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Cardiac arrest in the workplace and its outcome: a systematic review and meta-analysis

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Running title. **Meta-analysis Cardiac arrest in the workplace**

Key words: cardiac arrest; location; public; work; occupational; review; meta-analysis; prevention.

All authors have participated in the conception and design of the study, or the acquisition of data, or the analysis and interpretation of the data, drafting the article, or revising it critically for important intellectual content, and final approval of the version submitted.

Introduction. Out-of-hospital cardiac arrest (OHCA) in the workplace appears to be managed more effectively than OHCA occurring in other places. A systematic review and meta-analysis of the available epidemiological data was performed, comparing the rate of survival for OHCA in the workplace, versus survival in other locations.

Methods. Four databases (Pub-Med, Scopus, Web of science, “Base de Données de Santé Publique”, BDSP, i.e. the French Public Health Database) were searched since 2000, using the key words: (“Cardiac arrest”) and (“occupational” OR “workplace” OR “public location”). A two stage process with two independent readers was used to select relevant papers. Numbers of subjects who suffered from OHCA in the workplace versus other locations were extracted when possible, as well as their respective outcomes (admitted alive to the hospital, discharged alive, good neurological outcome). Meta risks were calculated using the generic variance approach (meta-odds ratios metaOR).

Results After full-text reading, 17 papers were included, from 9 countries, mostly published after 2005, and coming mostly from prospective registers. “Workplace” was defined differently in different studies, mostly in terms of industrial sites and offices. The workplace was an exceptional location for occurrences of OHCA (from 0.3% to 4.7 % of all OHCA, from 1.3 to 23.8 events per million people Per year), based on 2077 OHCA. In the quantitative analyses (survival available, 10 studies), MetaOR were found to be relatively consistent and high (from 1.9 (1.5-2.3) to 5.9(2.7-13.0)). When OHCA occurring at workplaces were compared to other public sites, no significant differences were found.

Conclusion. There is sufficient evidence to support the view that there will be better outcomes for OHCA cases that occur in the workplace than for those occurring elsewhere. Requirements for occupational health and safety should include prevention of such major (albeit rare) events.

Introduction Since the survival rate decreases exponentially with increases in the interval between out-of-hospital cardiac arrest (OHCA) and the chain of survival, the locations of first responders, their training level, and the location of automated external defibrillators (AED) are particularly important.^[1]

Despite its relatively low incidence, it has been suggested that OHCA in the workplace appears to be managed more effectively than OHCA occurring in other places, which encourages the setting up of first-aid programs in certain companies.^[2] Some studies that compare OHCA managed in the workplace versus OHCA managed at other locations have recently been published^[3–5].

The goal of this study was to undertake a systematic review and meta-analysis of the available epidemiological data, comparing the rate of survival for OHCA in the workplace, versus survival at other locations. The proportion of workplace OHCA in relation to other locations and its frequency are also described, if available.

Methods

Literature research

Four databases (Pub-Med, Scopus, Web of science, “Base de Données de Santé Publique”, BDSP, i.e. the French Public Health Database) were searched, using the key words: (“Cardiac arrest”) and (“occupational” OR “workplace” OR “public location”). No language limitation was added. Papers published before the recommendations of the International Liaison Committee on Resuscitation (ILCOR) of 2000 were considered too old^[6]. The first selection of articles was performed by two independent readers (A.D. and C.D.). The aim, based on the title and abstract, was to include only papers with (i) original studies dealing with cardiac

arrest, (ii) sufficient details to distinguish workplace locations from other locations (public or private), (iii) outcomes respecting the Utstein recommendations^[7,8]. The second stage included examination of full-text papers based on the same criteria. Studies meeting these criteria were included in the meta-analysis after a review by the independent readers (A.D. and C.D.).

Assessment of methodological quality

A list evaluating methodological quality in terms of four categories was created, adapted from Utstein style and Prisma recommendations^[7-9]. The five relevant questions were: (i) was the study design exhaustive? (i.e. with data from a register), (ii) was the workplace location defined precisely? (iii) did the outcome of OHCA patients include survival at 6 months with neurological evaluation? (iv) was the proportion of treatable OHCA available? (i.e. not traumatic, shockable, rhythm, with witnesses) (v) How recent were the studies? (performed in the last 10 years). Two reviewers (A.D. and C.D.) independently assessed the quality of each study by scoring each criterion as positive or negative. Disagreement was resolved by consensus. The fair quality score was based on a total score of 3 or higher.

