Survival to Discharge Rate and Favorable Neurological Outcome Related to Gender, Duration of Resuscitation and First Document of Patients In-Hospital Cardiac Arrest: A Systematic Meta-Analysis

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Objective: To investigate the relationship between outcomes and demographic-clinical variables in in-hospital cardiac arrest (IHCA).

Methods: The Medline database was searched along with Google Scholar, Scopus, Web of Science, and Persian language database without time limitation until January 6th, 2020. The inclusion criteria included papers published in journals or presented in English and Persian congress that reported the IHCA outcomes based on the Utstein criterion. All the descriptive, cross-sectional, and cohort studies on CPR were covered based on inclusion and exclusion criteria. Primary checks covered titles and abstracts followed by a full-text check of the remaining papers from the first screening stage. Data analysis was done using comprehensive meta-analysis (CMA) software version 2.0. The finding’s heterogeneity was checked using Q and Cochran tests with heterogeneity >50% and the random-effects model was used to estimate survival and favorable neurological outcome (FNO) in the analysis. To detect the publication bias of studies, the subgroup test, meta-regression test, sensitivity analysis test, funnel plot, and Egger’s regression test were used.

Results: Survival to discharge was 19.1% (95% CI=16.8-21.7) and FNO in the survived to discharge cases was 68.1% (95% CI=55.8-78.3). Survival to discharge and FNO were notably higher in men, CPR duration <15min, and shockable dysrhythmias.

Conclusion: IHCA outcomes are poor in developing countries. The outcomes of IHCA in terms of gender were inconsistent with the result reported by other meta-analyses.

Keywords: Cardiopulmonary resuscitation; CPR; Resuscitation; Cardiac arrest; Neurological.

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Introduction

Cardiopulmonary resuscitation (CPR) is a measure to compensate the function and return vital performance of the heart and lungs and was developed in 1950 [1]. The first instruction was published in 1996 which was later revised in 2020 [2]. Although CPR is the only efficient treatment in the case of cardiac arrest as a lethal condition, the success rate of the procedure is still too low and the survival-to-discharge rate ranges from 0 to 20%. There has been no significant improvement in this rate over the past 30 years [3-5]. This can be justified by the aging population, increased prevalence of physical health problems, and longer response time in the prehospital emergency system, which is due to the growing population and traffic jams in cities [5-9].

Assessing CPR outcomes yields a valuable indicator that is used by the American Heart Association to revise CPR instructions based on the Utstein criterion and its relationship with demographical variables, patient’s background and other variables [9-11]. Two studies of Shao et al., [12] and Movahedi et al., [13] showed that gender affects survival. Other studies have emphasized shockable dysrhythmias as an effective factor in survival to discharge. According to Bergum et al., [14], 53% of cardiac arrest cases with shockable dysrhythmia have led to successful CPR and discharge. Hirlekar et al., [9] and Salari et al., [15] have reported a significant relationship between survival to discharge and shockable rhythms.

The neurological outcomes and side effects are the risk factors of a successful CPR that can be affected by prolonged CPR duration and decreased heart output which in return decreases cerebral perfusion [16]. Although there is a specific instruction about the time of CPR termination in pre-hospital cases, the new instructions available in hospitals are ambiguous and challenging [17]. The American Heart Association has given room for clinical judgment in this regard [18]. At any rate, cerebral damages are generally considered a risk factor in cardiac arrest patients. The CPR duration is an efficient factor that needs further examination; still, there is no review study on the studies in this field. Therefore, the present systematic meta-analysis is based on the question of “is there any relationship between the CPR outcomes and demographic-clinical variables (first document, gender, CPR duration) in patients with In-hospital Cardiac arrest (IHCA)”?

Materials and Methods

Study Design

This systematic review and meta-analysis was funded by Hamadan University of Medical Sciences and reported following the PRISMA and MOOSE guidelines to report the systematic reviews and meta-analysis of observational studies [19, 20]. In this study, we aim to investigate the relationship between resuscitation outcomes include survival to discharge, and favorable neurological outcome (FNO) at discharge with the first document, gender, and duration of CPR in IHCA patients. As a result, PECO in the current study is defined as P (patients): Patients with IHCA, E (exposure): Advanced in-hospital resuscitation, C (comparison): Gender / First document (shockable with non-Shockable dysrhythmias)/ Duration of resuscitation (≤15min with >15 min), As for outcomes (O in PECO): Survival to discharge or 30-day survival and FNO at discharge included Cerebral Performance Category (CPC) ≤2.

