Review Article

Indonesian Journal of Cardiology
Indonesian J Cardiol 2020:41:177-198
pISSN: 0126-3773 / eISSN: 2620-4762
doi: 10.30701/ijc.1014

Modifiable Survival Factors of Out-of-Hospital Cardiac Arrest among Global Population: Systematic Review and Meta-Analysis

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Abstract

Out-of-hospital cardiac arrest (OHCA) is the most common type of cardiac arrest and causing much mortality and burden even preventive measure has been made. Therefore, we conducted study to give recommendation on OHCA approach by finding modifiable survival factors in-order to interfere them. We did systematic review of large cohort studies (n>100,000) on general population from four databases, then filtered 3,560 studies into 9 studies and appraised them using Newcastle-Ottawa scale for quality and Cochrane risk-of-bias before being synthesized. Among 486,012 subjects, we found out that age and shockable rhythm is unmodifiable but could be helped with lifestyle. Modifiable factors are grouped into two: bystander response including public location (OR=1.24; CI 95%=1.16–1.32), bystander witness (OR=1.45; CI 95%=1.36–1.56), bystander CPR (OR=1.45; CI 95%=1.36–1.56); and emergency service delivery including paramedic response <10 minutes (OR=1.55; CI 95%=1.41–1.70), ambulance physician (OR=1.52; CI 95%=1.37–1.68). Having OHCA in public means bigger chance of being resuscitated. However, resuscitation by uneducated bystander shown harmful thus public education was needed. Emergency services were considered important to arrive with competent workers, especially physicians who was trained on defibrillator usage and management regiment. Therefore, increasing public awareness, provide more ambulance and district health center facility, and training of health care workers are essential. In conclusion, management of OHCA involved multidisciplinary action throughout the nation to increase outcome of OHCA and lessen the burden. More area-specified and factor-specified studies should be conducted to improve applicability.

(Indonesian J Cardiol. 2020;41:187-198)

Keywords: cardiac arrest, healthcare, management, out-of-hospital, resuscitation

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Introdution

Cardiac arrest is phenomenon of sudden electrical distortion in heart, whether in pacemaker and/or bundles which disturb heart activity. Cardiac arrest should be differentiated from heart attack, in which there is a blockage in vascular systems which triggers electrical rhythm changes leading to cardiac arrest. Cardiac arrest is usually caused by arrhythmia, an irregular rhythm of heart which is not dangerous on a short term, however extremely dangerous if prolonged. Some causes of arrhythmia including coronary artery disease, heart attack, cardiomyopathy, valvular heart disease, congenital heart disease, and various electrical problems in heart such as Brugada's syndrome and long QT syndrome.[1] These causes are burdened by such conditions as personal and/or family history, smoking, and metabolic disorders. Cardiac arrest will reduce blood flow to brain leading to unconsciousness and brain damage if rhythm does not return to normal state. Brain damage will be followed by death as the worst complication.[2] All of these take place in matter of minutes, in which chance of survival reduce by 10% each minute patients left unattended or without any bystanders.[1]

Cardiac arrest could be caused by ischemic heart disease, which is world's leading cause of death in 2016, contributing up to 10,000,000 deaths per year.[3] It is also estimated in The United States that ischemic heart disease leads to cardiac arrest which kills more than 325,000 people yearly which are more to combination of breast cancer, lung cancer, and HIV/AIDS death toll. Cardiac arrest also causes economic burden of approximately USD 3,750 (IDR 53,000,000) per taxpayer family in The United States.[4] Indonesian fact sheets on 2018 also shown that cardiac arrest due to coronary heart disease contributed to 12.9% of national death, which is the highest and recently well distributed among all group of aged above 44 years which means every middle age and older share the risk almost equally.[5]

Out-of-hospital cardiac arrest (OHCA) is one example of cardiac arrest, involving emptiness of systemic circulation and mechanical cardiac function loss. It is estimated that 356,461 OHCA occur every year in The United States, which build up to 55% of all cardiac arrest events in which 90% of them are deadly.[4] This type of arrest is the most prone to continual brain cell death because of lack of perfusion. Various ways have been taken in order to increase survival of OHCA such as training to emergency health care workers and general populations. Even though it has positive impact on neurological outcomes, OHCA survival rate is still low as only less than 10% OHCA patient will survive.[6] Prior to latest knowledge, time for cardio-pulmonary resuscitation (CPR) holds most impact on OHCA survival. However, a successful OHCA management is based on chain of survival involving public bystanders, emergency services, and in-hospital providers.[7]

