Review Article

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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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ABSTRACT

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 Eagger'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 CRP 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, repetitious 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 (≤15min, >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

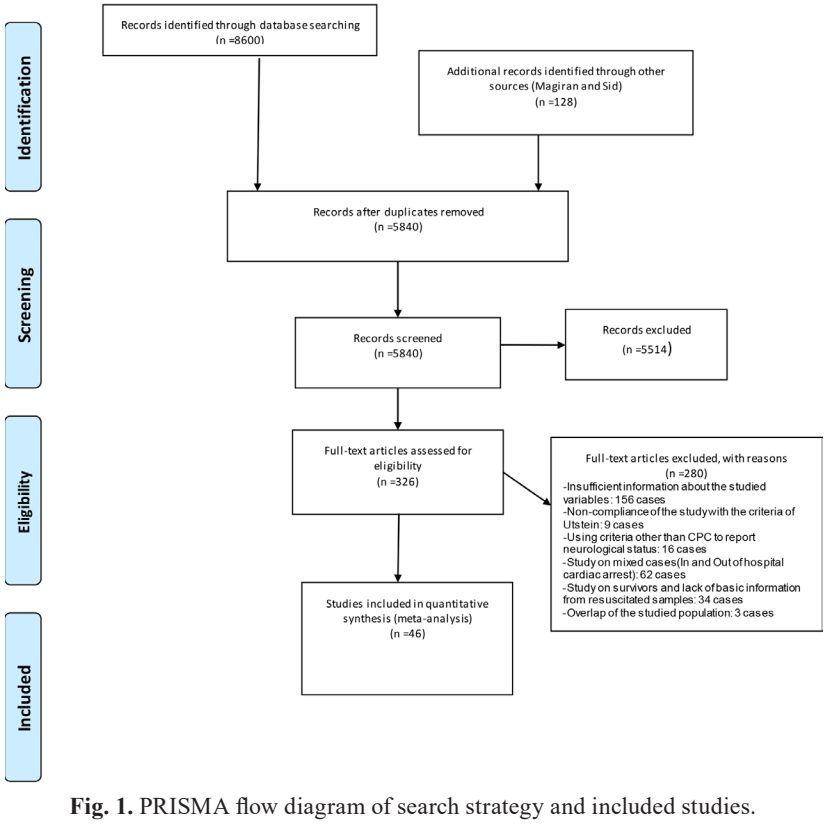

Fig. 1. PRISMA flow diagram of search strategy and included studies.

Table 1. Output information from related articles

Row	The first author	Study time (study type)	Study place	Survival to discharge or 30 days N (%)	FNO [a] N (%)	Total N	Total N	Total N
						Survival based on gender N (%)	Survival based on First Document N (%)	Survival based on CPR duration N (%)
						FNO based on gender N (%)	FNO based on the First Document N (%)	FNO based on CPR duration N (%)
			N (total)			Female	Male	Non-Shockable	Shockable	≤15min	>15min
1	Meaney et al., [22]	1999-2005 (Prospective)	U.S.	9125(17.57)	6850(75.07)	NR‡	NR	39391	12528	NR	NR
						NR	NR	4469(11.34)	4656(37.16)	NR	NR
			51919			NR	NR	3133(70.1)	3717(79.83)	NR	NR
2	Hessulf et al. [23]	2006-2015 (Retrospective)	Swedish Register	5113(28.3)	NR (93)	NR	NR	NR	NR	NR	NR
						NR	NR	NR	NR	NR	NR
			18069			NR	NR	NR	NR	NR	NR
3	Johnson et al., [24]	Unknown (Prospective)	South India	197(10.1)	161(81.73)	628	1327	1676	279	NR	NR
						70(11.1)	127(9.50)	146(8.71)	51(18.27)	NR	NR
			1955			NR	NR	114(78)	47(92)	NR	NR
4	Radeschi et al., [25]	2012-2014 (Retrospective)	Italy	228(14.8)	207(90.79)	575	964	1248	291	NR	NR
						89(15.48)	139(14.42)	116(9.29)	112(38.49)	NR	NR
			1539			NR	NR	NR	NR	NR	NR
5	Urberg et al., [26]	1983-1984 (Retrospective)	Michigan. US.	13(11)	NR	58	63	NR	NR	NR	NR
						6(10.34)	7(11.11)	NR	NR	NR	NR
			121			NR	NR	NR	NR	NR	NR
6	Hjalmarsson et al., [27]	2007-2015 (Retrospective)	Karolinska Stockholm	376(27.38)	NR	478	895	897	292	NR	NR
						125(26.15)	251(28.4)	151(16.83)	171(58.56)	NR	NR
			1373			NR	NR	NR	NR	NR	NR
7	Andersen et al., [28]	2017-2018 (Retrospective	Denmark	1124(27.8)	NR	NR	NR	2891	703	NR	NR
						NR	NR	466(16.1)	405(57.6)	NR	NR
			4049			NR	NR	NR	NR	NR	NR
8	Lundin et al., [29]	2015-2017 (Retrospective)	Swedish	1818(30.13)	1660(91.3)	NR	NR	3410	1356	NR	NR
						NR	NR	600(17.59)	857 (63.20)	NR	NR
			6033			NR	NR	543(90.5)	809(94.4)	NR	NR
9	Cicekci et al., [30]	2013-2015 (Retrospective)	Konya, Turkey	44(11.28)	25(56.82)	NR	NR	NR	NR	NR	NR
						10(NR)	34(NR)	10(NR)	34(NR)	29(NR)	15(NR)
			390			NR	NR	5(50)	20(58.82)	18(62.7)	7(46.67)
10	Rohlin et al., [31]	2007-2017 (Retrospective)	Swedish	471(29)	NR	NR	NR	NR	NR	635	133
						NR	NR	NR	NR	405(63.78)	36(27.7)
			1639			NR	NR	NR	NR	NR	NR
11	Nadkarni et al., [32]	2000-2004 (Retrospective)	US& Canadian's H	6485(17.57)	4390(67.69)	NR	NR	24978	8361	NR	NR
						NR	NR	2719(10.88)	3013(36)	NR	NR
			36902			NR	NR	1675(61.60)	2268(75.27)	NR	NR