Search Strategy

The searching process was initiated by selecting keywords that included both standardized medical subject heading (MESH) and text word includes. With the aim of obtaining papers published in journals and presented in congress, Medline database along Scopus, Web of Science, and Persian language databases including SID and Magiran was searched without time limitation until January 6th, 2020. In addition, a general search was performed in Google Scholar to obtain possibly missed manuscripts. All the found materials were checked based on exclusion and inclusion criteria and irrelevant cases were removed from the study. The search strategy is presented in Appendix 1.

Selection Criteria

The inclusion criteria included papers published in journals or presented in English and Persian congress on adults (older than 13 years old), that reported the outcomes of IHCA (survival to discharge or 30 days’ survival and FNO at discharge) based on the Utstein criterion, or they have reviewed the relationship between a “first document, gender or CPR duration”, and outcomes of IHCA. Qualitative works, letters to the editor, review studies, repetitive works, studies on animals, infants, children, studies limited to an initial success rate of CPR without any results about survival to discharge, studies with less than 30 subjects, meta-analysis, structured studies, studies on out of hospital cardiac arrest (OHCA) or both (undetermined of the type of cardiac arrest), studies with overlapped study populations, studies on survived patients and without information about the population under study were excluded.

Data Collection

All the descriptive, cross-sectional, and cohort studies on CPR were covered based on inclusion and exclusion criteria. Two independent reviewers screened titles and abstracts of the gathered papers and any disagreements within the process were resolved using a third researcher’s opinion. Primary checks covered titles and abstracts followed by a full-text check of the remaining papers from the first screening stage. Data extraction was performed by
two researchers, and the final and agreed information of articles was added to a researchers-designed checklist. The checklist included information about author name, publication year, time, type, and place of study, the total number of samples, outcomes (survival to discharge and FNO included CPC≤2), and outcomes based on gender, CPR duration, and first document of patients. Table 1 lists the information extracted from the articles.

**Outcome**
The primary outcome of the present meta-analysis was an overall survival rate to discharge or 30-day survival and FNO at discharge included CPC≤2. The secondary outcome was survival rate to discharge or 30-day survival and FNO at discharge based on gender, first document rhythm, and duration of resuscitation (≤15 min, >15 min).

**Methodological Quality (Risk of Bias) Assessment**
The Critical Appraisal Skills Program (CASP) for the cross-sectional study was used to the risk of bias assessment [21]. The searched articles were checked based on CASP checklist criteria by two independent researchers, and each researcher independently assessed the articles, and any disagreements within the process were resolved using a third researcher’s opinion.

**Statistical Analysis**
Data analysis was done using CMA version 2.0. The findings’ heterogeneity was checked using Q and Cochran tests with heterogeneity >50%, the random-effects model was used to estimate survival and FNO in the analysis. We used random effect model for analysis because of the high heterogeneity (>50%) of the studies, studies’ variation in terms of population, event rate of survival to discharge and location of studies. The subgroup test (to estimate the relationship between survival and FNO and qualitative variables like gender and first document), meta-regression test (to check the relationship between survival and FNO and quantitative variables like publication year); funnel plot, and Eagger’s regression test (to check publication bias) were used. Finally, the sensitivity analysis test was used to evaluate the effect of each study on the final results of the meta-analysis. Sensitivity analysis responses to the question “Are the findings robust to the decisions made in the process of obtaining them?”, if there are some studies that effects are too different from other studies, we should be dubious about the results and recommend more studies.

**Results**

**Study Characteristics**
Our search strategy retrieved 8728 records, of which 5840 remained after duplicates were removed. The parallel exclusion of studies resulted in 326 articles eligible for detailed assessment based on title and abstract. Finally, we included 46 studies in our systematic review and meta-analysis [12, 14, 15, 22-64] (Figure 1).

**Risk of Bias Assessment**
CASP checklist was used to the risk of bias assessment [21]. This checklist has 11 items that

