

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Effect of National Implementation of Utstein Recommendation from the Global Resuscitation Alliance on Ten Steps to improve Outcomes from Out-of-Hospital Cardiac Arrest: A Ten-Year Observational Study in Korea
AUTHORS	Kim, Young Taek; Shin, Sang Do; Hong, Sung Ok; Ahn, Ki Ok; Ro, Young Sun; Song, Kyoung Jun; Hong, Ki Jeong

VERSION 1 - REVIEW

REVIEWER	Freddy Lippert Emergency Medical Services Copenhagen, Denmark Member of the Global Resuscitation Alliance and chaired the Utstein meeting in 2015
REVIEW RETURNED	15-Apr-2017

GENERAL COMMENTS	<p>Title: Effect of National Implementation of Utstein Ten-step Cardiopulmonary Resuscitation Programs on Outcomes of Out-of-Hospital Cardiac Arrest: A Ten-Year Observational Study</p> <p>Summary of manuscript This study describes outcome of an out-of-hospital cardiac arrest population of 128,888 cases in South Korea from 2006 to 2015. ROSC, survival to discharge and good neurological all increased considerably. The authors use the 10 steps to improve survival strategy from the new Global Resuscitation Alliance and describes initiatives that have been implemented nationally and find a statistical association between improved outcome and implementation of these initiatives.</p> <p>General comments: This is a new and large national study of OHCA showing significantly improved outcome within a decade. The study also relate the improved outcome to various initiatives launched nationally in South Korea and use the newly introduced recommendations from an Utstein meeting in 2015 to assess the impact of introducing the strategy of the ten steps to improve outcome. It is a descriptive study comparing outcome in periods before and after implementation, however, these are national data, a very large population and also one of few national publications showing nearly a doubling in outcome. The study is original as it is the first study to related outcome to the commended ten steps from the Global Resuscitation Alliance and Resuscitation Academy. The effect of implementing the ten steps has never been investigated in one major study. The recommendations are based upon experts' opinions on best practices. Therefor this study is interesting, though</p>
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it is not a randomised controlled study.

Comments

1. The title is: Effect of National Implementation of Utstein Ten-step Cardiopulmonary Resuscitation Programs on Outcomes of Out-of-Hospital Cardiac Arrest: A Ten-Year Observational Study

The title refers to an Utstein meeting in 2015. The purpose of this meeting was to improve survival from Out-of-Hospital Cardiac Arrest and it came out with commended best practises including the so-called Ten Steps to improve cardiac arrest survival. Furthermore, this paper is now referred to as the Global Resuscitation Alliance recommendations on Ten Steps to improve Outcome from Out-of-Hospital Cardiac Arrest.

Therefor is seems more relevant to use the following title: Effect of National Implementation of Utstein Recommendation from the Global Resuscitation Alliance on Ten Steps to improve Outcomes from Out-of-Hospital Cardiac Arrest: A Ten-Year Observational Study

This will lead to similar changes throughout the manuscript and a short additional description of the Global Resuscitation Alliance.

2. The publication relates outcome to the implementation of some of the ten steps. Some of these steps can be fully or partially implemented and until now there are defined no common tool for assessing the individual steps. This is mentioned in the strengths and limitation. I would like the authors to elaborate on the lack of common assessment tool and a need for that for future benchmarking with this study.

3. Please comment on the increased number of cardiac arrest in the study period and the potential effect it might have on the interpretations of the results. Please estimate the incidence of CA per 100.000 population and the temporal trends

4. Please comment on the figure 3 showing a higher survival rated for discharge than prehospital ROSC.

Page 3

5. Line 8: "public CPR programs". The right wording is probably "community CPR programs"

6. Line 12 it says: However, it is unclear whether UTIS programs are associated with better outcomes or not. The reason for this to be unclear is that it has never been investigated. I suggest you use the term: However, it has not been documented whether UTIS....

7. Line 19: "excluding patients collapsed in ambulance..". The right term is probably cardiac arrest witnessed by ambulance personnel" as this includes cases with CA at scene or in the ambulance. Please note consistency throughout the manuscript.

8. Line 23: The phrase telephone CPR is used. A better term is Telephone assisted CPR or Dispatcher assisted CPR as recommended by the European Resuscitation Council.