12	Qvick et al., [33]	2007-2017 (Retrospective)	Karolinska University	470(29)	NR	650	989	NR	NR	NR	NR
						193(29.69)	277(28)	NR	NR	NR	NR
			1639			NR	NR	NR	NR	NR	NR
13	Heller et al., [34]	1984-1991 (Retrospective)	Australia	120(39)	NR	115	193	NR	NR	NR	NR
						45(39)	75(39)	NR	NR	NR	NR
			308			NR	NR	NR	NR	NR	NR
14	Kung et al., [35]	2008- 2011 (Retrospective)	Taiwan	28(5.1)	6(21.43)	224	320	523	21	NR	NR
						13(5.80)	15(4.68)	24(4.59)	4(19.04)	NR	NR
			544			NR	NR	NR	NR	NR	NR
15	Jones et al., [36]	2004-2006 (Retrospective)	New Zealand	113(27.2)	NR	169	246	267	148	NR	NR
						38(22.48)	75(30.49)	35(13.10)	78(52.70)	NR	NR
			415			NR	NR	NR	NR	NR	NR
16	Tok et al., [37]	2001-2002 (Prospective)	Turkey	12(11.7)	NR	36	55	80	23	NR	NR
						6(14.2)	6(10.7)	5(6.2)	7(30.4)	NR	NR
			103			NR	NR	NR	NR	NR	NR
17	Khatib et al., [38]	1995-2015 (Retrospective)	Afula, Israel	93(13.24)	NR	303	399	551	151	NR	NR
						37(12.21)	56(14.03)	57(10.34)	36(23.84)	NR	NR
			702			NR	NR	NR	NR	NR	NR
18	Kolte et al., [39]	2003-2011 (Retrospective)	USA	68477(24.62)	NR	311423	372915	NR	NR	NR	NR
						79724(25.6)	88753(23.8)	NR	NR	NR	NR
			684338			NR	NR	NR	NR	NR	NR
19	Thomas et al., [40]	1987-1988 (Prospective)	U. K	32(16.6)	NR	NR	NR	67	39	NR	NR
						NR	NR	8(11.4)	14(35.90)	NR	NR
			192			NR	NR	NR	NR	NR	NR
20	Wachira et al., [41]	2013 (Retrospective)	Kenya	12(11.1)	12(100)	NR	NR	83	14	NR	NR
						NR	NR	9(10.84)	1(7.1)	NR	NR
			108			NR	NR	9(100)	1 (100)	NR	NR
21	Widestedt et al., [42]	2012-2017 (Retrospective)	Stockholm, Sweden	191(33.27)	NR	234	340	384	131	NR	NR
						72(30.77)	119(35)	89(23.18)	78(59.54)	NR	NR
			574			NR	NR	NR	NR	NR	NR
22	Wang et al., [43]	2006-2014 (Retrospective)	Taiwan	215(14.1)	110(51.16)	598	926	NR	NR	NR	NR
						77(12.9)	138(14.9)	NR	NR	NR	NR
			1524			28(36.36)	82(59.42)	NR	NR	NR	NR
23	Rakic et al., [44]	2003 (Prospective)	Croatia	27(22.5)	NR	46	74	56	42	NR	NR
						11(23.9)	16(21.6)	6(10.71)	20(47.62)	NR	NR
			120			NR	NR	NR	NR	NR	NR
24	Shao et al., [12]	2014 (Prospective)	Beijing, China	247(9.10)	NR	NR	NR	2289	423	NR	NR
						NR	NR	154(6.73)	93(21.98)	NR	NR
			2712			NR	NR	NR	NR	NR	NR

