

Article details: 2014-0035	
Title	<b>Providing Optimal Care for Patients with ST-segment Elevation Myocardial Infarction Across a Large Region: Issues Beyond Timeliness of Reperfusion</b>
Authors	Mathew Mercuri, Michelle Welsford, Jon-David Schwalm, Shamir R. Mehta, Purnima Rao-Melacini, Nicholas Valettas, Tej Sheth, Michael Rokoss, Sanjit Jolly, James Velianou, Madhu Natarajan
Reviewer 1	<b>Kotb, Ahmed</b>
Institution	University of Ottawa
General comments	<p>It was a pleasure to review this paper. A great deal of research has focused on comparing the effectiveness of different strategies for reperfusion for patients with STEMI and exploring issues such as the timeliness of reperfusion. The authors of this paper go beyond what has already been studied and focus on the experiences and outcomes of all patients presenting with STEMI within a specific region, including those not receiving PPCI.</p> <p>So although PPCI, when delivered in a timely manner, is considered the evidence based standard of care, many patients do not receive PPCI due to a variety of reasons. For a regional program to improve patient outcomes, it is essential that the system approach taken ensures that the best available treatment is provided while also taking into consideration also the context under which it is delivered. The authors provide a detailed overview of the regional program in question and give a clear and thorough rationale for their research focus.</p> <p>The study design is strong and the methods used are appropriate and outlined in sufficient detail. The health outcomes and system related outcomes considered are relevant. The steps taken for statistical analysis transition nicely and demonstrate that the analysis was well thought and adequately preplanned. The results from their analyses are clearly summarized and presented. Their interpretation of their findings and description of the limitations of their research both demonstrate a great deal of thoughtfulness and thoroughness.</p> <p>However, I was concerned about the lack of adequately addressing the degree of missingness in the variables they accounted and adjusted for. When using large databases or dealing with a large sample that is followed over a long time period, certain variables are reported or collected better than others. It would be of interest to know whether or not data missingness was an issue and if so, how it was dealt with.</p> <p>Another important issue is that the authors have not provided a completed STROBE checklist along with their paper.</p> <p>Overall, the paper is very well written, its research methodology is strong and its clinical importance is evident. The thoughtfulness and time taken to properly plan the methods and analyses required to correctly address this research question are apparent in the quality of the work produced and the balance struck between statistical and clinical sense with regards to how the research was conducted.</p> <p>This lends itself well to the ability of readers to accept, with some degree of confidence, the conclusions made by the authors. The authors were able to better understand the factors impacting patient outcomes, reveal important gaps in the provision of care but also show a good understanding of the limitations of their research. Not only can this research provide great insight for their region of focus but their findings may be of great relevance to other similar regions facing similar to challenges in trying to deliver the best care to patients presenting with STEMI.</p>
Reviewer 2	<b>Toralben Patel</b>
Institution	Wright Center for Graduate Medical Education, Cardiology
General comments	<p>This paper is very well written by a group in Canada that has done substantial research in the field of ST Elevation Myocardial Infarction (STEMI). This study emphasizes that in addition to reducing the total ischemic time by choosing appropriate and timely reperfusion therapy in context of the available resources, broader system level initiatives are also needed to create public awareness, provide systematic approach for treatment of STEMI and improve resource allocation for adequate follow up and rehabilitation programs.</p> <p>It is a prospective cohort study conducted in 2247 patients between April 1 2010 and March 31 2013, that analyzes the difference in mortality between STEMI patients</p>