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**Fig. 1.** PRISMA flow diagram of search strategy and included studies.
| Row | The first author | Study time (study type) | Study place | N (total) | Survival to discharge or 30 days N (%) | FNO * N (%) | Total N | Survival based on gender N (%) | Survival based on First Document N (%) | Survival based on CPR duration N (%) |
|-----|------------------|-------------------------|-------------|----------|----------------------------------------|-------------|--------|---------------------------------|----------------------------------------|----------------------------------------|
|     |                  |                         |             |          |                                        |             |        | Female                           | Male                                   | ≤15min                                 |
| 1   | Meaney et al., [22] | 1999-2005 (Prospective) | U.S.        | 51919    | 9125 (17.57)                           | 6850 (75.07)|        | NR                               | NR                                    | NR                                     |
| 2   | Hessulf et al. [23] | 2006-2015 (Retrospective) | Swedish Register 18069 | 5113 (28.3) | NR (93)                               |              |        | NR                               | NR                                    | NR                                     |
| 3   | Johnson et al., [24] | Unknown (Prospective) | South India 1955 | 197 (10.1) | 161 (81.73)                           |              |        | 628                               | 1327                                   | 1676                                   |
| 4   | Radeschi et al., [25] | 2012-2014 (Retrospective) | Italy 1539 | 228 (14.8) | 207 (90.79)                           |              |        | 575                               | 964                                    | 1248                                   |
| 5   | Uberg et al., [26] | 1983-1984 (Retrospective) | Michigan, US. 121 | 13 (11) | NR                                    |              |        | 58                                | 63                                     | 116                                    |
| 6   | Hjalmansson et al., [27] | 2007-2015 (Retrospective) | Karolinska Stockholm 1373 | 376 (27.38) | NR                                    |              |        | 478                               | 895                                    | 897                                    |
| 7   | Andersen et al., [28] | 2017-2018 (Retrospective) | Denmark 4049 | 1124 (27.8) | NR                                    |              |        | 125 (26.15)                       | 251 (28.4)                           | 171 (58.56)                           |
| 8   | Lundin et al., [29] | 2015-2017 (Retrospective) | Swedish 6033 | 1818 (30.13) | 1660 (91.3)                           |              |        | NR                               | 2891                                   | 703                                    |
| 9   | Cicekci et al., [30] | 2013-2015 (Retrospective) | Konya, Turkey 390 | 44 (11.28) | 25 (56.82)                           |              |        | NR                               | 34 (NR)                               | 10 (NR)                               |
| 10  | Rohlin et al., [31] | 2007-2017 (Retrospective) | Swedish 1679 | 471 (29) | NR                                    |              |        | NR                               | 24978                                 | 8361                                   |
| 11  | Nadkarni et al., [32] | 2000-2004 (Retrospective) | US & Canada's H 36902 | 6485 (17.57) | 4390 (67.69)                           |              |        | NR                               | 2719 (10.88)                          | 3013 (36)                             |
| No. | Authors             | Year/Period        | Setting      | Number | Survival Rate | Follow-up | Other Details            |
|-----|---------------------|--------------------|--------------|--------|---------------|-----------|--------------------------|
| 12  | Qvick et al.,       | 2007-2017          | Karolinska University | 470(29) | NR            | 574       | 68477(24.62)             |
|     |                     | (Retrospective)    | 1639         | NR     |               | 684338    | 311423                   |
| 13  | Heller et al.,      | 1984-1991          | Australia   | 120(39) | NR            | 415       | 113(27.2)                |
|     |                     | (Retrospective)    |              | NR     |               | 38(22.48) | 169                   |
| 14  | Kung et al.,        | 2008-2011          | Taiwan      | 28(5.1) | 6(21.43)      | 544       | 224                     |
|     |                     | (Retrospective)    |              | NR     |               | 36(14.2)  | 36                     |
| 15  | Jones et al.,       | 2004-2006          | New Zealand | 113(27.2) | NR      | 415       | 6(10.7)                 |
|     |                     | (Retrospective)    |              | NR     |               | 6(10.7)   | 6(10.7)                 |
| 16  | Tok et al.,         | 2001-2002          | Turkey      | 12(11.7) | NR            | 103       | 36                      |
|     |                     | (Prospective)      |              | NR     |               | 36(14.2)  | 36(14.2)                |
| 17  | Khatib et al.,      | 1995-2015          | Afula, Israel | 93(13.24) | NR      | 702       | 303                     |
|     |                     | (Retrospective)    |              | NR     |               | 303       | 303                     |
| 18  | Kolte et al.,       | 2003-2011          | USA         | 68477(24.62) | NR      | 192       | 37(12.21)               |