Based on current knowledge, importance, urgency, and multi-aspects of OHCA management, we decided to study modifiable survival factors prior to OHCA in-hospital survival rate in order to give recommendation on OCHA approach. This recommendation expected to give indirect impact towards reduction of OHCA's mortality and morbidity thus improving its prognosis. It is also aimed to support sustainable development goals of United Nation which targeted to reduce by one third premature mortality from non-communicable diseases such as cancer, diabetes, respiratory disease, including cardiovascular disease by 2030 using multi-disciplinary approach in the dimension of public, emergency service, and hospital providers.[8]

Methods

Search strategy

We conducted systematic review of cohort studies based on Preferred Reporting for Systematic Reviews and Meta-analyses (PRISMA) statement which focused on general population who experienced OHCA as populations, survival factors as indicator with their respective controls, and survival rate as its outcome.[9] Based on that focus, we formulated a reseach questions as stated below:.

- What factors are contributing to the survival of out-of-hospital cardiac arrest?
- Are the factors modifiable? If not, is there any precaution step that could be taken according to that factor?
- How big the factors impact towards survival of out-of-hospital cardiac arrest?

Based on those questions, we conducted a qualitative research guided by Cochrane's handbook.10 We conducted searching on 25 September 2019 in four databases: PubMed, Scopus, ProQuest, and ScienceDirect using queries which could be seen in table1.

Table 1. Search strategies on various databases.

Database	Queries	Findings
PubMed	(((((Factor[Title/Abstract]) OR Factors[Title/Abstract]))) AND ((((("Survival"[Mesh] OR "Survival Rate"[Mesh])) OR "Survival"[Title/Abstract]) OR "Survival Rate"[Title/Abstract])) AND (("Out-of-Hospital Cardiac Arrest"[Mesh]) OR "Out-of-Hospital Cardiac Arrest"[Title/Abstract])	617
Scopus	(("Factor" OR "Factors") AND ("Survival" OR "Survival Rate" OR "Survive Rate") AND ("Out-of-Hospital Cardiac Arrest" OR "OHCA"))	1,470
ProQuest	(("Factor" OR "Factors") AND ("Survival" OR "Survival Rate") AND ("Out-of-Hospital Cardiac Arrest" OR "OHCA"))	4,554
ScienceDirect	(("Factor" OR "Factors") AND ("Survival" OR "Survival Rate") AND ("Out-of-Hospital Cardiac Arrest" OR "OHCA"))	5,268

Inclusion and exclusion criteria

Search results were assessed for duplication, which further assessed, including studies which mentioned OHCA. Studies then filtered using inclusion and exclusion criteria. Inclusion criteria are: (a) cohort/follow-up/population-based studies (b) general population (c) studying factors contributing to OHCA survival. Exclusion criteria are: (a) disease-centered outcome (b) studies including in-hospital factors (c) full text in other language due to researchers' limitation to hire a translator. Holistic process of literature research could be seen in figure 1. Criteria were fitted by two reviewers independently. Any disagreements are discussed together and resolved within two authors to reach agreements.

Quality assessment

All nine studies are assessed further using Newcastle-Ottawa scale which converted to Agency of Healthcare Research Quality (AHRQ) standard into good, fair, or poor quality.[11] Quality assessment using Newcastle-Ottawa scale was done with two reviewers assessed all studies respectively, which each other are blinded on others' scoring, then discussed further after scoring was done. In addition, studies were also assessed for risk of bias using revised Cochrane risk-of-bias tool with two reviewers also blinded and results discussed after assessment.[10]

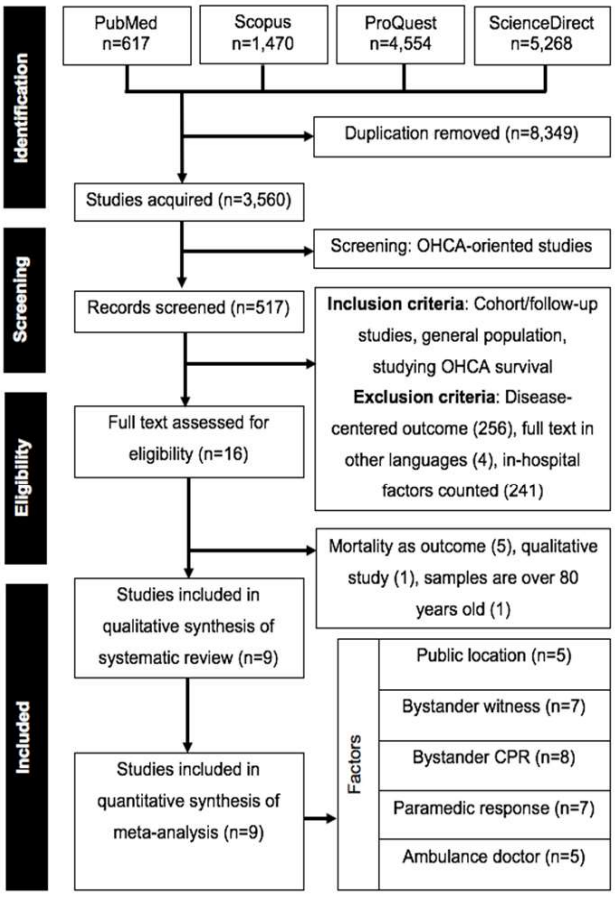


Figure 1. Search strategy and flow of literature search.