Data extraction and analysis

Relevant data were extracted from the articles: the number of workplace OHCA, their frequency, and their survival were extracted, as well as the number of those related to other locations. Frequency of OHCA was also extracted, if available. The core findings in each article were expressed using measures of association (odds ratio or OR) with a corresponding 95% confidence interval (CI). Three outcomes were considered: (i) admitted alive to hospital, (ii) discharged alive from hospital or still alive 30 days after the OHCA, (iii) favorable neurological outcome (i.e. Cerebral Performance Category (CPC) 1: return to normal cerebral function and normal living, or CPC 2: cerebral disability, but sufficient function for

independent activities of daily living). Whenever possible, these associations were directly extracted from the original article. In articles where this information was not available, associations were calculated when sufficient raw data was provided. Raw data were requested from all authors if needed. Some were unable to give us authorization for access to the raw data. Nevertheless, meta-ORs were calculated using the generic variance approach. The weight given to each study was the inverse of the variance of the estimated effect. Heterogeneity was tested with the Q statistic. From the Q statistic, we calculated a summary OR and 95% CI with the random effect method. This approach provides more conservative estimates (broader CI) than a fixed effect model, assuming that the differences between results are solely due to chance. For each outcome, all OHCA were included and only those considered as treatable (excluding OHCA without any witness, with traumatic cause, with non-shockable rhythm, depending on available data). To compare workplaces with other public sites, we also recalculated meta-OR for such treatable OHCA.

We tested the publication bias due to study size using Egger's regression approach. Meta-ORs were run on all studies, and on fair quality methodological studies only.

The meta-analysis was performed using STATA (Version 11.2; Stata Corp., College Station, TX, USA). The PRISMA checklist was used.^[9]

Results

In the four selected data bases, we found 30 papers corresponding to our first stage (Figure 1). Only two papers were included due to cross-references (in the reference list and not in the databases), and neither of these was selected after full-reading. After full-text reading, 17 papers were included^[10-12,3,13,14,4,15,5,16-23]. Agreement between the two reviewers was good (kappa 0.90). Selected studies came from nine countries (mostly from the United States, Japan, and France), and were mostly published after 2005 (Table 1). Data were obtained

mostly from prospective registers. No discrepancy between the readers was found (considering the simple but robust criteria). “Workplace” was defined differently in different studies, mostly in terms of industrial sites and offices. The workplace was an exceptional location for occurrences of OHCA (from 0.3% to 4.7 % of all OHCA, from 1.3 to 23.8 events per million people per year), based on 2077 OHCA.

Of the remaining 17 papers, 10 for which survival data were available and were selected in the quantitative analysis review: ^[10–12,3,13,14,4,15,5,16] Except for one of them, these studies found a better outcome for OHCA occurring in workplaces than OHCA occurring elsewhere (n=1383), and metaORs were found to be relatively consistent and high (Table 2), taking into account all outcomes. Sensitivity analyses based on recent and fair quality methodological studies found similar results. There was no significant publication bias (Egger’s test, $P > 0.05$). When OHCA occurring at workplaces were compared to those at other public sites, no significant differences were found.

Discussion

Results reported in the literature from the last fifteen years are consistent, and confirm that the workplace location seems to be a safer place than any other, with a better rate of survival observed in such locations, although such OHCA remain an exceptional event. However, improvement of OHCA handling in workplaces seems necessary when compared to outcomes involving other public places only.

Most of the difficulties with the studies about the management of OHCA in the workplace come from the heterogeneous definition of “workplace”, which ranges from small

shops to large factories, construction sites to small businesses etc. Thus, comparing outcomes involving different definitions of the workplace is debatable, given that the term “location elsewhere” is also very vague. Although most of the workplaces described were classified as “industry and business”, the definition of such locations remains quite broad. However, all workplaces share similar characteristics, such as relatively young age of the patient and the presence of witnesses, and similar interpretations for what counts as a workplace. Although studies are needed to analyze, in greater detail, differences in the survival chain for the different kinds of workplaces, the homogeneity of our results allows general recommendations to be proposed concerning the prevention and management of cardiac arrest cases in workplaces.