|     |                     | (Retrospective)    |              | NR     |               | 37(12.21) | 37(12.21)               |
| 19  | Thomas et al.,      | 1987-1988          | U. K        | 32(16.6) | NR            | 108       | 32(16.6)                |
|     |                     | (Prospective)      |              | NR     |               | 192       | 192                     |
| 20  | Wachira et al.,     | 2013               | Kenya       | 12(11.1) | NR            | 108       | 12(11.1)                |
|     |                     | (Retrospective)    |              | NR     |               | 108       | 12(11.1)                |
| 21  | Widestedt et al.,   | 2012-2017          | Stockholm, Sweden | 191(33.27) | NR      | 574       | 234                     |
|     |                     | (Retrospective)    |              | NR     |               | 234       | 234                     |
| 22  | Wang et al.,        | 2006-2014          | Taiwan      | 215(14.1) | 110(51.16) | 1524      | 215(14.1)               |
|     |                     | (Retrospective)    |              | NR     |               | 215(14.1) | 215(14.1)               |
| 23  | Rakic et al.,       | 2003               | Croatia     | 27(22.5) | NR            | 120       | 46                      |
|     |                     | (Prospective)      |              | NR     |               | 46(20.8)  | 46(20.8)                |
| 24  | Shao et al., [12]   | 2014               | Beijing, China | 247(9.10) | NR            | 2712      | 247(9.10)               |
|     |                     | (Prospective)      |              | NR     |               | 247(9.10) | 247(9.10)               |
| Study                     | Year       | Location          | Cases | Controls | Male | Female | Total | Male | Female | Total | Male | Female | Total | Male | Female | Total | Male | Female | Total |
|--------------------------|------------|-------------------|-------|----------|------|--------|-------|------|--------|-------|------|--------|-------|------|--------|-------|------|--------|-------|
| Chua et al., [45]        | 2008-2009  | Singapore         | 49(13.88) | NR       | NR   | NR     | 290   | NR   | NR     | 32(11) | NR   | NR     | 17(27) | NR   | NR     | NR    | NR   | NR     | NR    |
| Garry et al., [46]       | 2012-2013  | USA Stony Brook Univ | 65(24.49) | NR       | NR   | NR     | 96    | NR   | NR     | 159   | NR   | NR     | NR    | NR   | NR     | NR    | NR   | NR     | NR    |
| Chong et al., [47]       | 2017-2018  | Unknown           | 55(30) | NR       | NR   | NR     | 183   | NR   | NR     | 143   | 40    | NR     | NR    | NR   | NR     | NR    | NR   | NR     | NR    |
| Saklayen et al., [48]    | 1988-1990  | Dayton Ohio      | 44(13) | NR       | NR   | NR     | 340   | NR   | NR     | 113   | 61    | NR     | NR    | NR   | NR     | NR    | NR   | NR     | NR    |
| Skrifvars et al., [49]   | 1993-1997  | Finland           | 22(12.02) | NR       | NR   | NR     | 183   | NR   | NR     | 126   | 57    | NR     | NR    | NR   | NR     | NR    | NR   | NR     | NR    |
| Yokoyama et al., [50]    | 2008-2009  | Japan             | 136(27.8) | 105(77.21) | NR   | NR     | 491   | NR   | NR     | 347   | 138   | NR     | NR    | NR   | NR     | NR    | NR   | NR     | NR    |
| Topjian et al., [51]     | 2000-2008  | Philadelphia      | 16960(1769) | 13244(78.09) | NR   | NR     | 9852  | NR   | NR     | 42213 | 53639 | NR     | NR    | NR   | NR     | NR    | NR   | NR     | NR    |
| DeVoe et al., [52]       | 2007-2013  | New York          | 86(21) | NR       | NR   | NR     | 417   | NR   | NR     | 172   | 245   | 237    | 142   | NR   | NR     | NR    | NR   | NR     | NR    |
| Herlitz et al., [53]     | 1994-1998  | Sweden            | 208(37.34) | 192(92.31) | NR   | NR     | 557   | NR   | NR     | 217   | 340   | 240    | 261   | NR   | NR     | NR    | NR   | NR     | NR    |
| Oxlsion et al., [54]     | 2007-2010  | Sweden            | 58(20.2) | NR       | NR   | NR     | 287   | NR   | NR     | 111   | 176   | 207    | 80    | NR   | NR     | NR    | NR   | NR     | NR    |
| Parikh et al., [55]      | 2012 - 2018 | New York         | 125(18.38) | NR       | NR   | NR     | 680   | NR   | NR     | 262   | 418   | NR     | NR    | NR   | NR     | NR    | NR   | NR     | NR    |
| Al-Dury et al., [56]     | 2007-2014  | Swedish Register  | 4197(28.1) | NR       | NR   | NR     | 14933 | NR   | NR     | 5767   | 9166  | NR     | NR    | NR   | NR     | NR    | NR   | NR     | NR    |
| Goldberger et al., [57]  | 2000-2008  | (NRCPR) Michigan  | 9912(15.4) | 7034(80.6) | NR   | NR     | 64339 | NR   | NR     | 1517(26.30) | 2680(29.24) | NR     | NR    | NR     | NR    | NR   | NR     | NR    | NR   | NR     | NR    |
| Study Reference          | Study Period   | Location          | Survival Rate | Other Details |
|--------------------------|----------------|-------------------|---------------|---------------|
| Israelsson et al., [58]  | 2007-2011      | Swedish           | 107(37.4)     | NR            |
| Li et al., [59]          | 2012-2016      | Fujian, China     | 68(21.25)     | NR            |
| Ravipragasam et al., [60]| 2016-2017      | South India       | 44(17.50)     | NR            |
| Keivanpazhoh et al., [61]| 2010          | Iran              | 10(13.5)      | NR            |
| Jaber et al., [62]       | Unknown        | Iran              | 10(3.3)       | NR            |
| Salari et al., [15]      | 2006          | Iran              | 18(7.2)       | NR            |
| Mohnil et al., [63]      | 2004-2006      | Germany           | 57(30.2)      | NR            |
| Bergum et al., [14]      | 2009-2013      | Norway            | 71(25)        | NR            |
| Nolan et al., [64]       | 2011-2013      | UK                | 4153(18.35)   | NR            |