25	Chua et al., [45]	2008-2009 (Retrospective)	Singapore	49(13.88)	NR	NR	NR	290	63	NR	NR
						NR	NR	32(11)	17(27)	NR	NR
			353			NR	NR	NR	NR	NR	NR
26	Garry et al., [46]	2012-2013 (Prospective)	USA Stony Brook Univ	65(24.49)	NR	96	159	NR	NR	NR	NR
						22(22.9)	43(27)	NR	NR	NR	NR
			255			NR	NR	NR	NR	NR	NR
27	Chong et al., [47]	2017-2018 (Retrospective)	Unknown	55(30)	NR	NR	NR	143	40	NR	NR
						NR	NR	34(23.8)	21(52.5)	NR	NR
			183			NR	NR	NR	NR	NR	NR
28	Saklayen et al., [48]	1988-1990 (Retrospective)	Dayton Ohio	44(13)	NR	NR	NR	113	61	NR	NR
						NR	NR	1(1)	9(14.7)	NR	NR
			340			NR	NR	NR	NR	NR	NR
29	Skrifvars et al., [49]	1993-1997 (Prospective)	Finland	22(12.02)	NR	NR	NR	126	57	NR	NR
						NR	NR	7(5.55)	15(28)	NR	NR
			183			NR	NR	NR	13(86.67)	NR	NR
30	Yokoyama et al., [50]	2008-2009 (Prospective)	Japan	136(27.8)	105(77.21)	NR	NR	347	138	NR	NR
						NR	NR	73(21.04)	63(45.65)	NR	NR
			491			NR	NR	49(67.12)	56(88.89)	NR	NR
31	Topjian et al., [51]	2000-2008 (Prospective)	Philadelphia	16960(17.69)	13244(78.09)	42213	53639	NR	NR	NR	NR
						7593(17.99)	9817(18.30)	NR	NR	NR	NR
			95852			5782(76.15)	7462(76.01)	NR	NR	NR	NR
32	DeVoe et al., [52]	2007-2013 (Retrospective)	New York	86(21)	NR	172	245	237	142	NR	NR
						34(19.77)	52(21.22)	28(11.81)	46(32.39)	NR	NR
			417			NR	NR	NR	NR	NR	NR
33	Herlitz et al., [53]	1994-1998 (Prospective)	Sweden	208(37.34)	192(92.31)	217	340	240	261	NR	NR
						79(36.40)	129(37.94)	40(16.67)	147(56.32)	NR	NR
			557			71(91)	121(94)	NR	NR	NR	NR
34	Ohlsson et al., [54]	2007-2010 (Retrospective)	Sweden	58(20.2)	NR	111	176	207	80	NR	NR
						19(17.12)	39(22.16)	19(9.18)	39(48.75)	NR	NR
			287			NR	NR	NR	NR	NR	NR
35	Parikh et al., [55]	2012 - 2018 (Prospective)	New York	125(18.38)	NR	262	418	NR	NR	NR	NR
						33(12.50)	92(22)	NR	NR	NR	NR
			680			NR	NR	NR	NR	NR	NR
36	Al-Dury et al., [56]	2007-2014 (Prospective)	Swedish Register	4197(28.1)	NR	5767	9166	NR	NR	NR	NR
						1517(26.30)	2680(29.24)	NR	NR	NR	NR
			14933			NR	NR	NR	NR	NR	NR
37	Goldberger et al., [57]	2000-2008 (Prospective)	(NRCPR) Michigan	9912(15.4)	7034 (80.6)	NR	NR	NR	NR	NR	NR
						NR	NR	NR	NR	5838(NR)	2886(NR)
			64339			NR	NR	NR	NR	4738(81.2)	2296(79.56)