	<p>presenting to percutaneous intervention (PCI) capable and a non-PCI capable hospital. The authors did not find any significant difference in 90-day mortality rates between patients presenting to PCI vs. non-PCI capable centres. This an effort by the authors to recapitulate that the appropriate and timely use of some form of reperfusion therapy is likely more important than the choice of therapy. The authors also point out other important issues that needs to be addressed in improving outcomes of the STEMI patients presenting to regional hospitals. Such issues include creating public health awareness to avoid patient related delays, increase use of emergency medical service (EMS) for transport and enhance participation in cardiac rehabilitation and risk modification programs; and implementation of standardized approach for treatment and discharge of the STEMI patients. The data collection seems to be adequate, the data analyses are appropriate and the results are well presented.</p>
<p>Reviewer 3</p>	<p>April Manuel</p>
<p>Institution</p>	<p>Memorial University of Newfoundland, School of Nursing</p>
<p>General comments</p>	<p><b>Thank you for this opportunity to review the manuscript entitled “Providing Optimal Care for Patients with ST-segment Elevations Myocardial Infarction Across a Large Region: Issues Beyond timelines of Reperfusion”.</b> This is a relevant topic area, informs practice, and holds implications for further research in the field. In what follows I provide a brief synopsis of the main critiques of the article, keeping in alignment with the expectations of the CMAJ.</p> <p>I suggest that the title be rephrased to be more reflective of the content. The title should include the study type as per author submission guidelines for CMAJ. The abstract is presented clearly so that the main findings of the research are evident. I have noticed throughout the article starting at methods section of the abstract that all abbreviations are not consistently spelled out first. (e.g., PCI, ASA etc). Under <b>interpretation the wording should be “the type of reperfusion provided”</b></p> <p>The introduction provides a good overview into the topic under investigation however, the context of the current study is limited. Given that geographics is a primary factor influencing access to therapy some background to geographical plant of the existing study is needed earlier in the paper. Commas are missing after emergency medicine (paragraph one) and fibrinolysis, or not reperfusion therapy in paragraph two. Throughout the document I have noted that commas are missing when using a sequence of three items separated by <b>“and.”</b></p> <p><b>The objective(s) of the study are stated however the phrase “describe the experiences”</b> is not in alignment with the methodology (this should also be removed from the abstract as implies mixed methods). Given that the authors used standardized <b>questionnaires I would assume that they did not capture participants’ experiences but</b> health care outcomes. The literature incorporated is limited (and older); it should include other relevant/newer studies such as the article by Patel et al . (2010) Access to primary percutaneous coronary intervention for ST-segment elevation myocardial infarction in Canada: a geographic analysis . I do note that you incorporate more in your discussion but still a bit older.</p> <p>The methods section is presented using a narrative style. Under Regional STEMI Program the authors provide an overview of the region which should be included as background under the introduction or condensed into a section under setting in the methods section. I would condense this section and focus on the actual methods setting, sample, data analysis and statistical analysis. For example, is the second paragraph under the Methods needed?</p> <p>Under data collection the authors need to clearly separate out sample inclusion criteria and data collection. Rationale for the time frame of 90 days is not clear. Also, is this 90 days post incident ? You refer to a telephone call to determine health status however it is not clear as to if the health status is the same as health outcomes. if so use same language. Did you ask the participants in the telephone about system related outcomes <b>as well. I would consider moving up the sentence starting with “Health outcomes .....to fibrinolysis &lt; 30 min”, to follow the sentence that starts with “Chart reviews were used ...”</b> This would make the paragraph flow in a more logical manner. Ethics approval addressed.</p>