*Favorable Neurological Outcome (CPC<=2); *No Reported
Table 2. Methodological quality (risk of bias) assessment (CASP Checklist)

| Author; Year       | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 |
|--------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|---------|---------|
| Meaney and et al; 2010 | Y*     | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E       |         |
| Hessulf and et al; 2017 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E       |         |
| Johnson and et al; 2014 | Y      | Y      | C      | Y      | Y      | C      | Y      | Y      | E      | G†      |         |
| Radeschi and et al; 2017 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Urberg and et al; 1987 | Y      | Y      | N†     | Y      | N      | N      | C      | Y      | N      | F‡      |         |
| Hjalmarsson and et al; 2017 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Andersen and et al; 2019 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Lundin and et al; 2019 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Cieckci and et al; 2018 | Y      | Y      | Y      | N      | Y      | C      | C      | Y      | G      |         |         |
| Rohlin and et al; 2018 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Nadkarni and et al; 2006 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Vqivck and et al; 2018 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Heller and et al; 1995 | Y      | Y      | Y      | N      | Y      | Y      | Y      | Y      | E      |         |         |
| Kung and et al; 2014 | Y      | Y      | C      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Jones and et al; 2011 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Tok and et al; 2004 | Y      | Y      | Y      | N      | Y      | N      | Y      | C      | G      |         |         |
| Kolte and et al; 2014* | Y      | Y      | Y      | C      | Y      | Y      | C      | Y      | G      |         |         |
| Thomas and et al; 1990 | Y      | Y      | Y      | N      | Y      | C      | C      | Y      | G      |         |         |
| Wachira and et al; 2015 | Y      | Y      | Y      | N      | Y      | N      | N      | C      | Y      | N      | F      |
| Widestedt and et al; 2018 | Y      | Y      | Y      | C      | Y      | Y      | C      | Y      | E      |         |         |
| Wang and et al; 2016 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Rakic and et al; 2005 | Y      | Y      | N      | N      | Y      | Y      | Y      | N      | G      |         |         |
| Shao and et al; 2016 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Chua and et al; 2015* | Y      | Y      | C      | Y      | C      | C      | Y      | C      | E      |         |         |
| Garry and et al; 2015* | Y      | Y      | C      | Y      | C      | C      | C      | Y      | G      |         |         |
| Chong and et al; 2018* | Y      | Y      | C      | Y      | Y      | C      | C      | Y      | G      |         |         |
| Saklayen and et al; 1990 | Y      | Y      | Y      | N      | Y      | N      | C      | Y      | G      |         |         |
| Skritvars and et al; 2005 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Yokoyama and et al; 2011 | Y      | Y      | Y      | C      | Y      | Y      | Y      | E      |         |         |
| Toppijan and et al; 2010 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| DeVoe et al; 2016 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Herlitz et al; 2001 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Ohlsson et al; 2014 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Parikh et al; 2019 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Al-Dury et al; 2017 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Israelsson et al; 2014 | Y      | Y      | Y      | C      | Y      | Y      | Y      | E      |         |         |
| Mohnle et al; 2012 | Y      | Y      | Y      | C      | Y      | N      | Y      | Y      | E      |         |         |
| Ravipragasam and et al; 2019 | Y      | Y      | Y      | N      | Y      | Y      | Y      | Y      | E      |         |         |
| Li et al; 2019 | Y      | Y      | Y      | C      | Y      | Y      | Y      | Y      | E      |         |         |
| Jaberi et al; 2011 | Y      | Y      | Y      | N      | Y      | C      | N      | Y      | G      |         |         |
| Goldberger et al; 2012 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Nolan et al; 2014 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Bergum et al; 2015 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |
| Keivanpazhoh et al; 2011 | Y      | Y      | Y      | N      | Y      | N      | N      | C      | Y      | N      | F      |
| Salari et al; 2010 | Y      | Y      | Y      | N      | C      | Y      | N      | Y      | G      |         |         |
| Khatib and et al; 2017 | Y      | Y      | Y      | Y      | Y      | Y      | Y      | Y      | E      |         |         |

