

AHRQ Comparative Effectiveness Review Surveillance Program

CER #42:

Adjunctive Devices for Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention

Original release date:

December, 2011

Surveillance Report:

May, 2013

Key Findings:

- There have been relatively few new studies, and those that have been published report results consistent with the original conclusions. The relative effectiveness of thrombectomy versus abciximab may be out of date; this was a small portion of one key question

Summary Decision

This CER's priority for updating is **Low**

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Adjunctive Devices for Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention

1. Introduction

Comparative Effectiveness Review (CER) #42, Adjunctive Devices for Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention, was released in December 2011.¹ It was therefore due for a surveillance assessment in June 2012. Resource constraints at the Surveillance Center delayed this until April 2013. We contacted subject experts to get their opinions as to whether the conclusions had changed and need to be updated. We also conducted an update electronic literature search.

2. Methods

2.1 Literature Searches

Using the search strategy employed for the original report, we conducted a limited literature search of Medline for the years January 1, 2011-February 4, 2013. This search included five high-profile general medical interest journals (Annals of Internal Medicine, British Medical Journal, Journal of the American Medical Association, Lancet, and the New England Journal of Medicine) and seven specialty journals (American Journal of Cardiology, Journal of the American College of Cardiology, Circulation, Catherization and Cardiovascular Interventions, American Heart Journal, and the European Heart Journal). The specialty journals were the most highly represented among the references for the original report. Appendix A includes the search methodology for this topic.

2.2 Study selection

In general we used the same inclusion and exclusion criteria as the original CER.

2.3 Expert Opinion

We shared the conclusions of the original report with two experts in the field for their assessment of the need to update the report and their recommendations of any relevant new studies; both subject matter experts responded. Appendix C shows the questionnaire matrix that was sent to the experts.

2.4 Check for qualitative and quantitative signals

After abstracting the study conditions and findings for each new included study into an evidence table, we assessed whether the new findings provided a signal according to the Ottawa Method and/or the RAND Method, suggesting the need for an update. The criteria are listed in the table below.^{2,3}

Ottawa Method	
Ottawa Qualitative Criteria for Signals of Potentially Invalidating Changes in Evidence	
A1	Opposing findings: A pivotal trial or systematic review (or guidelines) including at least one new trial that characterized the treatment in terms opposite to those used earlier.
A2	Substantial harm: A pivotal trial or systematic review (or guidelines) whose results called into question the use of the treatment based on evidence of harm or that did not proscribe use entirely but did potentially affect clinical decision making.
A3	A superior new treatment: A pivotal trial or systematic review (or guidelines) whose results identified another treatment as significantly superior to the one evaluated in the original review, based on efficacy or harm.
Criteria for Signals of Major Changes in Evidence	
A4	Important changes in effectiveness short of “opposing findings”
A5	Clinically important expansion of treatment
A6	Clinically important caveat
A7	Opposing findings from discordant meta-analysis or nonpivotal trial
Quantitative Criteria for Signals of Potentially Invalidating Changes in Evidence	
B1	A change in statistical significance (from nonsignificant to significant)
B2	A change in relative effect size of at least 50 percent
RAND Method Indications for the Need for an Update	
1	Original conclusion is still valid and this portion of the original report does not need updating
2	Original conclusion is possibly out of date and this portion of the original report may need updating
3	Original conclusion is probably out of date and this portion of the original report may need updating
4	Original conclusion is out of date

2.5 Compilation of Findings and Conclusions

For this assessment we constructed a summary table that included the key questions, the original conclusions, and the findings of the new literature search, the expert assessments, and any FDA reports that pertained to each key question. To assess the conclusions in terms of the evidence that they might need updating, we used the 4-category scheme described in the table above for the RAND Method.

In making the decision to classify a CER conclusion into one category or another, we used the following factors when making our assessments:

- If we found no new evidence or only confirmatory evidence and all responding experts assessed the CER conclusion as still valid, we classified the CER conclusion as still valid.
- If we found some new evidence that might change the CER conclusion, and /or a minority of responding experts assessed the CER conclusion as having new evidence that

might change the conclusion, then we classified the CER conclusion as possibly out of date.

- If we found substantial new evidence that might change the CER conclusion, and/or a majority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as probably out of date.
- If we found new evidence that rendered the CER conclusion out of date or no longer applicable, we classified the CER conclusion as out of date. Recognizing that our literature searches were limited, we reserved this category only for situations where a limited search would produce prima facie evidence that a conclusion was out of date, such as the withdrawal of a drug or surgical device from the market, a black box warning from FDA, etc.

