare no competing interests.

References