	<p>Page 4</p> <p>9. Line 35: "Emergency medical services with low service level were different from North America or</p> <p>10. European countries where advanced life support are given to OHCA at the field. Therefore the</p> <p>11. generalization should be cautious." I agree, however, there are huge variations of level of care in both Europe and North America. I therefor suggest that you rephrase these sentences.</p> <p>12. See also page 14, line 6-10</p> <p>Page 5</p> <p>13. Line 30. The link does not work. I suggest you use: www.resuscitationacademy.org as the main site</p> <p>Page 6</p> <p>14. The two links (line 22 and 26) end up with a website in Korean language. Please provide English sites if possible.</p> <p>Page 9</p> <p>15. Line 4: Misspelling in "dispatcher assistance".</p> <p>16. Page 11. Discussion Please start the discussion-paragraph by summarizing the finding.</p> <p>Page 14,</p> <p>17. line 13 misspelling in headline Conclusion.</p> <p>18. Line 17-23. I would prefer a more precise conclusion so that it can be read and understood without reading the whole paper.</p> <p>19. References. I suggest that you include the national study by Wissenberg et al from JAMA 2013 (http://jamanetwork.com/journals/jama/fullarticle/1745678) This study used a similar methodology and found a doubling in survival from OHCA and related the improvement to various national initiatives. However, they did not do it as detailed as this publication and did not relate the changes to the ten steps that were not recommend until 2015.</p>
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REVIEWER	Yoshikazu Goto Kanazawa University Hospital, Department of Emergency and Critical Care, Japan
REVIEW RETURNED	18-Apr-2017

GENERAL COMMENTS	<p>Thank you for the opportunity to review this manuscript, which reports on a study to show that national implementation of the Utstein ten-step implementation strategy programs was associated with better out-of-hospital cardiac arrest (OHCA) outcomes in Korea. This well written before- and after-intervention study was based on patients from the Korean registry. However, several issues have to be addressed by the authors.</p> <p>Major issue:</p> <p>1. As mentioned in the discussion, based on the Utstein criteria, the subjects of study should be limited to patients with witnessed, presumed cardiac etiology, and initial shockable rhythm after OHCA to evaluate outcomes trends after OHCA by year.</p>
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	<p>2. Many confounders would influence the outcomes. Particularly, the change of CPR guidelines is crucial. Therefore, I suggest that the CPR guidelines by year should be put into an analyzed model (multivariable logistic regression model). Moreover, in-hospital medication should be also considered to establish an analyzed model.</p> <p>Minor issue:</p> <ol style="list-style-type: none"> 1. Precise description of background concerning resuscitation techniques by EMS providers should be stated: e.g., epinephrine administration, rule of termination at the field, etc. 2. Statistics: A significant level should be mentioned in the texts. Which trend test did the authors applied; Cochran-Armitage test or others? Description of software are required. <p>3. Results:</p> <ol style="list-style-type: none"> 1) Page 11, line10; 'p for trend >0.001' may be wrong. 2) Page 11, line 10 to line 13; In the sentence 'proportion of women and elderly patients...' 'elderly patients' may be only patients aged >80 years. The words 'as well as shorter response time interval (4 min)' may be correctively 'as well as shorter response time interval (<4 min).' 3) Page, line 18; Last phrase 'and were correlated with better outcomes' should be deleted, because no results of relationship between variables and outcomes were shown in the Table 3. 4) Page 13, line 20; 'wase' may be 'was,' simply typographic error.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Freddy Lippert

Institution and Country: Emergency Medical Services Copenhagen, Denmark

Please state any competing interests or state 'None declared': Member of the Global Resuscitation Alliance and chaired the Utstein meeting in 2015

Please leave your comments for the authors below

Title: Effect of National Implementation of Utstein Ten-step Cardiopulmonary Resuscitation Programs on Outcomes of Out-of-Hospital Cardiac Arrest: A Ten-Year Observational Study

Summary of manuscript

This study describes outcome of an out-of-hospital cardiac arrest population of 128,888 cases in South Korea from 2006 to 2015. ROSC, survival to discharge and good neurological all increased considerably. The authors use the 10 steps to improve survival strategy from the new Global Resuscitation Alliance and describes initiatives that have been implemented nationally and find a statistical association between improved outcome and implementation of these initiatives.