	<p><b>Statistical analysis methods appropriate for study.</b> The sentence " Patients presenting by EMS and brought directly to the catheterization laboratories were included in the PCI center group" <b>needsto the moved to the discussion on sample.</b> I assume univariate logical regression was used to determine which variables were associated with mortality at 90 days post incident? I find the description of the statistical analysis somewhat confusing and wonder if other readers will find it easy to follow and understand. Further clarification as to the rationale for selection of statistical methods chosen would help her (e.g Bootstrap re-sampling). A p value of &lt;0.15 being considered significant is weak.</p> <p>In the results section there is an overview of the sample which should be moved to a <b>section title "Sample". Table one reports no significant difference between PCI and non-PCI outcomes</b> this should be the focus of this section . Under outcomes the authors introduce odds ratio and Hosmer and Lemeshow test which should be introduced under section statistical analysis. As well, the second last sentence wherein the authors reference a history of diabetes in 40% of sample is not clear; seems like an ad lib statement; while significant it is not addressed. Under Risk Factor Modification post <b>STEMI the sentence "Approximately 85% of patients reported a history of at least 1 risk factor for coronary disease "is a repetitive statement from page 7.</b></p> <p>While the key finding of the study is reinforced in the first paragraph the first sentence <b>in the discussion is unclear. The same is also true for the line 44 starting with "We infer.....safe care". Again, in this section the authors refer to the experiences</b> of the participants however, how this information is captured and analyzed remains unknown.</p> <p>In the discussion the authors identify five areas of concern that should be addressed to improve optimal patient health care outcomes; being that Diabetes was noted in 40% of risk population interventions should encompass this population.; being that only 4.2% of patients included smoking cessation into their health this might be another area for concern/discussion. The findings are compared with existing literature some of the literature is a bit older.</p> <p>Limitations to the study were addressed. Main conclusions were appropriate and in line with studies objectives. Future directions for care briefly addressed. Although the authors refer to geographics as a factor limiting access to PCI no relationship was explored as to level of care and geographic location of the participants. This would be an interesting point.</p> <p>The reference list does not adhere in many places to Vancouver style of referencing (e.g. referencing of 6 or more authors, name of article not in quotations) .</p>
<p><b>Author response</b></p>	<p>Reviewer: 1</p> <p>Ahmed Kotb</p> <p>University of Ottawa, Ottawa Heart Institute</p> <p>It was a pleasure to review this paper. A great deal of research has focused on comparing the effectiveness of different strategies for reperfusion for patients with STEMI and exploring issues such as the timeliness of reperfusion. The authors of this paper go beyond what has already been studied and focus on the experiences and outcomes of all patients presenting with STEMI within a specific region, including those not receiving PPCI.</p> <p>So although PPCI, when delivered in a timely manner, is considered the evidence based standard of care, many patients do not receive PPCI due to a variety of reasons. For a regional program to improve patient outcomes, it is essential that the system approach taken ensures that the best available treatment is provided while also taking into consideration also the context under which it is delivered. The authors provide a detailed overview of the regional program in question and give a clear and thorough rationale for their research focus.</p> <p>The study design is strong and the methods used are appropriate and outlined in sufficient detail. The health outcomes and system related outcomes considered are</p>

relevant. The steps taken for statistical analysis transition nicely and demonstrate that the analysis was well thought and adequately preplanned. The results from their analyses are clearly summarized and presented. Their interpretation of their findings and description of the limitations of their research both demonstrate a great deal of thoughtfulness and thoroughness.

1. However, I was concerned about the lack of adequately addressing the degree of missingness in the variables they accounted and adjusted for. When using large databases or dealing with a large sample that is followed over a long time period, certain variables are reported or collected better than others. It would be of interest to know whether or not data missingness was an issue and if so, how it was dealt with.

**The degree of "missingness" of data is described in the revised manuscript/ See points 6, 9 , and 11 of the editor's comments, above.**

2. Another important issue is that the authors have not provided a completed STROBE checklist along with their paper.

The manuscript has been revised to conform to the STROBE recommendations on reporting. A copy of the STROBE checklist has been submitted with the revised manuscript. Any discrepancies have been noted on the checklist.

Overall, the paper is very well written, its research methodology is strong and its clinical importance is evident. The thoughtfulness and time taken to properly plan the methods and analyses required to correctly address this research question are apparent in the quality of the work produced and the balance struck between statistical and clinical sense with regards to how the research was conducted.

This lends itself well to the ability of readers to accept, with some degree of confidence, the conclusions made by the authors. The authors were able to better understand the factors impacting patient outcomes, reveal important gaps in the provision of care but also show a good understanding of the limitations of their research. Not only can this research provide great insight for their region of focus but their findings may be of great relevance to other similar regions facing similar to challenges in trying to deliver the best care to patients presenting with STEMI.

The authors thank Dr Kotb for reviewing the manuscript and providing feedback on how to improve the reporting of the presented data.