2.6 Determining Priority for Updating

We used the following two criteria in making our final conclusion for this CER:

- How much of the CER is possibly, probably, or certainly out of date?
- How out of date is that portion of the CER? For example, would the potential changes to the conclusions involve refinement of original estimates or do the potential changes mean some therapies are no longer favored or may not exist? Is the portion of the CER that is probably or certainly out of date an issue of safety (a drug withdrawn from the market, a black box warning) or the availability of a new drug within class (the latter being less of a signal to update than the former)?

3. Results

3.1 Search

The literature search identified 52 titles. After title and abstract review, we further reviewed the full text of seven journal articles. The remaining titles were rejected because they clearly did not meet inclusion criteria for any of the review questions or were unlikely to impact the CER conclusions. In addition to the electronic database searches, we followed up suggestions from the topic experts for studies not already included in the original report. We reference-mined articles that met inclusion criteria as well as systematic reviews identified by the literature searches to identify additional articles that may have been published since the publication of the report.

Thus, 14 articles went on to full text review. Of these, 11 articles were rejected because they did not meet the inclusion criteria of the original report. The three remaining articles, were abstracted into an evidence table (Appendix B) for this assessment.⁴⁻⁶

3.2 Expert Opinion

One expert thought one key question had new evidence, and the others were still valid. The other expert thought that the conclusions for all key questions were still valid, but identified a number of issues relevant to PCI that could impact the relative value of adjunctive devices.

3.3 Identifying qualitative and quantitative signals

Table 1 shows the original key questions, the conclusions of the original report, the results of the literature and drug database searches, the experts' assessments, the recommendations of the Southern California Evidence-based Practice Center (SCEPC) regarding the need for update, and qualitative signals.

Table 1: Summary Table

Conclusions From CER Executive Summary	RAND Literature Search	FDA / Health Canada / MHRA (UK)	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC
Conclusion #1				
<p>In the catheter aspiration trials, the risks of major adverse cardiovascular events (MACE) and coronary dissection were significantly lower in the overall analysis and the good-quality trial analyses. The risks of mortality, myocardial infarction, stroke, target revascularization, and side branch occlusion were not significantly different from control. Eight of nine trials and one controlled observational study found a nonsignificant prolongation of the time needed to conduct the PCI procedure compared with control. Intermediate health outcomes showed significant reductions in distal embolization and no reflow, and significantly more patients experienced ST segment resolution, higher MBG, and near-normal (TIMI-3) blood flow through the target vessel compared with control. More research is needed to truly determine the balance of benefits to harms.</p>	<p>One new meta-analysis reported better outcomes in patients treated with aspiration thrombectomy than patients treated with PCI alone⁶</p>	<p>None</p>	<p>1 expert thought this was still valid</p> <p>1 expert thought a new meta-analysis would refine these conclusions</p>	<p>This conclusion is still valid, although there are now more data</p>
Conclusion # 2				
<p>Mechanical thrombectomy device use did not result in any significant differences in the risk of mortality, stroke, MACE, coronary dissection, and coronary perforation in the overall analyses and analyses limited to good-quality trials. However, these devices significantly increased the time needed to conduct the PCI procedure in three trials. While the risks of myocardial infarction, target revascularization, mortality, and MACE were not significantly different from control, these findings may be misleading since many of the trials evaluating this procedure versus control had a short duration of followup. When we evaluated mortality and MACE in studies of 365 days or longer, we saw no significant</p>	<p>One new meta-analysis reported no difference in outcomes in patients treated with mechanical thrombectomy than patients treated with PCI alone⁵</p>	<p>None</p>	<p>Both experts thought this conclusion was still valid</p>	<p>This conclusion is still valid, although there are now more data</p>

Conclusions From CER Executive Summary	RAND Literature Search	FDA / Health Canada / MHRA (UK)	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC
<p>Unlike the case with catheter aspiration devices, there were no significant beneficial effects on intermediate health outcomes with mechanical thrombectomy devices, and while most were in the right direction of effect, the chance of achieving near normal (TIMI-3) blood flow was not significantly different from control. More research is needed to truly determine the balance of benefits to harms with mechanical thrombectomy devices.</p>				
Conclusion # 3				
<p>The use of embolic protection devices was based on a limited number of studies. One significant finding on final health outcomes (effect of distal filter on target revascularization) was seen in overall analyses or those limited to good-quality trials. It was difficult to assess the impact of these devices on final health outcomes and intermediate outcomes. In STEMI, distal balloon devices significantly increased the chance of achieving MBG-3 and near-normal (TIMI-3) blood flow but did not significantly impact the achievement of ST-segment resolution, prevention of no reflow, or the risk of distal embolization. Distal filter devices did not significantly impact ST-segment resolution, distal embolization, no reflow, attainment of near-normal (TIMI-3) blood flow, or MBG. There was a paucity of trials available to evaluate adverse events with any of the embolic protection devices. The only significant finding was increased time to perform a PCI procedure compared with control for all three types of embolic protection devices individually and when evaluated all together. The balance of benefits to harms cannot be determined for these device classes.</p>	No new data	None	Both experts thought this conclusion was still valid	This conclusion is still valid
Conclusion #4				
Given the inadequate power in overall	One new RCT reported that	None	Both experts thought this	This conclusion