General comments:

This is a new and large national study of OHCA showing significantly improved outcome within a decade. The study also relates the improved outcome to various initiatives launched nationally in South Korea and use the newly introduced recommendations from an Utstein meeting in 2015 to assess the impact of introducing the strategy of the ten steps to improve outcome.

It is a descriptive study comparing outcome in periods before and after implementation, however, these are national data, a very large population and also one of few national publications showing nearly a doubling in outcome. The study is original as it is the first study to related outcome to the commended ten steps from the Global Resuscitation Alliance and Resuscitation Academy. The effect of implementing the ten steps has never been investigated in one major study. The recommendations

are based upon experts' opinions on best practices. Therefore this study is interesting, though it is not a randomized controlled study.

Comments

1. The title is: Effect of National Implementation of Utstein Ten-step Cardiopulmonary Resuscitation Programs on Outcomes of Out-of-Hospital Cardiac Arrest: A Ten-Year Observational Study

The title refers to an Utstein meeting in 2015. The purpose of this meeting was to improve survival from Out-of-Hospital Cardiac Arrest and it came out with commended best practises including the so-called Ten Steps to improve cardiac arrest survival. Furthermore, this paper is now referred to as the Global Resuscitation Alliance recommendations on Ten Steps to improve Outcome from Out-of-Hospital Cardiac Arrest.

Therefore it seems more relevant to use the following title: Effect of National Implementation of Utstein Recommendation from the Global Resuscitation Alliance on Ten Steps to improve Outcomes from Out-of-Hospital Cardiac Arrest: A Ten-Year Observational Study

This will lead to similar changes throughout the manuscript and a short additional description of the Global Resuscitation Alliance.

(Answer)

Yes. We changed the title and added a bit information Global Resuscitation Alliance as follows

(Title)

Effect of National Implementation of Utstein Recommendation from the Global Resuscitation Alliance on Ten Steps to improve Outcomes from Out-of-Hospital Cardiac Arrest: A Ten-Year Observational Study in Korea

(Background)

The Utstein Implementation Meeting was held in 2015 in Stavanger, Norway to discuss ways to implement scientific recommendations at the community level. From this meeting, the ten programs and ten actions for improving outcomes after OHCA were agreed as core public health CPR programs, The Utstein Ten-step Implementation Strategy (UTIS). The UTIS recommended the following steps derived from expert consensus: 1) Cardiac arrest registry, 2) Telephone CPR, 3) High-performance CPR, 4) Rapid dispatch, 5) Measurement of professional resuscitation, 6) Automatic external defibrillator (AED) program for first responders, 7) Smart technologies for CPR and AED use, 8) Mandatory training for CPR and AED, 9) Accountability, and 10) Culture of excellence. The UTIS was agreed and accepted by the Global Resuscitation Alliance, a new international collaborating organizations for facilitating and implementing the UTIS to the communities, in the following meeting during the EMS 2016 in Copenhagen.

2. The publication relates outcome to the implementation of some of the ten steps. Some of these steps can be fully or partially implemented and until now there are defined no common tool for assessing the individual steps. This is mentioned in the strengths and limitation. I would like the authors to elaborate on the lack of common assessment tool and a need for that for future benchmarking with this study.

(Answer)

Thanks for comments. We added the limitation in the Strength and limitation as follows.

(Strength and limitation)

The degree of implementation or real change by implementation were not fully measured. This might be related with measurement bias. This study relates outcome to the implementation of some of the ten steps. Some of these steps can be fully or partially implemented and until now there are defined no common tool for assessing the individual steps.

3. Please comment on the increased number of cardiac arrest in the study period and the potential effect it might have on the interpretations of the results. Please estimate the incidence of CA per

100,000 population and the temporal trends

(Answer)

Yes. We added the crude incidence rates per 100,000 of each year in the Methods and Results section as follows.

(Methods)

We estimated the crude incidence rates (IRs) for 100,000 population of each year. The IRs were calculated from the total number of OHCA with all causes in all gender/ age group divided by the total number of population multiplying 100,000.

(Results)

The crude incidence rates per 100,000 were 18.2 in 2006 and 41.1 in 2015, respectively.

4. Please comment on the figure 3 showing a higher survival rate for discharge than prehospital ROSC.

(Answer) Thanks for the comments. We added the following sentences in the Results and Discussion.

(Results)

The prehospital ROSC was higher than survival to discharge rate in 2015.