Item1: Did the study address a clearly focused issue?  
Item2: Did the authors use an appropriate method to answer their question?  
Item3: Were the subjects recruited in an acceptable way?  
Item4: Were the measures accurately measured to reduce bias?  
Item5: Were the data collected in a way that addressed the research issue?  
Item6: Did the study have enough participants to minimize the play of chance?  
Item7: How are the results presented and what is the main result?  
Item8: Was the data analysis sufficiently rigorous?  
Item9: Is there a clear statement of findings?  
Item10: Can the results be applied to the local population?  
Item11: How valuable is the research?  

* presented in Congress; †. Yes; ‡. Can’t Tell; †. NO; €.Excellent; ¥.GOOD; ¥. Fair
10 items evaluate the content of the article from different angles and item 11 is related to commenting on the overall quality of the article based on the result obtained from the first 10 items. Based on the researchers’ evaluation of the articles, about 74% of the articles published in journals were evaluated as an excellent and only 2 articles were in an acceptable condition. In 12 articles, bias measurement and classification methods could not be deduced, and in 6 articles, there are enough participants to minimize the play of chance (Table 2).

**Publication Bias**

There were no evidences of publication bias in the assessment of survival to discharge on women (t=0.33, p=0.13), survival to discharge on men (t=1.5, p=0.74) and the rate of FNO (t=0.65, p=0.52) based on the results of funnel plot and Eagger’s regression test (Figure 2).

**Sensitivity Analysis**

The results of the sensitivity analysis test showed the parallel effect of each study on the conclusion and the robustness of the model; therefore, we did not delete any studies to compare with the remaining results (Figure 3).

**Meta-analysis**

**Survival to Discharge**

Based on the results of systematic and meta-analysis review on 46 articles of 1,020,799 cases with IHCA, survival to discharge was equal to 19.1% (95% CI=16.8-21.7) (Figure 4). In addition, meta-regression results showed that survival to discharge rate had a declining trend over the past few years. Figure 5 illustrates heterogeneity in survival to discharge in different studies and countries, therefore, the higher survival rates are in Australia (39%), Sweden with (32.7%) and Germany (30.2%), and the lowest survival rates are in Iran (6.9%) and Taiwan (8.7%) (Q-value=20707.47, p≤0.001).

The results about survival to discharge in men and women showed that survival to discharge to women with 364,593 cases was 19.8% (95% CI=17.6-22.2) and this figure for men with 444,463 cases was 22.2% (95% CI=20.2-24.3) (Figure 6).

Only three studies used a similar pattern to report the survival to discharge based on CPR duration. The meta-analysis results on these studies indicated that out of 2,148 cases with initial successful resuscitation (ROSC) and CPR duration ≤15 min, survival rate was 47.3% (95% CI=28.9-66.6) and in CPR duration>15min in 359 cases, this rate was...
Fig. 3. The results of sensitivity analysis test

Fig. 4. Survival to discharge (Survival rate: 19.1%, Q-value=11896.47, P<0.001)

Fig. 5. Survival rate to discharge based on study location

Fig. 6. Comparison of survival to discharge in female with male
Survival to discharge rate of patients in-hospital cardiac arrest

significantly lower (13.2%) (95% CI=6.5-25) (Figure 7). Also, survival rate to discharge in 135,996 cases under study with shockable and non-shockable dysrhythmias was 39.3% (95% CI=35.6-43.1) and 12.1% (95% CI=11-13.3), respectively (p<0.001) (Figure 8).

**FNO (CPC≤2) at Discharge**

From 46 articles entered to the meta-analysis, 15 articles with total cases of 302,850 reported FNO at discharge. This index relative to survivors until discharge was equal to 68.1% (95% CI=55.8-78.3) (Figure 9). Meta-regression results on survival to discharge and FNO showed that the higher of survival to discharge and the higher of FNO (p<0.001) (Figure 2).