38	Israelsson et al., [58]	2007-2011 (Retrospective)	Swedish	107(37.4)	NR	90	196	NR	NR	NR	NR
						27(30)	80(40.82)	NR	NR	NR	NR
			286			NR	NR	NR	NR	NR	NR
39	Li et al., [59]	2012-2016 (Retrospective)	Fujian, China	68(21.25)	NR	NR	NR	180	140	90	43
						NR	NR	15(8.33)	53(37.86)	55(61.11)	12(27.91)
			320			NR	NR	NR	NR	NR	NR
40	Ravipragasam et al., [60]	2016-2017 (Prospective)	South India	44(17.50)	NR	115	137	195	57	127(<10min)	125(>10min)
						11(9.56)	33(24.09)	28(14.36)	16(28.08)	26(20.47)	18(14.4)
			252			NR	NR	NR	NR	NR	NR
41	Keivanpazhoh et al., [61]	2010 (Prospective)	Iran	10(13.5)	NR	NR	NR	NR	NR	NR	NR
						NR	NR	NR	NR	NR	NR
			74			NR	NR	NR	NR	NR	NR
42	Jaberi et al., [62]	Unknown (Prospective)	Iran	10(3.3)	NR	NR	NR	NR	NR	NR	NR
						NR	NR	NR	NR	NR	NR
			302			NR	NR	NR	NR	NR	NR
43	Salari et al., [15]	2006 (Retrospective)	Iran	18(7.2)	NR	101	149	172	78	NR	NR
						8(7.9)	10(6.7)	3(1.7)	15(19.2)	NR	NR
			250			NR	NR	NR	NR	NR	NR
44	Mohnle et al., [63]	2004-2006 (Retrospective)	Germany	57(30.2)	NR	57	132	126	61	83(NR)	41(NR)
						15(26.31)	42(31.82)	27(21.43)	30(49.18)	45(54.22)	12(29.27)
			189			NR	NR	NR	NR	NR	NR
45	Bergum et al., [14]	2009-2013 (Prospective)	Norway	71(25)	NR	NR	NR	207	72	NR	NR
						NR	NR	30(14.29)	38(52.8)	NR	NR
			306			NR	NR	NR	NR	NR	NR
46	Nolan et al., [64]	2011-2013 (Prospective)	UK	4153(18.35)	3759(97.5)	NR	NR	17018	3982	NR	NR
						NR	NR	1735(10.19)	1727(49)	NR	NR
			22628			NR	NR	1524(96)	1602(99.1)	NR	NR

[a] Favorable Neurological Outcome (CPC<=2); [b]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	Y	E€
Hessulf and et al;2017	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Johnson and et al;2014	Y	Y	Y	C‡	Y	Y	C	C	Y	Y	G¥
Radeschi and et al;2017	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Urberg and et al;1987	Y	Y	Y	N†	Y	N	N	C	Y	N	F£
Hjalmarsson and et al;2017	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Andersen and et al;2019	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Lundin and et al;2019	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Cicekci and et al;2018	Y	Y	Y	N	Y	Y	C	C	Y	Y	G
Rohlin and et al;2018	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Nadkarni and et al;2006	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Qvick and et al;2018	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Heller and et al;1995	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	E
Kung and et al;2014	Y	Y	Y	C	Y	Y	Y	Y	Y	Y	E
Jones and et al;2011	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Tok and et al;2004	Y	Y	Y	N	Y	N	Y	C	Y	C	G
Kolte and et al;2014*	Y	Y	Y	C	Y	Y	C	C	Y	Y	C
Thomas and et al;1990	Y	Y	Y	N	Y	Y	C	C	Y	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	Y	C	Y	Y	E
Wang and et al;2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Rakic and et al;2005	Y	Y	Y	N	Y	N	Y	Y	Y	N	G
Shao and et al;2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Chua and et al;2015*	Y	Y	Y	C	Y	Y	C	C	Y	Y	C
Garry and et al;2015*	Y	Y	Y	C	Y	Y	C	C	Y	Y	C
Chong and et al;2018*	Y	Y	Y	C	Y	Y	C	C	Y	Y	C
Saklayen and et al;1990	Y	Y	Y	N	Y	Y	N	C	Y	Y	G
Skrifvars and et al;2005	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Yokoyama and et al;2011	Y	Y	Y	Y	Y	Y	C	Y	Y	Y	E
Topjian and et al;2010	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
DeVoe et al;2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Herlitz et al;2001	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Ohlsson et al;2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Parikh et al;2019	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Al-Dury et al;2017	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Israelsson et al;2014	Y	Y	Y	C	Y	C	Y	Y	Y	Y	E
Mohnle et al;2012	Y	Y	Y	C	Y	N	Y	Y	Y	Y	E
Ravipragasam and et al;2019	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	E
Li et al;2019	Y	Y	Y	C	Y	Y	Y	Y	Y	Y	E
Jaberi et al;2011	Y	Y	Y	N	Y	Y	C	N	Y	Y	G
Goldberger et al;2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Nolan et al;2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	E
Bergum et al;2015	Y	Y	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	Y	C	Y	N	Y	Y	G
Khatib and et al;2017	Y	Y	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 in 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 ≤15min, survival rate was 47.3% (95% CI=28.9-66.6) and in CPR duration>15min in 359 cases, this rate was