(Discussion)

The prehospital ROSC was higher than survival to discharge rate in 2015. The survival to discharge rate was not increased than 2014, while the good neurological recovery rates and prehospital ROSC rates continuously increased. Increase in bystander CPR might contribute the continuous improvement in prehospital ROSC and good brain recovery.

Page 3

5. Line 8: "public CPR programs". The right wording is probably "community CPR programs"

(Answer) We changed it.

6. Line 12 it says: However, it is unclear whether UTIS programs are associated with better outcomes or not. The reason for this to be unclear is that it has never been investigated. I suggest you use the term: However, it has not been documented whether UTIS....

(Answer) We changed it.

7. Line 19: "excluding patients collapsed in ambulance..". The right term is probably cardiac arrest witnessed by ambulance personnel" as this includes cases with CA at scene or in the ambulance.

Please note consistency throughout the manuscript.

(Answer) We changed it.

8. Line 23: The phrase telephone CPR is used. A better term is Telephone assisted CPR or Dispatcher assisted CPR as recommended by the European Resuscitation Council.

(Answer) We changed it throughout the manuscript.

Page 4

9. Line 35: "Emergency medical services with low service level were different from North America or

10. European countries where advanced life support are given to OHCA at the field. Therefore the

11. generalization should be cautious." I agree, however, there are huge variations of level of care in both Europe and North America. I therefore suggest that you rephrase these sentences.

12. See also page 14, line 6-10

(Answer) Thanks for comments. We changed the sentences with following.

(Limitations)

The third limitation is related to the study setting. In Korea, the emergency services are intermediate, which is very different from the advanced services provided in some communities in North America or Europe. Thus, one should be cautious with respect to generalizability.

Page 5

13. Line 30. The link does not work. I suggest you use: www.resuscitationacademy.org as the main site

(Answer) Thanks for comments. We dropped out the link which was recommended by Editor-in Chief of the journal. Instead, we added more explanation on GRA meeting because relevant references were not available.

Page 6

14. The two links (line 22 and 26) end up with a website in Korean language. Please provide English sites if possible.

(Answer) Thanks for comments. We dropped out the link which was recommended by Editor-in Chief of the journal. The link was not required.

Page 9

15. Line 4: Misspelling in "dispatcher assistance".

(Answer) We changed it.

16. Page 11. Discussion Please start the discussion-paragraph by summarizing the finding.

(Answer) We changed it.

(Discussion)

The implementation of the Utstein ten-steps programs was associated with increase in prehospital ROSC, survival to discharge and good neurological recovery during 10-years observational period in Korea.

Page 14,

17. line 13 misspelling in headline Conclusion.

18. Line 17-23. I would prefer a more precise conclusion so that it can be read and understood without reading the whole paper.

(Answer) We changed it.

(Discussion)

Implementation of national OHCA registry, regular public reports, mandatory CPR training program, telephone-assisted CPR program, and medical oversight for EMS CPR performance, which are recommended by the Global Resuscitation Alliance, were significantly associated with better outcomes in the 10-years of before-and after-study in Korea.

19. References. I suggest that you include the national study by Wissenberg et al from JAMA 2013 (<http://jamanetwork.com/journals/jama/fullarticle/1745678>) This study used a similar methodology and found a doubling in survival from OHCA and related the improvement to various national initiatives. However, they did not do it as detailed as this publication and did not relate the changes to the ten steps that were not recommend until 2015.

(Answer) Thanks for the comments. We added the following discussion paragraph and added the reference.

(Discussion)

There were several reports on the association between community implementation of CPR programs and improved outcomes. One report from Denmark showed the significant improvement in outcomes by implementation of community programs (13). Analysis using resuscitation attempted OHCA between 2001 and 2010 in the nationwide Danish Cardiac Arrest Registry (n=19468 showed the significant increase in bystander CPR rate (21.1% in 2001 to 44.9% 2010) and increase in survival on hospital arrival (7.9% in 2001 to 21.8% in 2010), and finally improvement in 30-days survival (3.5% in 2001 to 10.8% in 2010) and 1-year survival (2.9% in 2001 to 10.2% in 2010) (All p-values < .001). Although the study did not analyze the association between the phase of the national initiatives or

implementation of CPR programs and outcome, the findings were very similar to those of our study.