The similarity in results observed for workplaces raises the question of why outcomes are better there than elsewhere. Three explanations are plausible: first, people are usually healthier at work than elsewhere: the “healthy worker effect”. This major difference between workplaces and private and/or other public sites, is visible in the younger ages of patients, and the rarity of this type of event, even though the medical condition, usually better, is not reported in these studies. Some studies have tried to minimize the impact of such effects. Two authors used matched controls on age to have similar patterns for subjects, and were considered in the meta-analysis. However, chronic illnesses were not considered, and the better survival observed is partly explained by the fact that people in workplaces generally are healthier than those in other locations, which would explain the low incidence. Nevertheless, it also is quite plausible that improved management of OHCA at workplace locations might be very efficient, taking into account the high number of years of life saved in good conditions. Second, for business and industry, in general, the workplace is also characterized by a higher density of people working together, as with other public locations. However, specific

guidelines for workplaces also result in better management of events, with first-aid, and automated external defibrillator implementation, recommended.^[2,24] Third, specific efforts have been made by many employers and occupational health practitioners to improve working conditions and prevent, as much as possible, the occurrence of cardiac arrest (prevention of major injuries, suicide attempts related to occupational psychosocial factors, etc...). Since we were not able to find better outcomes for workplaces than for other public sites, improvement in prevention and OHCA management guidelines should be a priority all over the world, again considering the gain in number of years of life under good conditions ^[25].

Some limitations should be considered concerning the methodology used. First, publication bias should be discussed. Even though the meta-analysis is based on a small number of studies retained, the results of the papers included seem to be coherent and quite homogeneous, and Egger's test do not reveal a major publication bias, such as Funnel plot (results not shown). The choice of the outcomes used to express the results of the meta-analysis may also raise questions. We decided not to include returns to spontaneous circulation as an outcome, and to adopt a broad definition of treatable OHCA. However, these simplifications did allow us to group the data using broad definitions based on different criteria. Furthermore, if raw data had been accessible, better definitions of treatable OHCA would have been available, but would probably have led to higher odds ratios. Pooled meta-Analysis was not possible because some data were not accessible, even though some authors did send us raw data.

In conclusion, there is insufficient evidence to support the view that there are better outcomes for OHCA cases that occur in the workplace than for those occurring elsewhere.

Requirements for occupational health and safety should include prevention of such major (albeit rare) events, by requiring first-aid and automated external defibrillators, as some countries already do ^[26,27,24]. Research papers should also distinguish the workplace from other public sites, with a special focus on the details of the workplace environment.

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Conflict of interest statement

No relevant conflicts of interest. The authors are paid for their respective affiliations. In addition, Alexis Descatha has received money for his editing work (He is Editor in chief of Archives des maladies professionnelles) from Elsevier Masson.

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Table 1. Studies included.