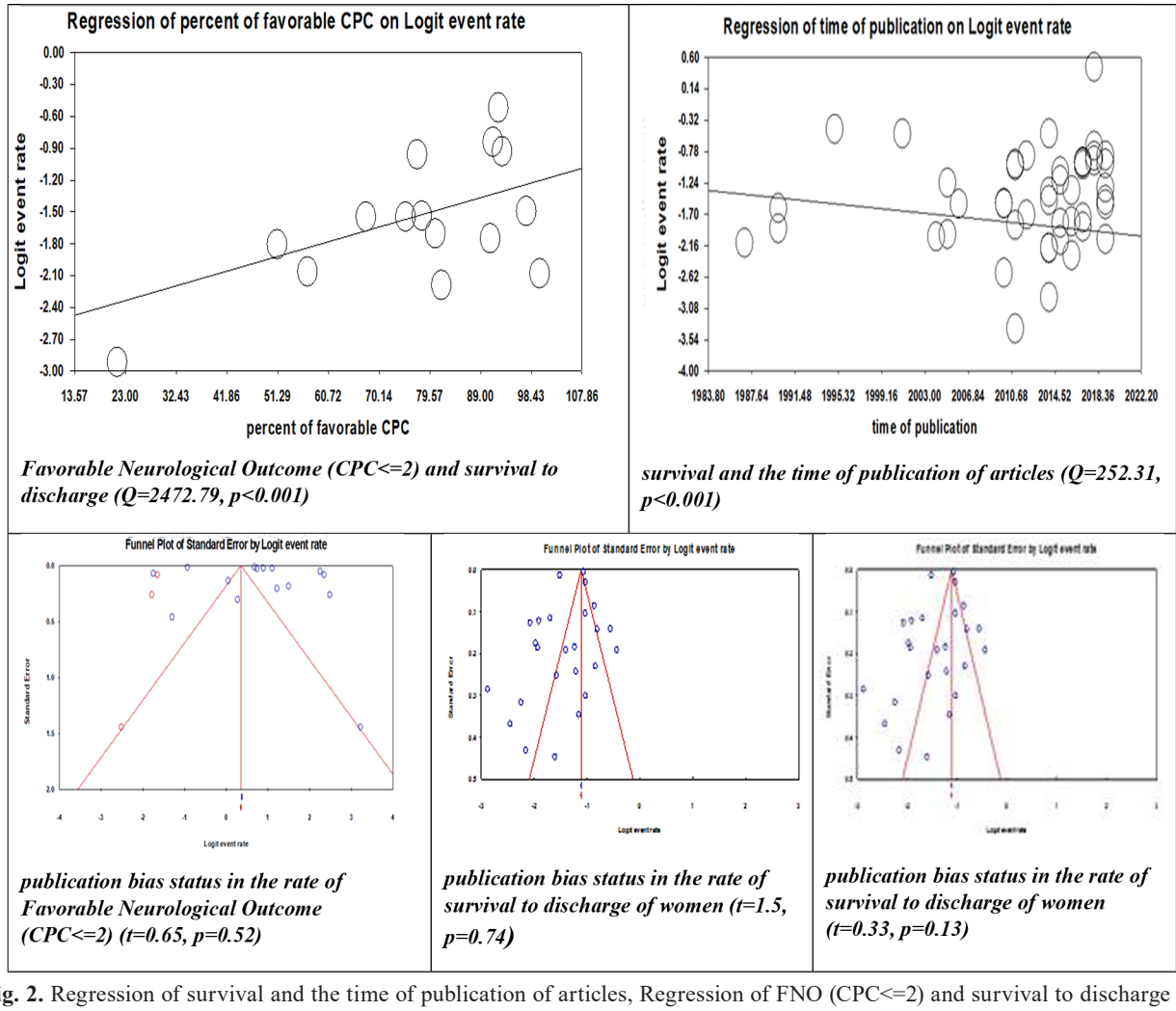

Fig. 2. Regression of survival and the time of publication of articles, Regression of FNO (CPC<=2) and survival to discharge and Funnel plot for publication bias in survival to discharge of women, men and FNO