Reviewer: 2

Reviewer Name: Yoshikazu Goto

Institution and Country: Kanazawa University Hospital, Department of Emergency and Critical Care, Japan

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

Thank you for the opportunity to review this manuscript, which reports on a study to show that national implementation of the Utstein ten-step implementation strategy programs was associated with better out-of-hospital cardiac arrest (OHCA) outcomes in Korea. This well written before- and after-intervention study was based on patients from the Korean registry. However, several issues have to be addressed by the authors.

Major issue:

1. As mentioned in the discussion, based on the Utstein criteria, the subjects of study should be limited to patients with witnessed, presumed cardiac etiology, and initial shockable rhythm after OHCA to evaluate outcomes trends after OHCA by year.

(Answer) Thanks for the comments. We did analyze not only the Utstein criteria-based OHCA (cardiac, witnessed, and shockable), but also the whole OHCA with cardiac etiology (unwitnessed and non-shockable). The CPR programs are usually targeting the whole OHCA regardless of witness or rhythm status. We added the sensitivity analysis results for the Utstein criteria patients in the Table 6. The results were similar with those of whole study population in Table 4. We added this additional analysis in the Method section, Results Section, and Discussion Section.

(Methods)

We performed the sensitivity analysis for appropriate comparison on the Utstein OHCA population who had cardiac etiology, witnessed status, and initial shockable rhythm using the same multivariable logistic regression according to study period on outcomes.

(Results)

Sensitivity analysis was performed for the Utstein OHCA population. The AORs (95% CIs) on good neurological recovery in the model with adjusted for the full confounders (Model 2) were 1.36 (1.03-1.80) for phase 1 and 5.72 (4.51-7.26) for phase 2. The AORs (95% CI) were 1.25 (1.00-1.55) (phase 1) and 3.78 (3.11-4.59) (phase 2) on survival to discharge and 1.11 (0.75-1.62) (phase 1) and 14.00 (10.35-18.93) (phase 2) on pre-hospital ROSC.

(Discussion)

From the sensitivity analysis on Utstein OHCA population whose proportion was 4.6% of original study population, we found the similar effect of Utstein ten-steps CPR programs on outcomes according to phases. The good neurological recovery was significantly improved in both phase 1 and phase 2, and survival to discharge and prehospital ROSC was significantly improved in phase 2. The results were similar to those of original OHCA population.

2. Many confounders would influence the outcomes. Particularly, the change of CPR guidelines is crucial. Therefore, I suggest that the CPR guidelines by year should be put into an analyzed model (multivariable logistic regression model). Moreover, in-hospital medication should be also considered to establish an analyzed model.

(Answer) Thanks for your comments. The 2006-2010 followed the 2005 guidelines, and 2011-2015 followed the 2010 guidelines. As reviewer commented, the implementation year of guidelines was added in the model for adjustment. We changed the following section.

(Method)

We performed a multivariate logistic regression analysis for the UTIS on the outcomes, adjusted for

potential confounders such as age, gender, urbanization level of the event location, place (private, public, unknown), event witness (witnessed, unwitnessed, unknown), primary ECG rhythm (VF/pulseless VT, PEA, and asystole), response time intervals from call to ED arrival, scene time interval (STI) from arrival to the scene and departure to ED, advanced airway management (ETI, SGA, BVM, PV), level of ED (level 1 to 4), and implemented international CPR guidelines (2005 vs. 2010) for all patients. The 2005 and 2010 guideline were implemented during 2006-2010 and 2011-2015, respectively.

(Result)

(Main analysis)

AORs (95% CIs) on good neurological recovery in model 2 were 1.82 (1.53-2.15) for phase 1 and 2.21 (1.78-2.75) for phase 2. AORs (95% CI) in model 2 were 1.79 (1.62-1.98) (phase 1) and 1.78 (1.56-2.04) (phase 2) on survival to discharge and 2.20 (1.86-2.59) (phase 1) and 3.47 (2.84-4.24) (phase 2) on pre-hospital ROSC, respectively.

(Sensitivity analysis)

AORs (95% CIs) on good neurological recovery in model 2 were 1.32 (1.00-1.75) for phase 1 and 5.76 (4.56-7.28) for phase 2. AORs (95% CI) in model 2 were 1.22 (0.98-1.51) (phase 1) and 3.79 (3.14-4.58) (phase 2) on survival to discharge and 1.09 (0.74-1.60) (phase 1) and 14.36 (10.66-19.36) (phase 2) on pre-hospital ROSC, respectively.