Conclusions From CER Executive Summary	RAND Literature Search	FDA / Health Canada / MHRA (UK)	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC
analyses and lack of data, we could not definitively determine the impact of therapy in subpopulations. No data were available to determine if the results differed based on ethnicity or ejection fraction. Given the available data, the concomitant use of a glycoprotein IIb/IIIa receptor antagonist and a device may be associated with a survival benefit.	the use of abciximab, but not aspiration thrombectomy reduced myocardial infarct size ⁴		conclusion was still valid	is possibly out of date based on the new RCT

Legend: CABG: Coronary Artery Bypass Grafting; MACE: Major Adverse Cardiovascular Events; PCI: Percutaneous Coronary Intervention; SCEPC: Southern California Evidence-based Practice Center

References

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5. Vink MA, Dirksen MT, Tijssen JGP, et al. Lack of long-term clinical benefit of thrombus aspiration during primary percutaneous coronary intervention with paclitaxel-eluting stents or bare-metal stents: post-hoc analysis of the PASSION-trial. *Catheterization & Cardiovascular Interventions.* 2012 May 1;79(6):870-7. PMID: 21735533.
6. Kumbhani DJ, Bavry AA, Desai MY, et al. Role of aspiration and mechanical thrombectomy in patients with acute myocardial infarction undergoing primary angioplasty: An updated meta-analysis of randomized trials. *J Am Coll Cardiol.* 2013 May 8 PMID: 23665372.

Appendices

Appendix A: Search Methodology

Appendix B: Evidence Tables

Appendix C: Questionnaire Matrix

Appendix A. Search Methodology

Update: January 1, 2011- February 4, 2013

Search Strategy for MEDLINE (via OVID)

1. myocardial infarction.mp. or Myocardial Infarction/
2. acute myocardial infarction.mp.
3. AMI.mp.
4. MI.mp.
5. STEMI.mp.
6. ST-segment elevation.mp.
7. ACS.mp.
8. NSTEMI.mp.
9. acute coronary syndrome.mp. or Acute Coronary Syndrome/
10. ST-segment resolution.mp.
11. unstable angina.mp. or Angina, Unstable/
12. Q-wave.mp.
13. no-reflow.mp.
14. distal embolization.mp.
15. Angioplasty, Transluminal, Percutaneous Coronary/ or percutaneous coronary intervention.mp.
16. PCI.mp.
17. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
18. thrombectomy.mp. or Thrombectomy/
19. embolic protection.mp.
20. distal protection.mp.
21. proximal protection.mp.
22. thrombus aspiration.mp.
23. aspiration catheter.mp.
24. rescue catheter.mp.
25. diver CE.mp.
26. Export catheter.mp.
27. transvascular aspiration catheter.mp.
28. TVAC.mp.
29. Pronto.mp.
30. x-sizer.mp.
31. angiojet.mp.
32. filterwire.mp.
33. spiderx.mp.
34. spiderfx.mp.
35. angioguard.mp.
36. proxis.mp.
37. interceptor plus.mp.
38. rinspirator.mp.
39. microvena trap.mp.

40. percusurge.mp.
41. triactiv.mp.
42. cardioshield.mp.
43. thrombobuster.mp.
44. rio catheter.mp.
45. fetch catheter.mp.
46. quickcat.mp.
47. rubicon catheter.mp.
48. parodi anti-embolisation.mp.
49. 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48
50. 17 and 49
51. 50 not carotid.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
52. limit 51 to humans
53. "annals of internal medicine".jn.
54. bmj.jn.
55. jama.jn.
56. lancet.jn.
57. "new England journal of medicine".jn.
58. "American journal of cardiology".jn.
59. "journal of the American college of cardiology".jn.
60. circulation.jn.
61. catheterization & cardiovascular interventions.jn.
62. American heart journal.jn.
63. European heart journal.jn.
64. heart.jn.
65. 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64
66. 52 and 65
67. limit 66 to yr="2011-Current"