First author	Country	Where/When?	Type of study	Type of Workplace	Number of OHCA at workplace	Proportion of OHCA at workplace/elsewhere	Number of OHCA at workplace/Inhabitants (in number by years/millions of inhabitants)	Survival on workplace versus elsewhere (respectively)	Fair quality?(Score)
Descatha 2005(11)	France	Paris West Suburb 1993-2002	Retrospective Case-Control study from a prospective database	All workplace type (detailed and checked);	72	2.00%	14.9	Adm. _{all} 22.2% vs 17.7% Adm. _{Treatable} 25.5% vs 18.0% Disch. _{All} 8.3% vs 4.2% Disch. _{Treatable} 9.1% vs 6.0%	No (1)
Descatha 2009 (4)	France	Paris Suburb 2004	Retrospective analysis of a prospective register	Workplace (not specified)	61	2.65%	7.4	Adm. _{all} 31.1% vs 19.6% Adm. _{Treatable} 45.5% vs 26.3%	No (2)
Descatha 2013 (15)	France	France 2011-2012	Case –control study in a prospective nationwide register	Workplace (not specified)	113	4.70%	1.6	Adm. _{all} 36.3% vs 15.6% Adm. _{Treatable} 25.5% vs 18.0% CPC1/2 _{All} 9.7% vs 2.9% CPC1/2 _{treatable} 15.7% vs 3.3%	Yes (3)
Eisenberg 2006 (12)	Austria	Vienna 1993-2002	Retrospective study from prospective register	Office and construction site	16	0.99%	1.0	Adm. _{Treatable} 25.0% vs 29.5%	No (2)
Iwami 2006 (14)	Japan	Osaka 1998-2000	Retrospective study from prospective register	Workplace (not specified)	241	1.77%	9.1	Disch. _{All} 5.8% vs 1.4% Disch. _{Treatable} 10.3% vs 2.6%	Yes (3)
Murakimi 2014 (5)	Japan	Osaka 2005-2011	Prospective population-based study	Workplace (not specified)	306	0.68%	5.0	Adm. _{Treatable} 51.6% vs 39.5% Disch. _{Treatable} 32.0% vs 12.7% CPC1/2 _{treatable} 22.2% vs 7.3%	Yes (4)
Muraoka 2006 (3)	Japan	Takatsuki city 1999-2004	Retrospective study from prospective register	Factory/office and Storehouse	17	1.54%	7.9	Disch. _{Treatable} 23.5% vs 4.7% CPC1/2 _{treatable} 17.6% vs 1.0%	Yes (3)
Pell 2002 (10)	United Kingdom	Scotland 1991-1998	Retrospective cohort study from prospective register	Other place of work	466	3.12%	12.8	Disch. _{Treatable} 11.9% vs 7.8%	No (2)
Reed 2006 (13)	United States and Canada	PAD data -3 2000-2003	Post-hoc analysis of a randomized-control trial	Offices and industrial complex	19	3.04%	8.0	Disch. _{Treatable} 6.3% vs 18.2%	Yes (3)
Weisfeldt 2010 (16)	United States and Canada	US and Canada 2005-2007	Prospective cohort study for a from prospective register	Industrial site	72	0.52%	2.4	Disch. _{Treatable} 16.7% vs 9.6%	Yes (4)
Brooks 2013 (22)	Canada	Toronto 2006-2010	Retrospective study from prospective register	Industrial	39	0.27%	1.3	NI*	NI*
Engdahl 2005 (20)	Sweden	Göteborg 1994-2002	Retrospective study from prospective register	Worksites not accessible to the public such as industrial sites and warehouses	22	1.00%	5.4	NI*	NI*
Folke 2009 (19)	Danemark	Copenhagen 1994-2005	Retrospective study from prospective register	Large industrial business	164	1.29%	22.8	NI*	NI*
Hansen 2013 (23)	Danemark	Copenhagen 1994-2011	Retrospective study from prospective register	Office	257	1.48%	23.8	NI*	NI*

Moon 2015 (21)	United States	MetropolitanPhenix 2000-2012	Retrospective study from prospective register	Public business/Office/workplace	65	1.29%	1.3	NI*	NI*
Malcom 2004 (18)	United States	Georgia State 2000	Retrospective study from prospective register	Industrial	62	0.98%	7.5	NI*	NI*
Zakaria 2014 (17)	Singapore	Singapore 2001-2004	Retrospective study from prospective register	Office and industrial building	63	2.80%	5.0	NI*	NI*

* Not included (no survival extractable), OHCA = out of hospital cardiac arrest, Adm.= Admission alive at hospital, Disch = Discharge alive from hospital
CPC1/2 = Good neurological outcome (cerebral performance category 1 or 2)

Table 2. Summary of meta-odds ratio (Meta-OR) of studies included in the quantitative analysis (with 95% confidence interval or CI95%).