Only three studies reported FNO related to gender. According to the meta-analysis results, FNO in men and women at discharge was 79.1 (95% CI=63-89.4) and 71.2 (95% CI=41.3-89.7), respectively; therefore, men had better outcomes (Figure 10). In addition to gender, shockable background dysrhythmias were another factor in neurological outcome. With shockable and non-shockable dysrhythmias, FNO was equal to 86.4 (95% CI=79.9-91) and 76.9 (95% CI=67.4-84.3), respectively (Figure 11). In addition, taking into account the limitations of the studies, it was not possible to assess the relationship between FNO and CPR duration (only two articles entered the meta-analysis). The assessment of the results of these two studies showed the duration of CPR affected the FNO at discharge, therefore, it will be high in CPR duration and low in FNO index (Table 1).

**Fig. 7.** Survival rate to discharge based on CPR duration

**Fig. 8.** Survival to discharge based on the first document rhythm

**Fig. 9.** Favorable neurological outcome during discharge (CPC<2)

**Fig. 10.** Favorable Neurological Outcome (CPC<2) by gender

**Fig. 11.** Favorable Neurological Outcome (CPC<2) based on the first document rhythm
Discussion

This systematic review study and meta-analysis were conducted to assess the relationship between resuscitation outcomes and demographic-clinical variables in patients with IHCA. By resuscitation outcome, survival to discharge or 30-day survival and FNO were intended. Survival to discharge or 30-day discharge results of 46 articles was 19.1% based on meta-analysis [12, 14, 15, 22-64]. In addition, the results of our study showed that the survival to discharge rate had a declining trend over the past few years. According to the updated report by the American Heart Association, survival to discharge is equal to 25%, in addition, D’Arrigo et al., reported this index equal to 37.9% [65, 66]. One reason for the declining statistics can be the inclusion of studies conducted in developing countries.

FNO at discharge was 68.1%, compared to the results of the meta-analysis performed in-hospital cardiac arrest which shows a declining trend over the past few years [65]. According to the results, FNO has a direct relationship with patients’ survival, therefore, it will be high in the survival to discharge and the FNO. The decrease in survival to discharge can explain the decrease in FNO.

Survival to discharge or 30-day survival and FNO were notably higher in men compared to women. Bougouin et al., [67] systematically assessed out-of-hospital cardiac arrest patients and reported results inconsistent with the present study. The different survival rates between men and women are indicative to a pathophysiological difference of cardiac arrest in women and men, and the results of our study challenge the classic paradigm of better prognosis in women. According to this paradigm, female hormones improve vascular performance at higher fertility ages by lowering lipoproteins levels and decreasing the risk of cardiac arrest [68-70]. This finding is also contradictory to the fact that estrogen has a protective effect on the nervous and cardiac system [71, 72]. The studies showed that the rate of shockable dysrhythmias in men was higher than in women [9, 14, 15, 22, 33]. Sensitivity of shockable dysrhythmias to timely shocks [14] can be a reason for different survival rates and better neurological outcomes in men.

Survival to discharge and FNO with shockable dysrhythmias were notably higher than those with non-shockable dysrhythmias. One of the predictors of survival to discharge in D’Arrigo et al., [66] was the shockable background dysrhythmia. Only in one study with a small sample group, survival to discharge was higher with non-shockable dysrhythmias [41]. On the other hand, studies on several clinics and large sample groups showed that shockable dysrhythmias were determinants of survival to discharge and FNO [11, 32, 64]. There is reliable evidence of reversibility, survival to discharge, and FNO when a defibrillator is used soon enough [14].

The results indicated that CPR duration was a determinant of survival to discharge, therefore, survival to discharge was notably higher when less than 15min compared with CPR duration >15min.

In conclusion, inconsistent with some of the meta-analysis studies on OHCA, our results showed that survival to discharge rate with strong evidence, and FNO in adults (CPC≤2) in men was higher than women. Despite limitations in studies with a similar time pattern on the effect of CPR duration on survival to discharge and FNO, the results of the present meta-analysis showed this factor effect on the mentioned outcomes. Adherence to the same pattern in the classification of the variables studied in the report on the outcomes of CPR will pave the way for future meta-analysis studies.

The results of our study showed that the outcomes of cardiac arrest in developing countries are weak and make it clearer to health care providers for identifying gaps in the survival chain and improve the quality of cardiopulmonary resuscitation. Although non-
shockable dysrhythmias and prolonged resuscitation time were identified as factors associated with weaker resuscitation outcomes, patient’s significant percentage with non-shockable dysrhythmias or prolonged resuscitation, with FNO was discharged. Therefore, adherence to guidelines until the end of resuscitation time and these factors non-interference in the quality of resuscitation is recommended for rescuers. On the other hand, about 32% of discharged resuscitated people are in the CPC>2 and will experience-dependent life. This result can be considered by health policymakers for rehabilitation needs and planning.