Qualitative and quantitative analysis

We used evidence-based analysis to conduct a systematic review. two reviewers assessed studies' outcome and highlight significant contributing factors to intra-hospital survival of OHCA independently, then discussed further which resulted in form of a table. Studies will be extracted by source, location, design, number of participants, mean age, gender, follow-up period, drop-out rate, and outcome. Agreed factors will be discussed by reviewers with regards to relation strength and mechanisms. Factors which are sufficient for quantitative analysis are admitted for meta-analysis. Factors were put as study code, log of odds ratio, and standard of error which will be calculated for study weight, fixed odds ratio and its 95% confidence interval (CI) which will be presented in forest plot. Studies were also assessed for statistical heterogeneity using chi-squared test which samples would be considered heterogenous if p-value is lower than 0.10 and using I-squared statistic which would be considered heterogenous over 50% level according to the Cochrane handbook.[11] Heterogeneity assessment's results will be presented in funnel plot. All qualitative statistical analyses were done using Review Manager software for iOS.

Results

Literature search

We conducted a literature search using search strategy mentioned above and found 3,560 studies after duplication removed from PubMed, Scopus, ProQuest, and ScienceDirect. We filtered studies based on inclusion and exclusion criteria and finally retrieved 16 studies which were further assessed by full-text-reading. However, five studies which presented mortality instead of survival as outcome, one study with geriatric samples, and one study with qualitative design were thus omitted and we came to a total 9 studies assessed for both qualitative and quantitative analysis.

Study characteristics

We found nine studies which consisted of three retrospective and six prospective cohort studies across three continents: Asia (n=4), Europe (n=3), and America (n=2).11–21 This study involved >100,000 samples with >1,000 samples from each study, thus considered as meta-analysis of large cohort trials (Higgins et al., 2011). This study collected data from 486,012 subjects with various characteristics which have been analyzed and proven there are no chance of these characteristics to be confounding factor as they are distributed equally when the studies started as in table 2. They are mean age which distributed among >55 years, sex which was slightly to moderately dominated by male, and level of evidence which distributed among 2a–1b. However, there are deviance in drop-out rate by Liu et al.[17] and length of follow up by Mathiesen et al.[18] but do not give negative effect to the study as those studies were classified as good studies by Newcastle-Ottawa scale. This scale also has proven studies were in good condition to be assessed, even reaching full points of excellent for all studies beside of study by Liu et al and all appraised studies were in low risks of bias according to Cochrane tools which could be seen clearly in table 3.[17] However, studies which accumulated altogether are subject to risk of publication bias which will be explained further.

Factors contributing to survival of OHCA

Based on qualitative review of two reviewers, we concluded that factors contributing to OHCA intra-hospital survival could be classified as unmodifiable and modifiable, as seen in Table 4. Unmodifiable factors were older age which contributed negatively to survival according to all nine studies and shockable rhythm which contributed positively in six studies, while sex did not have any clear relation. However, we were more concerned about modifiable factors which mainly focused on multi-disciplinary actions of emergency medicine involving health care workers, emergency team, and public bystanders. These include public location as mentioned in five studies, bystander witness in seven studies, bystander CPR in eight studies, paramedic response <10 minutes in seven studies, advanced life support (ALS) skill in one study, return of spontaneous circulation unit at emergency department in one study, physician in ambulance in five study which all correlated positively to survival in addition with drug given on transport.

Table 2. Characteristic of selected studies.

Studies, year	Studies characteristics								
	Location	Design	Final Participants	Mean age (year)	Sex (M:F)	Study period	Drop-out rate (%)	Follow-up (month)	Level of evidence*
Buick et al., 2016	Toronto	R	9,485	69.6	5:3	2006–14	7.8	1	2a
Fukuda et al., 2016	Japan	P	243,140	71.6	3:1	2006–9	8.2	1	1b
Kida et al., 2004	Nagoya	P	1,600	70.4	3:2	1994–6	7.3	1	1b
Kitamura et al., 2012	Japan	P	169,360	72.3	3:2	2005–9	2.8	1	1b
Liu et al., 2008	Milwaukee	R	1,702	>55	7:5	1995–2005	24.6	1	2a
Mathiesen et al., 2018	Stavanger	P	1,138	N/A	N/A	2006–15	N/A	12	1b
O'Keefe et al., 2010	England	P	1,161	71.0	2:1	1996–2000	7.7	1	1b
Tanaka et al., 2017	Asia	P	56,575	72.7	3:2	2009–12	14.9	1	1b
Vonvopelius et al., 2015	Southwest England	R	1,851	75.0	N/A	2011–3	7.6	1	2a