Minor issue:

1. Precise description of background concerning resuscitation techniques by EMS providers should be stated: e.g., epinephrine administration, rule of termination at the field, etc.

(Answer) Thanks for your comments. We added more information on EMS resuscitation technique as following.

(Methods)

The 2005 and 2010 CPR guidelines recommended by the International Liaison Committee on Resuscitation (ILCOR) were accepted by the academic societies and implemented in the CPR training for lay persons, first responders, and EMS providers in 2006 and 2011, respectively.(11, 12) The EMS CPR protocol was developed by EMS medical directors in 2011 on the basis of 2010 guidelines. The protocol allowed the EMS providers to perform chest compression and automatic defibrillation, and endotracheal intubation or supraglottic airway under direct medical control during prehospital CPR. The epinephrine or other resuscitation drugs were not permitted to infuse. The termination of resuscitation declared by emergency medical technicians was not allowed and all OHCA should be transported to the emergency department with providing CPR on ambulance transport if the patients did not achieve the prehospital return of spontaneous circulation.

2. Statistics: A significant level should be mentioned in the texts. Which trend test did the authors applied; Cochran-Armitage test or others? Description of software are required.

(Answer) Thanks for your comments. We added more information as followings.

(Methods)

Demographic findings were described as percentages (%) for categorical variables or medians (q1 and q3) and were compared using the Chi-square test or Wilcoxon rank sum test with a significance level (p value<0.05).

All trends were tested by the Cochran-Armitage test.

All statistical analyses were performed using SAS software, version 9.4 (SAS institute Inc., Cary, NC, USA).

3. Results:

1) Page 11, line10; 'p for trend >0.001' may be wrong.

(Answer) Thanks. We corrected with p<0.001.

2) Page 11, line 10 to line 13; In the sentence 'proportion of women and elderly patients...' 'elderly patients' may be only patients aged >80 years. The words 'as well as shorter response time interval (4

min)' may be correctively 'as well as shorter response time interval (<4 min).'

(Answer) Thanks. We corrected with elderly patients older than 80 years and (<4 min.)

3) Page, line 18; Last phrase 'and were correlated with better outcomes' should be deleted, because no results of relationship between variables and outcomes were shown in the Table 3.

(Answer) Thanks. We deleted the sentence.

4) Page 13, line 20; 'wase' may be 'was,' simply typographic error.

(Answer) Thanks. We deleted the sentence.

VERSION 2 – REVIEW

REVIEWER	<p>Freddy K. Lippert Emergency Medical Services Copenhagen, University of Copenhagen, Denmark</p> <p>Member of the Global Resuscitation Alliance</p>
REVIEW RETURNED	25-Jun-2017

GENERAL COMMENTS	<p>Thanks for the opportunity to review this revised version. All comments have been addressed adequately.</p> <p>As for one of my comments: "4. Please comment on the figure 3 showing a higher survival rate for discharge than prehospital ROSC. (Answer) Thanks for the comments. We added the following sentences in the Results and Discussion. (Results) The prehospital ROSC was higher than survival to discharge rate in 2015. (Discussion) The prehospital ROSC was higher than survival to discharge rate in 2015. The survival to discharge rate was not increased than 2014, while the good neurological recovery rates and prehospital ROSC rates continuously increased. Increase in bystander CPR might contribute the continuous improvement in prehospital ROSC and good brain recovery."</p> <p>My comment addressed figure 3 and the fact that prehospital ROSC rates were lower than the actual survival to discharge rates in the first year of the study. Usually the prehospital ROSC rate is higher than the final survival rates. As this is not the case in this study it probably reflects that prehospital care was more scoop and run and ROSC and survival was achieved after arrival to hospital. So the change in 2015 is probably due to increased bystander CPR AND better prehospital care. Anyhow, I agree with the changes made also in the paragraph.</p>
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REVIEWER	<p>Yoshikazu Goto Kanazawa University Hospital, Department of Emergency and Critical Care, Japan</p>
REVIEW RETURNED	21-Jun-2017

GENERAL COMMENTS

This new version of manuscript has fulfilled my previous suggestions. Thank you.