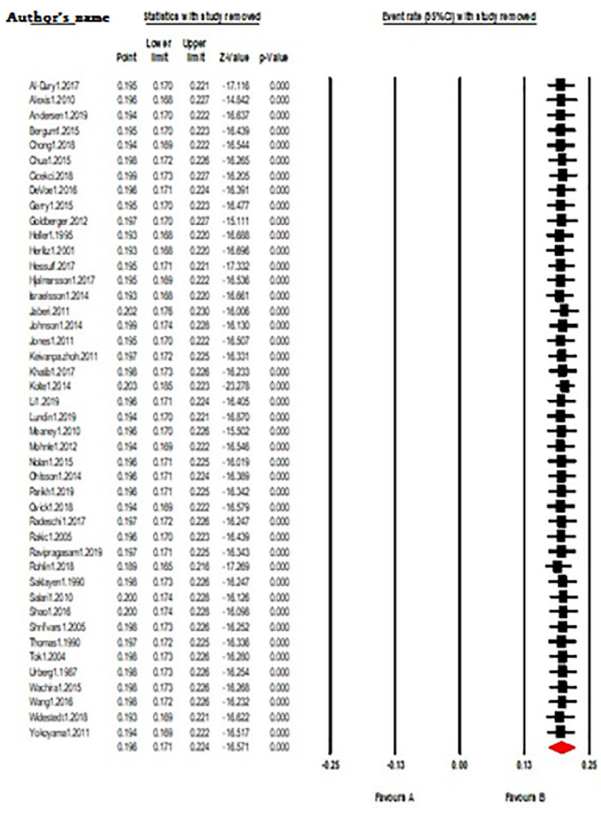

Fig. 3. The results of sensitivity analysis test

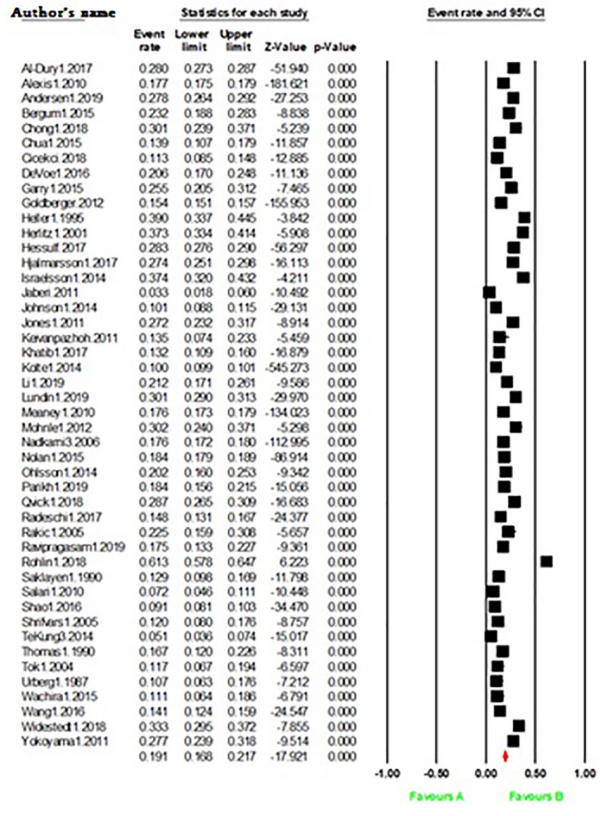

Fig. 4. Survival to discharge **(**Survival rate: 19.1%, Q-value=11896.47, P<0.001**)**