	MetaOR for admission alive at hospital (CI95%), Number of studies (related references), Q statistic	MetaOR for discharge alive from hospital (Number of studies) (CI95%), Number of studies, Q statistic	MetaOR for a good neurological outcome i.e. CPC1/2 (CI95%), Number of studies, Q statistic
All OHCA	2.1 (1.3-3.2), n=3 (4,11,15), P=0.136	2.4 (1.3-4.4), n=4 (10,11,13,14), P=0.051	<i>Not enough studies, n=1 (15), OR=3.6 (1.5-8.6)</i>
All treatable OHCA	1.9 (1.5-2.3), n=4 (5,11,12,15), P=0.402	2.4 (1.6-3.7), n=7 (3,5,10,11,13,14,16), P=0.002	5.9(2.7-13.0), n=3 (3,5,15) P=0.037
All treatable OHCA, only high quality studies included	2.0 (1.6-2.4), n=2(5,15), P=0.521	2.9 (1.8-4.7), n=5(3,5,13,14,16), P=0.041	5.9(2.7-13.0), n=3 (3,5,15), P=0.037
OHCA restricted to workplaces or other public sites	<i>Not enough studies, n=1 (5), OR=1.1 (0.8-1.4)</i>	1.1 (0.8-1.6), n=6(3,5,10,3,14,16),P=0.054	1.4(0.5-3.9), n=3 (3,5,15) , P=0.038

CPC Cerebral performance category

Figure 1.Flow chart.