Abbreviations: R, retrospective cohort; P, prospective cohort; M, male; F, female
*According to Center for Evidence-based Medicine, Oxford University (CEBM, 2009)

Table 3. Quality assessment of selected studies.[1]

Studies, year	Selection				Comparability	Outcome			AHRQ Standard	Risk of
	1	2	3	4	1	1	2	3		
Buick et al., 2016	a(*)	a(*)	a(*)	a(*)	b(*)	a(*)	a(*)	a(*)	Good	Low
Fukuda et al., 2016	a(*)	a(*)	a(*)	a(*)	b(*)	b(*)	a(*)	a(*)	Good	Low
Kida et al., 2004	a(*)	a(*)	a(*)	a(*)	b(*)	a(*)	a(*)	a(*)	Good	Low
Kitamura et al., 2012	a(*)	a(*)	a(*)	a(*)	b(*)	b(*)	a(*)	a(*)	Good	Low
Liu et al., 2008	a(*)	a(*)	a(*)	a(*)	b(*)	b(*)	a(*)	d	Good	Low
Mathiesen et al., 2018	a(*)	a(*)	a(*)	a(*)	b(*)	b(*)	a(*)	a(*)	Good	Low
O'Keefe et al., 2010	a(*)	a(*)	a(*)	a(*)	a(*)	b(*)	a(*)	a(*)	Good	Low
Tanaka et al., 2017	a(*)	a(*)	a(*)	a(*)	b(*)	a(*)	a(*)	a(*)	Good	Low
Vonvopelius et al., 2015	a(*)	a(*)	a(*)	a(*)	b(*)	a(*)	a(*)	a(*)	Good	Low

[1]Study is considered:
- Good: 3 or 4 stars in selection domain AND 1 star in comparability domain AND 2 or 3 stars in outcome domain.
- Fair: 2 stars in selection domain AND 1 star in comparability domain AND 2 or 3 stars in outcome domain.
- Poor: 0 or 1 stars in selection domain AND 0 star in comparability domain AND 0 or 1 stars in outcome domain.
(*) Stars given for each of study aspect.
[2] According to revised Cochrane risk-of-bias tool for randomized trials (Higgins et al., 2019, p. 1–66).

Table 4. Survival factors of intra-hospital OHCA survival.

Survival Factors	Studies, year								
	Odd ratio (95% CI)								
	Buick et al., 2016	Fukuda et al., 2016	Kida et al., 2004	Kitamura et al., 2012	Liu et al., 2008	Mathiesen et al., 2018	O'Keefe et al., 2010	Tanaka et al., 2017	Vonvopelius et al., 2015
Older Age	0.86 (0.74–1.00)	0.75** (0.39–0.85)	0.42** (0.21–0.99)	0.65** (0.61–0.69)	0.56** (0.44–0.70)	0.77** (0.67–0.87)	0.97 (0.95–1.00)	0.56** (0.44–0.70)	0.96** (0.95–0.98)
Male sex	0.82** (0.73–0.92)	1.02 (0.86–1.20)	0.79 (0.41–1.49)	0.89** (0.81–0.97)	0.81** (0.66–0.99)	1.94** (1.51–2.51)			
Public location*	1.30** (1.01–1.57)		3.27** (2.30–4.58)		2.06** (1.39–3.06)	1.20** (1.10–1.30)			4.40 (0.55–36.20)
Bystand witness*	2.09** (1.85–2.35)	3.15** (2.65–3.75)		1.87** (1.77–1.97)		4.12** (3.12–5.44)	1.64 (0.52–5.19)	1.98** (1.75–2.24)	3.64** (1.71–7.50)
Bystand CPR*	1.1 (0.98–1.24)	0.89 (0.75–3.75)		1.42** (1.33–1.52)	1.32** (1.20–1.55)	1.98** (1.52–2.58)	1.32 (0.46–3.8)	1.59** (1.34–1.88)	1.58 (0.99–2.84)
Paramedic Response*1	1.09 (0.95–1.25)	1.20** (1.02–1.38)	1.78 (0.59–5.40)		1.35 (0.91– 2.02)		1.24** (1.04–1.48)	1.59** (1.34–1.88)	1.12** (1.06–1.20)
Shock-able rhythm	2.36** (2.07–2.71)	5.20** (4.26–6.33)			2.49** (1.75–3.55)	8.25** (6.21–10.95)	5.57** (1.44–21.60)	3.25** (2.58–4.10)	
ALS skill	2.25** (1.96–2.58)								
ROSC at ED	28.93** (20.52–40.77)								
Doctor in ambulance*		3.45** (2.71–4.37)	2.46** (1.18–5.15)			2.63** (1.86–3.74)	2.50** (2.12–2.88)		1.51 (0.82–2.78)
Drug given								1.48** (1.40–1.59)	