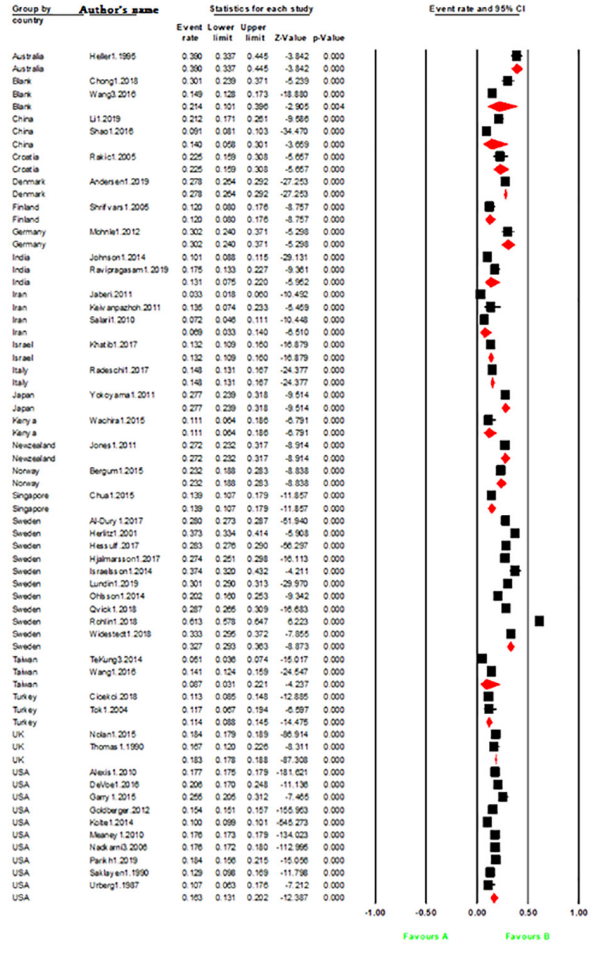

Fig. 5. Survival rate to discharge based on study location

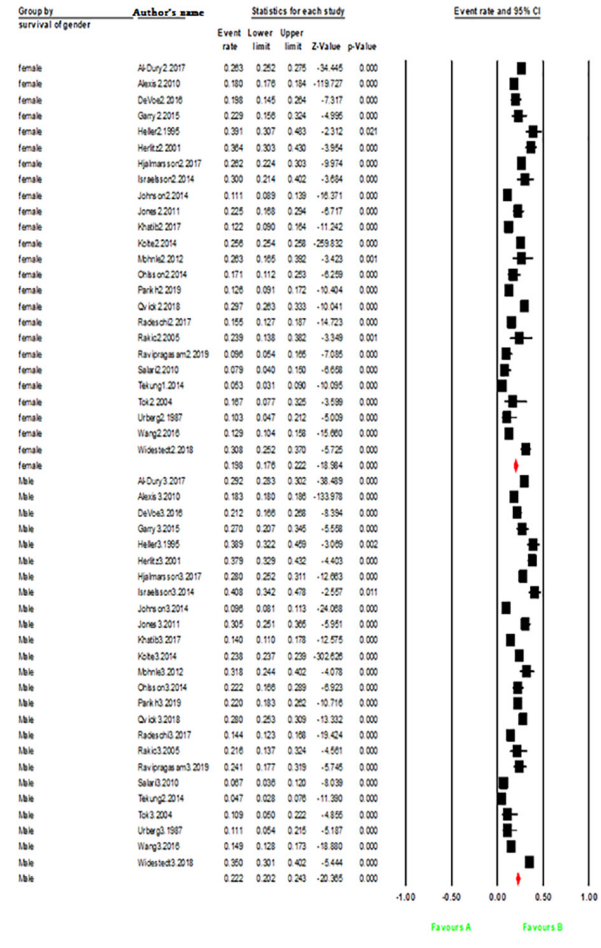

Fig. 6. Comparison of survival to discharge in female with male

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 ($p \leq 0.001$) (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).

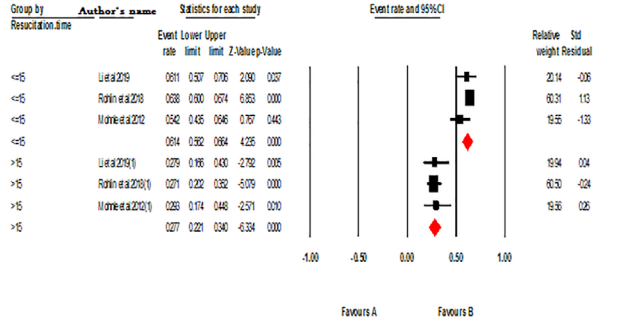

Fig. 7. Survival rate to discharge based on CPR duration

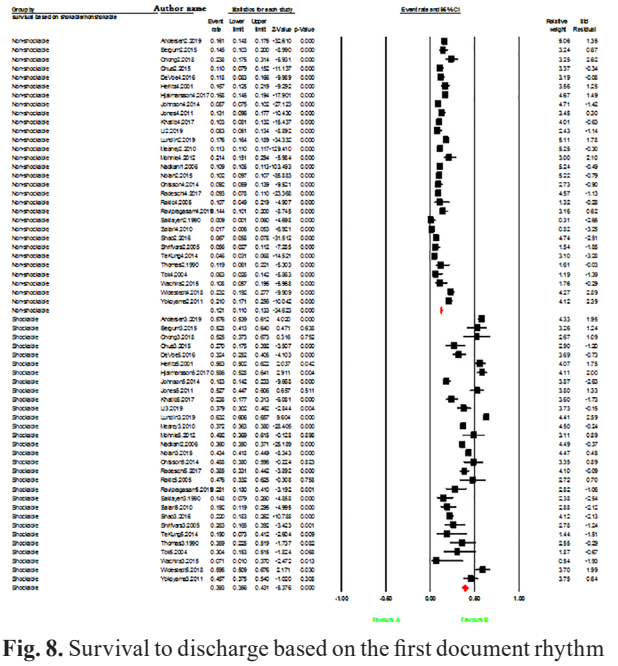

Fig. 8. Survival to discharge based on the first document rhythm

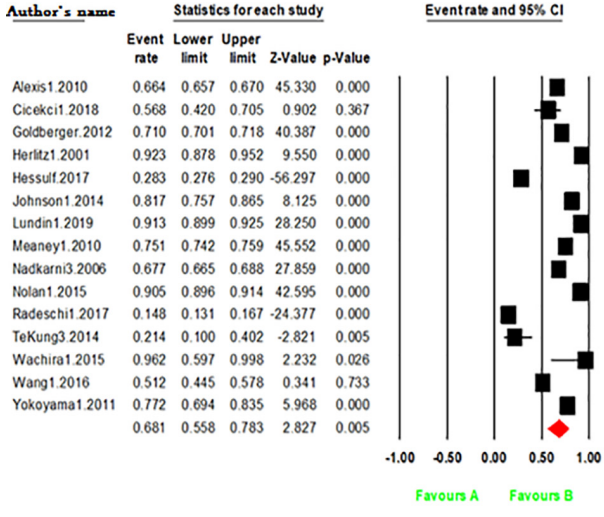

Fig. 9. Favorable neurological outcome during discharge (CPC<=2)