Declarations

Ethics approval: The Institutional Review Board and the Ethics Committee of Hamadan University of Medical Sciences, Hamadan, Iran, approved this study (codes: 9803282410 and IR.UMSHA.REC.1398.208).

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Appendix 1. Search query

Filters applied: Full text, Congress, Observational Study, Humans, English, Persian, Adolescent: 13-18 years, Adult: 19+ year

Search terms:

**Medline search query**
1. ("Cardiopulmonary resuscitation"[Title/Abstract]) OR ("Advanced life support"[Title/Abstract]) OR ("Cardiac arrest"[Title/Abstract]) OR ("In-hospital Cardiac arrest"[Title/Abstract]) OR (IHCA[Title/Abstract]) AND ("Neurological outcome"[Title/Abstract]) OR ("success rate of Cardiopulmonary resuscitation"[Title/Abstract]) OR ("Survival to discharge"[Title/Abstract]) OR ("Favorable neurological outcome"[Title/Abstract])
2. ("Cardiopulmonary resuscitation"[Title/Abstract]) OR ("In-hospital Cardiac arrest"[Title/Abstract]) OR ("Neurological outcome"[Title/Abstract]) OR ("success rate of Cardiopulmonary resuscitation"[Title/Abstract]) OR ("Survival to discharge"[Title/Abstract]) OR ("Favorable neurological outcome"[Title/Abstract]) AND (Sex[Title/Abstract] OR gender[Title/Abstract] OR "Duration of resuscitation"[Title/Abstract] OR Shockable[Title/Abstract] OR "non-shockable"[Title/Abstract])

**Scopus search query**
1. "Cardiopulmonary resuscitation" OR ("Cardiac arrest" OR "In-hospital Cardiac arrest" OR (IHCA AND ("Neurological outcome" OR "success rate of Cardiopulmonary resuscitation" OR "Survival to discharge" OR "Favorable neurological outcome")) OR (Sex OR gender OR "Duration of resuscitation" OR Shockable OR "non-shockable")
2. (("Cardiopulmonary resuscitation" OR "Cardiac arrest" OR "In-hospital Cardiac arrest" OR (IHCA AND ("Neurological outcome" OR "success rate of Cardiopulmonary resuscitation" OR "Survival to discharge" OR "Favorable neurological outcome")) OR (Sex OR gender OR "Duration of resuscitation" OR Shockable OR "non-shockable")
3. (("Cardiopulmonary resuscitation" OR "Cardiac arrest" OR "In-hospital Cardiac arrest" OR (IHCA AND ("Neurological outcome" OR "success rate of Cardiopulmonary resuscitation" OR "Survival to discharge" OR "Favorable neurological outcome")) OR (Sex OR gender OR "Duration of resuscitation" OR Shockable OR "non-shockable")

**Science direct query**
1. ("Cardiopulmonary resuscitation" OR "Advanced life support" OR "Cardiac arrest" OR "In-hospital Cardiac arrest" OR IHCA AND ("Neurological outcome" OR "success rate of Cardiopulmonary resuscitation" OR "Survival to discharge" OR "Favorable neurological outcome")) OR ("Cardiopulmonary resuscitation" OR "In-hospital Cardiac arrest" OR (IHCA AND ("Neurological outcome" OR "success rate of Cardiopulmonary resuscitation" OR "Survival to discharge" OR "Favorable neurological outcome")) AND (Sex OR gender OR "Duration of resuscitation" OR Shockable OR "non-shockable")
2. ("Cardiopulmonary resuscitation" OR "Cardiac arrest" OR "In-hospital Cardiac arrest" OR (IHCA AND ("Neurological outcome" OR "success rate of Cardiopulmonary resuscitation" OR "Survival to discharge" OR "Favorable neurological outcome")) AND (Sex OR gender OR "Duration of resuscitation" OR Shockable OR "non-shockable")
3. ("Cardiopulmonary resuscitation" OR "Cardiac arrest" OR "In-hospital Cardiac arrest" OR (IHCA AND ("Neurological outcome" OR "success rate of Cardiopulmonary resuscitation" OR "Survival to discharge" OR "Favorable neurological outcome")) AND (Sex OR gender OR "Duration of resuscitation" OR Shockable OR "non-shockable")