Abbreviations: CPR,cardio-pulmonary resuscitation; ALS, advanced life support; ROSC, return of spontaneous circulation; ED, emergency department

*selected for quantitative analysis by doing meta-analysis.

**statistically significant on independent basis.

1 response time of <10 minutes

Quantitative analysis of factors contributing to survival of OHCA

We found that five aspects were eligible for quantitative analysis which is meta-analysis: physician in ambulance, paramedic response, bystander witness, by stander CPR, and public location as they are modifiable survival factors and met minimum requirements for meta-analysis according to Cochrane handbook.10 Meta-analysis showed the cumulative fixed odds ratio of each study after calculated with its weight and presented the final odd ratio of analysis with all study weighted-in. According to meta-analysis, physician in ambulance, paramedic response, bystander witness, bystander CPR, and public location increase the chance of OHCA intra-hospital survival by 1.51 (1.37–1.68), 1.55 (1.41–1.70), 1.45 (1.36–1.56), 1.11 (1.05–1.18), and 1.24 (1.16–1.32) times respectively and were reliable results as no final 95% CI of odd ratio passed the line of OR=1 which could make them insignificant as could be seen in Figure 2.

Heterogeneity and sensitivity analysis

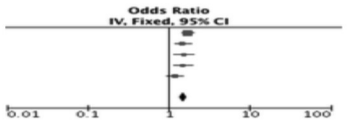
Heterogeneity of studies were assessed using chi-square with threshold of $p<0.10$ and I-statistic with threshold of $I^2>50\%$. All studies were presented in homogenous order according to these factors: physician in ambulance ($p=0.18$; $I^2=37\%$), paramedic response

1. Physician in ambulance

Study or Subgroup	log[Odds Ratio]	SE	Weight (%)	Odds Ratio IV, Fixed, 95% CI
Fukuda, 2016	0.54	0.08	40.0	1.72 (1.47, 2.01)
Kida, 2004	0.39	0.12	17.8	1.48 (1.17, 1.87)
Mathiesen, 2018	0.42	0.15	11.4	1.52 (1.13, 2.04)
O'Keefe, 2018	0.40	0.14	13.1	1.49 (1.13, 1.96)
Vonvopelius, 2015	0.18	0.12	17.8	1.20 (0.95, 1.51)
Total (95% CI)			100	1.52 (1.37, 1.68)

Heterogeneity Chi2=6.33, df=4 (P=0.18), I2=37%

Test for overall effect: Z=8.25 (P<0.00001)

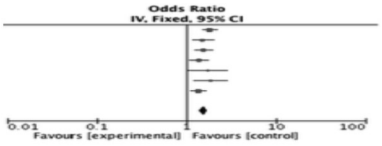


2. Paramedic response

Study or Subgroup	log[Odds Ratio]	SE	Weight (%)	Odds Ratio IV, Fixed, 95% CI
Buick, 2016	0.60	0.10	23.5	1.82 (1.50, 2.22)
Fukuda, 2016	0.42	0.14	12.0	1.52 (1.16, 2.00)
Kida, 2004	0.44	0.12	16.3	1.55 (1.23, 1.96)
Liu, 2008	0.32	0.12	16.3	1.38 (1.09, 1.74)
O'Keefe, 2018	0.55	0.26	3.5	1.73 (1.04, 2.89)
Tanaka, 2017	0.62	0.22	4.9	1.86 (1.21, 2.86)
Vonvopelius, 2015	0.31	0.10	23.5	1.36 (1.12, 1.66)
Total (95% CI)			100	1.55 (1.41, 1.70)

Heterogeneity Chi2=6.12, df=6 (P=0.41), I2=2%

Test for overall effect: Z=9.03 (P<0.00001)