Reviewer: 2

Toralben Patel

Wright Center for Graduate Medical Education, Cardiology

Comments to the Author

This paper is very well written by a group in Canada that has done substantial research in the field of ST Elevation Myocardial Infarction (STEMI). This study emphasizes that in addition to reducing the total ischemic time by choosing appropriate and timely reperfusion therapy in context of the available resources, broader system level initiatives are also needed to create public awareness, provide systematic approach for treatment of STEMI and improve resource allocation for adequate follow up and rehabilitation programs.

It is a prospective cohort study conducted in 2247 patients between April 1 2010 and March 31 2013, that analyzes the difference in mortality between STEMI patients presenting to percutaneous intervention (PCI) capable and a non-PCI capable hospital. The authors did not find any significant difference in 90-day mortality rates between patients presenting to PCI vs. non-PCI capable centres. This an effort by the authors to recapitulate that the appropriate and timely use of some form of reperfusion therapy is likely more important than the choice of therapy. The authors also point out other important issues that needs to be addressed in improving outcomes of the STEMI patients presenting to regional hospitals. Such issues include creating public health awareness to avoid patient related delays, increase use of emergency medical service (EMS) for transport and enhance participation in cardiac rehabilitation and risk modification programs; and implementation of standardized approach for treatment and discharge of the STEMI patients.

The data collection seems to be adequate, the data analyses are appropriate and the results are well presented.

The authors thank Dr Patel for reviewing the manuscript.

Reviewer: 3  
April Manuel

Memorial University of Newfoundland School of Nursing

Thank you for this opportunity to review the manuscript entitled **"Providing Optimal Care for Patients with ST-segment Elevations Myocardial Infarction Across a Large Region: Issues Beyond timelines of Reperfusion"**. This is a relevant topic area, informs practice, and holds implications for further research in the field. In what follows I provide a brief synopsis of the main critiques of the article, keeping in alignment with the expectations of the CMAJ.

1a. I suggest that the title be rephrased to be more reflective of the content. The title should include the study type as per author submission guidelines for CMAJ. The abstract is presented clearly so that the main findings of the research are evident.

The authors have changed the title as per the reviewer's suggestion. The revised title is as follows:

**"Providing Optimal Regional Care for ST-segment Elevation Myocardial Infarction: Results from a Prospective Cohort Study of Patients in a Large Provincial Health Region"**

1b. I have noticed throughout the article starting at methods section of the abstract that all abbreviations are not consistently spelled out first. (e.g., PCI, ASA etc). Under interpretation the wording should be **"the type of reperfusion provided"**

The manuscript has been revised as per the reviewer's suggestions. We have spelled out all abbreviations in the manuscript and tables, and have provided acronyms on first mention for those that appear regularly throughout the manuscript.

The authors have also changed the interpretation section to **"the type of reperfusion provided"**, as per the reviewer's suggestion.

2a. The introduction provides a good overview into the topic under investigation however, the context of the current study is limited. Given that geographics is a primary factor influencing access to therapy some background to geographical plant of the existing study is needed earlier in the paper.

The revised manuscript includes mention of the Patel et al. paper (2010) that discusses geographic issues regarding STEMI care resource allocation (as per the reviewer's suggestion, below). However, we have not added greater detail regarding this issue to the introduction in an effort to keep the paper concise.

2b. Commas are missing after emergency medicine (paragraph one) and fibrinolysis, or not reperfusion therapy in paragraph two. Throughout the document I have noted that **commas are missing when using a sequence of three items separated by "and."**

We thank the reviewer for bringing this to our attention. We have carefully reviewed the manuscript to ensure such grammar errors are corrected.

**3a. The objective(s) of the study are stated however the phrase "describe the experiences" is not in alignment with the methodology (this should also be removed from the abstract as implies mixed methods).** Given that the authors used standardized questionnaires I would assume that they did not capture participants' experiences but health care outcomes.