Results: 52

Appendix B. Evidence Table

Author, year	Study design	Comparison	Sample size	Results
Kumbhani, 2013 ^b	Meta-analysis	Patients with acute myocardial infarction treated with aspiration or mechanical thrombectomy vs. conventional PCI	25 trials including 5,534 patients	Major adverse cardiac events were significantly lower in patients treated with aspiration thrombectomy than PCI alone [RR=0.76, p=0.006]. Mechanical thrombectomy patients did not have improved outcomes compared to PCI alone [RR=1.60, p=0.77]
Stone, 2012 ⁴ (INFUSE-AMI)	RCT	Patients with ST segment elevation myocardial infarction randomized to manual aspiration thrombectomy, bolus intracoronary abciximab or both	452	Infarct size was smaller at 30 days in patients treated with abciximab and not in patients treated with aspiration thrombectomy
Vink, 2012 ⁵ (PASSION)	Post hoc analysis of RCT	Patients being randomized to drug-eluting stents vs. bare metal stents who were also treated with thrombus aspiration	619	Patients treated with thrombus aspiration did not have better outcomes than those treated with PCI alone (composite outcome of death, myocardial infarction, or target lesion revascularization 13.0% vs. 13.5%)

Legend: CABG: PCI: Percutaneous Coronary Intervention; RCT: Randomized Controlled Trial

Appendix C. Questionnaire Matrix

Surveillance and Identification of Triggers for Updating Systematic Reviews for the EHC Program

Title: Adjunctive Devices for Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
Conclusion #1			
<p>In the catheter aspiration trials, the risks of major adverse cardiovascular events (MACE) and coronary dissection were significantly lower in the overall analysis and the good-quality trial analyses. The risks of mortality, myocardial infarction, stroke, target revascularization, and side branch occlusion were not significantly different from control. Eight of nine trials and one controlled observational study found a nonsignificant prolongation of the time needed to conduct the PCI procedure compared with control. Intermediate health outcomes showed significant reductions in distal embolization and no reflow, and significantly more patients experienced ST segment resolution, higher MBG, and near-normal (TIMI-3) blood flow though the target vessel compared with control. More research is needed to truly determine the balance of benefits to harms.</p>	<input type="checkbox"/>	<p>New Evidence:</p>	<input type="checkbox"/>
Conclusion # 2			
<p>Mechanical thrombectomy device use did not result in any significant differences in the risk of mortality, stroke, MACE, coronary dissection, and coronary perforation in the overall analyses and analyses limited to good-quality trials.</p>	<input type="checkbox"/>	<p>New Evidence:</p>	<input type="checkbox"/>

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
<p>However, these devices significantly increased the time needed to conduct the PCI procedure in three trials. While the risks of myocardial infarction, target revascularization, mortality, and MACE were not significantly different from control, these findings may be misleading since many of the trials evaluating this procedure versus control had a short duration of followup. When we evaluated mortality and MACE in studies of 365 days or longer, we saw no significant difference in mortality risk, although a single trial found a significant reduction in MACE. Unlike the case with catheter aspiration devices, there were no significant beneficial effects on intermediate health outcomes with mechanical thrombectomy devices, and while most were in the right direction of effect, the chance of achieving near normal (TIMI-3) blood flow was not significantly different from control. More research is needed to truly determine the balance of benefits to harms with mechanical thrombectomy devices.</p>			
Conclusion # 3			
<p>The use of embolic protection devices was based on a limited number of studies. One significant finding on final health outcomes (effect of distal filter on target revascularization) was seen in overall analyses or those limited to good-quality trials. It was difficult to assess the impact of these devices on final health outcomes and intermediate outcomes. In STEMI, distal balloon devices significantly increased the chance of achieving MBG-3 and near-normal (TIMI-3) blood flow but did not significantly impact the achievement of ST-segment resolution, prevention of no reflow, or the risk of distal embolization. Distal filter devices did not significantly impact ST-segment resolution, distal embolization, no reflow, attainment of near-normal (TIMI-3) blood flow, or</p>	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
<p>MBG. There was a paucity of trials available to evaluate adverse events with any of the embolic protection devices. The only significant finding was increased time to perform a PCI procedure compared with control for all three types of embolic protection devices individually and when evaluated all together. The balance of benefits to harms cannot be determined for these device classes.</p>			
Conclusion #4			
<p>Given the inadequate power in overall analyses and lack of data, we could not definitively determine the impact of therapy in subpopulations. No data were available to determine if the results differed based on ethnicity or ejection fraction. Given the available data, the concomitant use of a glycoprotein IIb/IIIa receptor antagonist and a device may be associated with a survival benefit.</p>	<input type="checkbox"/>	<p>New Evidence:</p>	<input type="checkbox"/>
<p>Are there new data that could inform the key questions that might not be addressed in the conclusions?</p>			