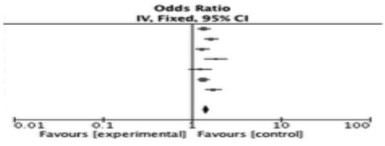


3. Bystander witness

Study or Subgroup	log[Odds Ratio]	SE	Weight (%)	Odds Ratio IV, Fixed, 95% CI
Buick, 2016	0.32	0.08	19.5	1.38 (1.18, 1.61)
Fukuda, 2016	0.50	0.09	15.4	1.65 (1.38, 1.96)
Kitamura, 2012	0.27	0.09	15.4	1.31 (1.10, 1.57)
Mathiesen, 2018	0.62	0.15	5.5	1.85 (1.38, 2.48)
O'Keefe, 2018	0.22	0.14	6.4	1.24 (0.94, 1.63)
Tanaka, 2017	0.30	0.07	25.4	1.35 (1.17, 1.54)
Vonvopelius, 2015	0.56	0.10	12.5	1.75 (1.44, 2.13)
Total (95% CI)			100	1.45 (1.46, 1.56)

Heterogeneity Chi2=12.22, df=6 (P=0.06), I2=51%

Test for overall effect: Z=10.59 (P<0.00001)

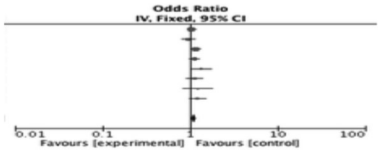


4. Bystander cardiopulmonary resuscitation

Study or Subgroup	log[Odds Ratio]	SE	Weight (%)	Odds Ratio IV, Fixed, 95% CI
Buick, 2016	0.04	0.06	24.7	1.04 (0.93, 1.17)
Fukuda, 2016	-0.05	0.09	11.0	0.95 (0.80, 1.13)
Kitamura, 2012	0.15	0.06	24.7	1.16 (1.04, 1.31)
Liu, 2008	0.12	0.07	18.2	1.13 (0.98, 1.29)
Mathiesen, 2018	0.30	0.14	4.5	1.35 (1.02, 1.77)
O'Keefe, 2018	0.12	0.11	7.4	1.13 (0.91, 1.40)
Tanaka, 2017	0.20	0.20	2.2	1.22 (0.83, 1.81)
Vonvopelius, 2015	0.20	0.11	7.4	1.22 (0.98, 1.51)
Total (95% CI)			100	1.11 (1.05, 1.18)

Heterogeneity Chi2=7.67, df=7 (P=0.36), I2=9%

Test for overall effect: Z=3.54 (P<0.0004)



5. Public location

Study or Subgroup	log[Odds Ratio]	SE	Weight (%)	Odds Ratio IV, Fixed, 95% CI
Buick, 2016	0.11	0.04	67.1	1.12 (1.04, 1.21)
Kida, 2004	0.52	0.11	8.9	1.67 (1.35, 2.08)
Liu, 2008	0.31	0.11	8.9	1.37 (1.10, 1.70)
Mathiesen, 2018	0.08	0.13	6.3	1.08 (0.84, 1.40)
Vonvopelius, 2015	0.64	0.11	8.9	1.90 (1.53, 2.36)
Total (95% CI)			100	1.24 (1.16, 1.32)

Heterogeneity Chi2=30.83, df=4 (P<0.00001), I2=87%

Test for overall effect: Z=6.47 (P<0.00001)

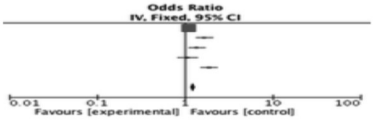


Figure 2. Forest plot presenting relation between respective factors and OHCA survival.

(p=0.41; I^2=2%), and bystander CPR (p=0.36; I^2=9%). However, aspect of public location (p<0.00001; I^2=87%) and bystander witness (p=0.06; I^2=51%) was presented heterogeneously but enough to present the results with reliable 95% CI. Variance of factors' effect was accounted for substantial heterogeneity. We do not conduct further sensitivity analyses as we considered that all studies have affected pool estimate properly. Analysis of heterogeneity could be seen in figure 3.

Publication bias

All of our meta-analysis concerning physician in ambulance, paramedic response, bystander witness, and bystander CPR were proven homogenous in the funnel plot and statistic examination, except for public location. However, Cochrane handbook suggest that heterogeneity examination using funnel plot demands at least 10 studies to present sufficient power for studies