The authors appreciate that "experiences" might denote something different than what was examined in the study. We believe that "clinical management" might better reflect what was examined. The manuscript has been revised to reflect this change.

3b. The literature incorporated is limited (and older); it should include other relevant/newer studies such as the article by Patel et al. (2010) Access to primary percutaneous coronary intervention for ST-segment elevation myocardial infarction in

Canada: a geographic analysis . I do note that you incorporate more in your discussion but still a bit older.

**The author's thank the reviewer for the suggestion regarding the Patel et al. paper.** This has been included in the revised manuscript.

4. The methods section is presented using a narrative style. Under Regional STEMI Program the authors provide an overview of the region which should be included as background under the introduction or condensed into a section under setting in the methods section. I would condense this section and focus on the actual methods setting, sample, data analysis and statistical analysis. For example, is the second paragraph under the Methods needed?

[Editor's note: a brief description of the site and program is appropriate as context for readers.]

The manuscript has been revised to make this section more concise. We have removed this section from the methods. It now appears as part of the introduction.

5. Under data collection the authors need to clearly separate out sample inclusion criteria and data collection. Rationale for the time frame of 90 days is not clear. Also, is this 90 days post incident?

In our past experience 30 days was too short to fully document some post discharge activities. For example, waitlist for cardiac rehabilitation in our region are >6 weeks, and thus, attendance would not be fully captured for some patients by 30 days. 90 days is commonly used as an important end point in large clinical trials for STEMI (e.g. Assent 4 –Lancet 2006; APEX-AMI, 2012).

6. You refer to a telephone call to determine health status however it is not clear as to if the health status is the same as health outcomes, if so use same language.

**The authors agree that "health status" may be too broad. We have changed the mention of "health status" to "health outcomes", so as to better reflect what was measured in the study, and to be consistent throughout the report.**

7. Did you ask the participants in the telephone about system related outcomes as well.

System related outcomes were related to experiences in hospital or prior to arrival for care for first MI event, and thus, were captured prior to discharge. Information on system outcomes was not required at the time of follow-up, and thus, it was not included as part of the follow-up.

**8. I would consider moving up the sentence starting with "Health outcomes .....to fibrinolysis < 30 min", to follow the sentence that starts with "Chart reviews were used ...". This would make the paragraph flow in a more logical manner.** Ethics approval addressed.

The manuscript has been revised to reflect the change suggested by the reviewer.

**Ethics approval for the project was obtained from each participating hospital's** institutional review board. We have noted this in the methods section.

Statistical analysis methods appropriate for study.

**9. The sentence " Patients presenting by EMS and brought directly to the catheterization laboratories were included in the PCI center group" needsto the moved to the discussion on sample.**

A more explicit definition of the patient sample is included in the revised methods section. We have moved the above-mentioned statement to that section, as per the reviewer's suggestion.

10. I assume univariate logical regression was used to determine which variables were associated with morality at 90 days post incident? I find the description of the statistical analysis somewhat confusing and wonder if other readers willfind it easy to follow and understand. Further clarification as to the rationale for selection of statistical methods chosen would help her (e.g Bootstrap re-sampling).

Follow-up data was measured at 90 days post the initial MI. We have noted this in the revised manuscript. We have also done our best to revise the manuscript to better describe the logistic regression modeling methods.

11. A p value of <0.15 being considered significant is weak.

A p-value of 0.05 was considered significant in the presented analysis. The author's note the typo regarding the 0.15 in reference to the Wald Score (which should be 0.1). However, in that case, we are referring to the threshold for including variables in the multivariable model (our threshold for inclusion was set at 0.1 based on univariate analysis, as per convention). We maintained a p-value 0.05 for all variables when drawing conclusions regarding the significance of a variable in predicting mortality based on the final model. We have revised the manuscript to correct the error pointed out by the reviewer.

12. In the results section there is an overview of the sample which should be moved to a section title "Sample". (the CMAJ editors found this point to be of less importance)

The manuscript includes information regarding the number of patients presenting with STEMI during the study period, and the number of patients excluded from analysis due to death prior to presentation to hospital. The authors have included this information in the results section rather than the methods section, as per convention when reporting results from clinical studies (similar to those reported in CMAJ Open). We have ensured that all other sample information is included in the methods section.