Figure 1 : Flow Chart

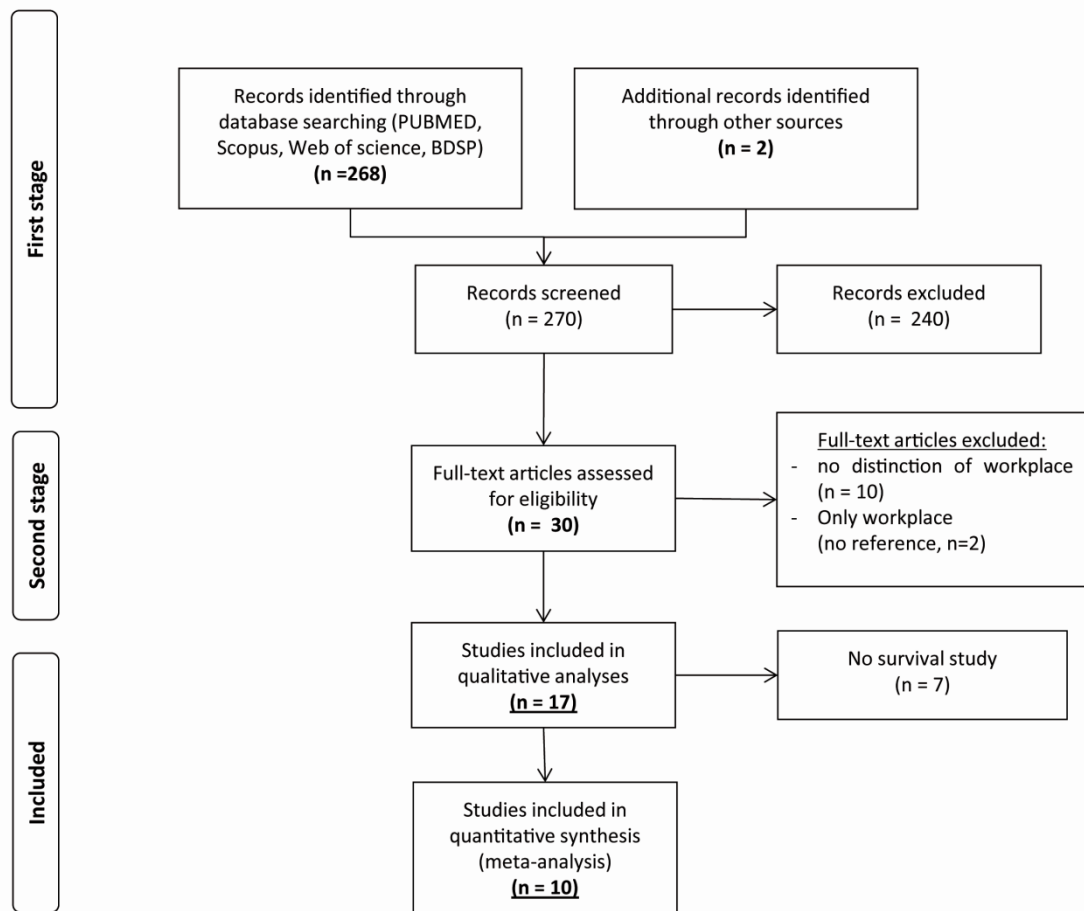


Figure 2. Related Forrest plots of table 2

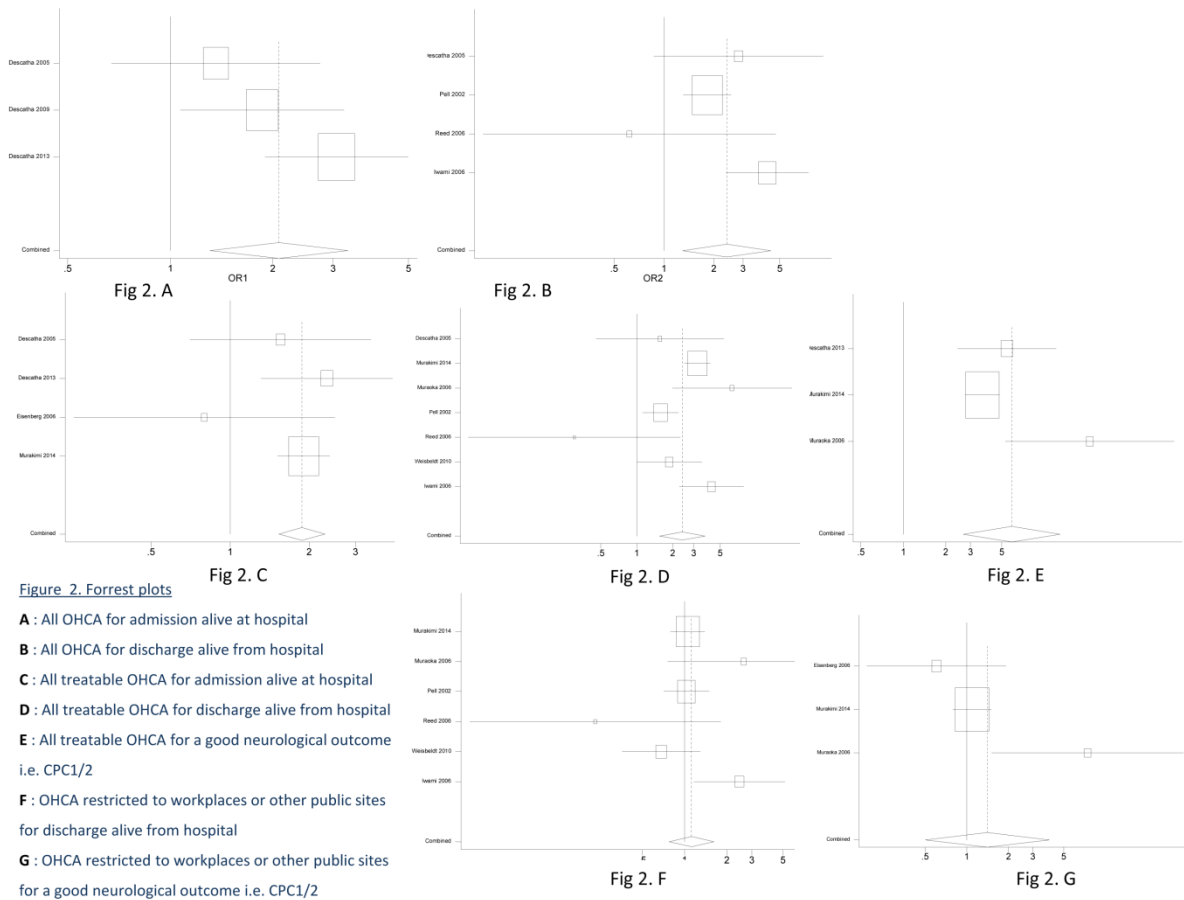


Figure 2. Forrest plots

- A** : All OHCA for admission alive at hospital
- B** : All OHCA for discharge alive from hospital
- C** : All treatable OHCA for admission alive at hospital
- D** : All treatable OHCA for discharge alive from hospital
- E** : All treatable OHCA for a good neurological outcome i.e. CPC1/2
- F** : OHCA restricted to workplaces or other public sites for discharge alive from hospital
- G** : OHCA restricted to workplaces or other public sites for a good neurological outcome i.e. CPC1/2