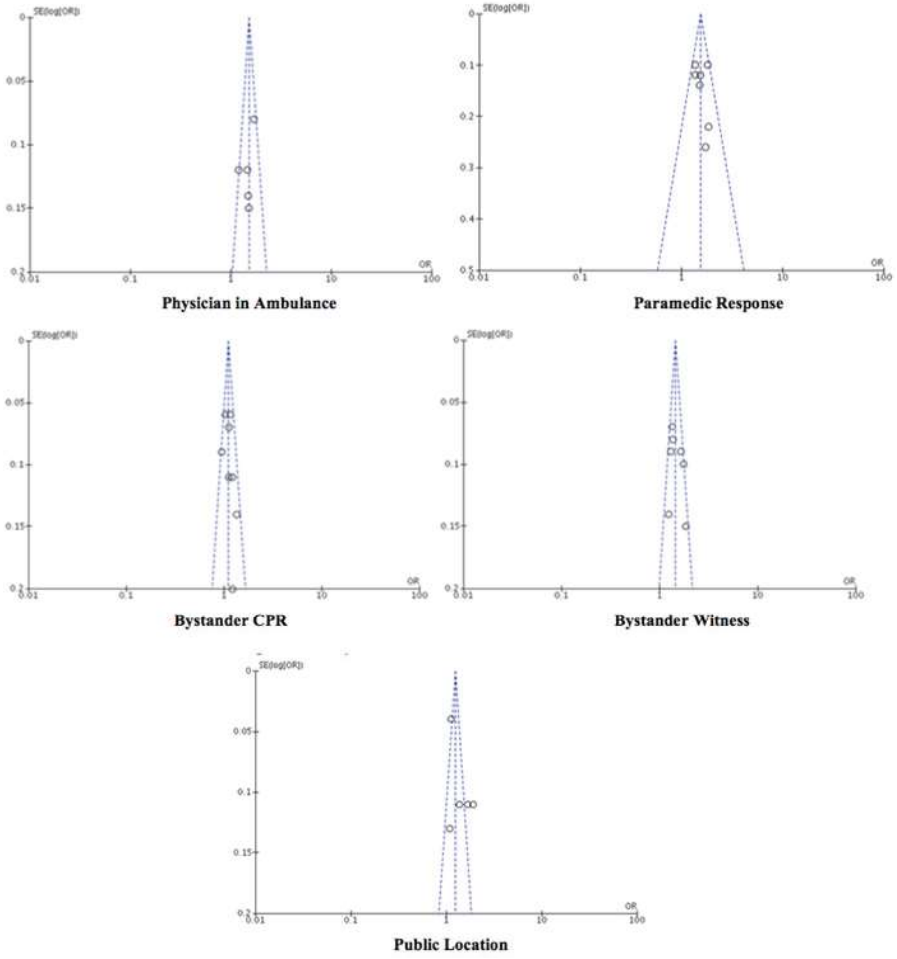


Figure 3. Funnel plot presenting heterogeneity analyses of factors calculated in meta-analysis.

heterogeneity.10 Therefore, this study is still subject to publication bias which is limited to amount of publication. Despite all limitations, this study is still currently applicable as it included all studies available at the moment, thus applicable in clinical and emergency settings.

Discussion

Unmodifiable survival factors of OHCA

Study showed that age correlated negatively with chance of surviving OHCA. This is explainable by the fact that older patients have reduction on their heart electrical activities. Sinoatrial and atrioventricular nodes are proven to be less powerful as human age, thus provide less pace-making activity.[22] Older age is also linked with increased comorbidities such as history of diabetes and renal failure which could damage nerves and vessels, history of congestive heart failure and myocardial infarct which lessened heart's capacity to overcome cardiac arrest.[23] Other comorbidities along with slow rate of physical recovery in elderly also put physicians in doubt when they consider performing CPR to seniors, in which 40% of CPR leads to recovery, but 50% of them died in hospitals.[24] Mainly, elderly also do not have normal ventricular fibrillation (VF) which is shockable and give good prognosis for CPR. Therefore, shockable rhythm was contributing positively to survival in this study.

On the other hand, there is no clear difference between sex and survival of OHCA. Men have more comorbidities such vascular damage and less heart electrical activity but are more likely to get bystander CPR than women because of ethical reason, therefore survival between gender could not be determined.[25] These factors could not be changed but should be taken as note to reduce comorbidities such as high blood glucose and metabolic status by diet and physical activity and give CPR equally both to men and women without taking age factor aside.

Modifiable survival factors of OHCA

Survival factors of OHCA are multi-disciplinary actions involving every elements of population: bystanders, emergency service, and health care workers. This study proved that bystander did increase survival of OHCA by 1.45 times (OR=1.45; 95% CI=1.36–1.56), which explained why people having OHCA in public place had a better chance of survival than those in private places (OR=1.24; 95% CI=1.16–1.32). This also confirmed by Yan et al on his meta-analysis which state that witnessed OHCA and unwitnessed OHCA have discharge survival rate of 10.5% and 4.4% respectively.[26] Public place and being seen by bystanders on the event of OHCA have two similar mechanisms: faster emergency response and faster emergency service delivery.