13. Table one reports no significant difference between PCI and non-PCI outcomes this should be the focus of this section.

While we agree with the reviewer as to the importance of this observation, this information is not included in the text so as to avoid repeating information that appears in the tables; respecting the limitations on paper length the authors felt it important to avoid repetition where possible.

14. Under outcomes the authors introduce odds ratio and Hosmer and Lemeshow test which should be introduced under section statistical analysis.

We have moved mention of the Hosmer-Lemeshow test and the c-statistic into the analysis section as per the reviewer's suggestion. The results of these tests are presented with Table 4.

15. As well, the second last sentence wherein the authors reference a history of diabetes in 40% of sample is not clear; seems like an ad lib statement; while significant it is not addressed.

Here the manuscript is referring to results of the bootstrap model, rather than the rate of diabetes in the population. That is, when applying 1000 simulations of the model, diabetes was a significant predictor in only 40% of the simulation samples. The manuscript has been revised to clarify this point, as follows:

**"The bootstrap analysis indicated that optimal time to treatment, symptom onset to ED arrival >6 hours, and history of diabetes were significant in <50% of the simulation samples."**

16. Under Risk Factor Modification post STEMI the sentence "Approximately 85% of patients reported a history of at least 1 risk factor for coronary disease" is a repetitive statement from page 7.

The manuscript has been revised in order to minimize repetition, as per the reviewer's suggestion. We have revised the statement in the "Risk Factor" section to the following:

**"While the vast majority of patients presented with at least 1 risk factor for coronary disease, the baseline use of medications for prevention of MI or risk factor modification prior to presentation was low."**

17. While the key finding of the study is reinforced in the first paragraph the first sentence in the discussion is unclear. The same is also true for the line 44 starting with "We infer.....safe care". Again, in this section the authors refer to the experiences of

the participants however, how this information is captured and analyzed remains unknown.

**We have revised the first two sentences of the first paragraph in the "Interpretation" (Main Findings) in order to clarify their meaning, as follows:**

**"In this large regional program there were variations in reperfusion management of STEMI patients that reflect local capabilities. However, median time to reperfusion met evidence-based benchmarks, and there was no difference in 90-day mortality rates between patients presenting to PCI vs. non-PCI capable centres."**

18. In the discussion the authors identify five areas of concern that should be addressed to improve optimal patient health care outcomes; being that Diabetes was noted in 40% of risk population interventions should encompass this population.; being that only 4.2% of patients included smoking cessation into their health this might be another area for concern/discussion. The findings are compared with existing literature some of the literature is a bit older.

Diabetes was only present in approximately 20% of the population, consistent with other cardiac disease populations. The 40% refers to the bootstrapping method to assess the regression model. We have **clarified this point (see reviewer's point 15, above).**

The authors agree that smoking cessation is a significant area of concern. Fortunately, the majority of patients reported quitting at 90 days post STEMI. The need to improve participation in smoking cessation and other risk modification programs is mentioned in the interpretation section:

**"3) participation in cardiac rehabilitation and risk modification programs was suboptimal despite a formalized discharge practice and availability of a bridging clinic/phone call at 7 days post-discharge for all patients at the PCI centre."**

19. Limitations to the study were addressed. Main conclusions were appropriate and in line with studies objectives. Future directions for care briefly addressed. Although the authors refer to geographics as a factor limiting access to PCI no relationship was explored as to level of care and geographic location of the participants. This would be an interesting point.

We agree with the reviewers comment. However, we do not collect postal codes for this analysis, and thus, could not perform a detailed analysis on this issue. Fortunately, we do have plans to explore this issue in a subsequent research program.

20. The reference list does not adhere in many places to Vancouver style of referencing (e.g. referencing of 6 or more authors, name of article not in quotations)

**The reference section has been revised, as per the Journal's preferred format.**