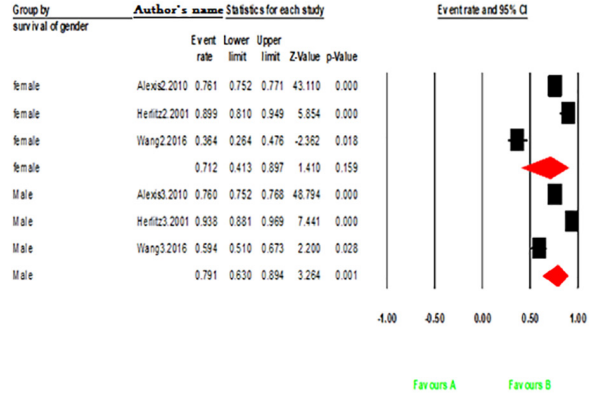

Fig. 10. Favorable Neurological Outcome (CPC<=2) by gender

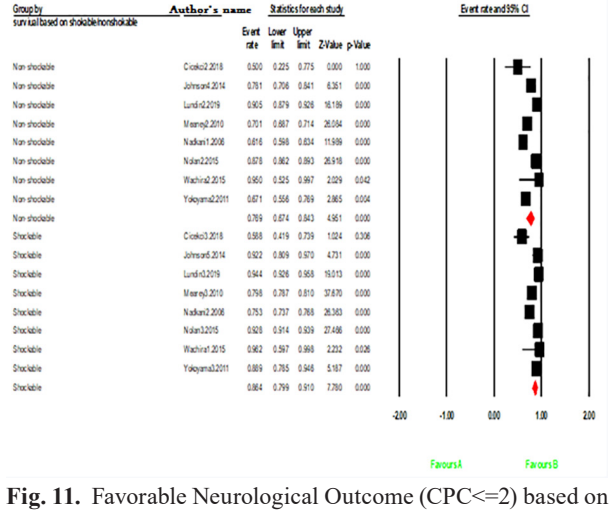

Fig. 11. Favorable Neurological Outcome (CPC<=2) based on the first document rhythm

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 larg 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. There were a limited number of the evaluated CPR studies duration effect on survival to discharge; still, the results supported the higher survival to discharge with shorter CPR duration [31, 59, 60, 63]. In addition, despite the limited findings of the duration of CPR and FNO (CPC≤2) at discharge that did not allow a meta-analysis, the results showed that the duration of CPR affected neurological performance at discharge [30, 57]. Schultz *et al*., [73] argued that CPR duration affected the resuscitation outcomes and concluded that the survival rate for CPR duration >10min was only 2%. Ballew *et al*., [74] reported similar results so the survival to discharge with CPR duration <5min and CPR duration >20min was 45% and 5%, respectively. These findings and other studies show that resuscitation duration is an independent factor to predict the low survival rate in patients after CPR [75]. Goldberger *et al*., [57] reported contrary results. The results of a multi-center study by Goldberger *et al*., [57] showed a better survival to discharge at hospitals with longer CPR duration. They argued that computation of total CPR duration for the survived distribute results toward a shorter duration of resuscitation. However, like other studies, Goldberger noted that duration of resuscitation was a factor in the poor neurological outcome in discharged patients.

We are aware that our research may have some limitations. Search bias in Persian and English languages, unavailability of some of the studies full-text, and lack of adequate information in the available summaries were some of the limitations. In addition, limitations includes using of different models by studies on the relationship of CPR duration, the outcome of CPR and failure to report the results based on different age groups.

Conclusion

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).

Consent for publication: Not applicable.

Conflict of interests: The authors declare that they have no competing interests

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Authors' contributions: Study design: AG, KO, and MKH; Data collection: AG and ARA; Data extraction: AG and ARA; Analysis: AG and ARA; Drafting: AG, KO, ARA; Critically revised the paper: All authors.

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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])\ Scince direct query[Due to limited acceptance of booleans connectors (max 8 per field)] 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]) 3. (“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 (shockable[Title/Abstract] OR “non-shockable”[Title/Abstract]) Scopus search query 1. TITLE-ABS-KEY (“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”) 2. TITLE-ABS-KEY (“Cardiopulmonary resuscitation” OR “In-hospital Cardiac arrest” OR “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”)