Faster emergency response means that OHCA patient could get faster response from bystanders, expectedly getting a CPR. CPR is the first line treatment which should be given to OHCA patient to create artificial circulation in order to re-oxygenate body and brain to prevent cell destruction and induce biochemical and electrical activity especially in the heart. It has been proven in this study that bystander CPR could increase survival chance by 1.11 times (OR=1.11; 95% CI=1.05–1.18) and 1.49 times in every unbreathing event.[22] However, sometimes CPR could be harmful for OHCA patient and give rather deadly outcome when given by uneducated bystanders which cause 13% of injuries in all CPR cases, consisting of broken sternum/ribs (9%), lung injuries (3%), and internal bleeding (3%) which could deplete chance of OHCA survival instead.[14,27,28] This fact was also supported by meta-analysis by Yan et al which stated that bystander CPR, emergency medical system CPR, and unspecific CPR have discharge survival rate of 11.3%, 10.7%, and 7.7% respectively. To sum up, public location makes better access for bystander to perform CPR. CPR is beneficial for OHCA survival if given by bystanders who are capable and well-informed about CPR itself, thus education of CPR must be given to all elements of citizens nationwide to increase OHCA survival by CPR.

This study found that emergency service delivery is an important factor determining survival of OHCA which includes paramedic response and physician presence in ambulance. Paramedic response less than 10 minutes did increase chance of OHCA survival by 1.55 times (OR=1.55; 95% CI=1.41–1.70). This is explained by the fact that ambulance comes with emergency care worker and equipment such as defibrillator which

is needed for OHCA management. Defibrillator delivers electrical current called "counter shock" which depolarizes a large amount of myocardium, nodes, and bundles to recover the heart out of dysrhythmia phase, as shown by the rebuilding of its normal sinus rhythm by the sinoatrial node for normal heart activity.29 This is why the world has set standards for response time, in which maximum 8 minutes for urgent case such OHCA and 90% of any emergency responses recorded, and maximum 19 minutes for serious but non-urgent case. This standard has been implemented in first-world countries such as The United States, United Kingdom, Japan, and Australia.30 Moreover, it is needed to increase number of emergency department and its ambulance, alongside with making emergency medical system more familiar to increase emergency response of all matters, including to OHCA which is the most common case seen among all emergencies.

Emergency services delivery also relies on workforce involved. This study showed that physician's presence in ambulance could increase risk of OHCA survival by 1.52 times (OR=1.52; CI 95%=1.37–1.68). This is explained by the fact that physician is more trained of defibrillator usage and medication regiments, thus explains why medication admission in transport is favorable for OHCA survival.20 Vasopressors and anti-arrhythmic medications are important for OHCA immediate management after CPR and defibrillation, the administration of which requires physician's knowledge of their forms, dosages, and other pharmacology traits. Therefore, the provision of standardized emergency medicine training to all physicians and health care workers is essential as the first step towards emergency service knowledge and deploy physicians and nurses in every ambulance in order to increase service and management of emergencies, including OHCA to increase its chance of survival.[1] Moreover, ambulance services must be subsidized by government or stakeholders to increase participation ability of every population elements.

Limitation and strength of study

This study is a broad study to define the overview of barriers and boundaries in OHCA management, thus open fields for other more detailed studies to be conducted and interventions done in these field of factors independently and extensively in order to increase survival and quality of life of OHCA patients. In addition, this study provided add-on from previous meta-analysis by stating more complete data on one-month survival on OHCA patients and discussing more about emergency medical system performance as OHCA's survival factor. This study also realized us that OHCA needs a multidisciplinary management involving all layers of citizens and all fields of knowledge, thus collaboration and good management skills are needed to be improved and applied.

However, this study is limited to English-language-only journals due to writers' capability and possibility of publication bias, in which no aspect collected 10 studies or more for analysis as trusted-minimum according to Cochrane's handbook. Even though there are some language limitation, we still found 8 journals with almost perfect score for NCS-OTW scale. That means the studies we used is reliable and represented.

Conclusion

Intra-hospital survival of OHCA was favored by physician's presence in ambulance, swift paramedic response, presence of bystander witness, performance of CPR by bystander, and public location by range of 1.11 to 1.55 times. Thus bystander response, emergency service delivery, and health care workers performance were considered important. Therefore, it is recommended to take multidisciplinary actions to strengthen performance of bystander, medical staff, and medical system and facility. These recommendations perhaps will give indirect effect to reduce by one third premature mortality by non-communicable diseases by 2030 as aimed by The United Nations.

Acknowledgement

This research is not funded by any institutions. Writers declared that this research has no conflict of interest. Writer would like to thank Faculty of Medicine Universitas Indonesia for the knowledge given on scientific writing.

Publication approval

All authors read and approved the final manuscript

Conflict of Interest

This paper received no specific grant from any funding agency, commercial, or not-for-profit sectors.

Funding

None.

Ethical Clearance

Not applicable.

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