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LETTER

Association of prehospital acetylsalicylic acid and heparin administration with favorable neurological outcome after out-of-hospital cardiac arrest: a matched cohort analysis of the German Resuscitation Registry

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Dear Editor,

Out-of-hospital cardiac arrest (OHCA) is associated with high morbidity and mortality. Only approximately 5–14% of patients who survive OHCA are discharged with favorable neurological outcome [1, 2]. No prehospitally administered drug has shown to improve neurological outcome in these patients. Acute myocardial infarction (AMI) is a major cause of OHCA. We recently found AMI in 48.2% of patients with OHCA and showed that prehospital administration of acetylsalicylic acid and heparin (AH) was associated with improved survival to hospital discharge, particularly in patients with AMI [3].

In this study, we evaluated the effect of prehospital AH administration on favorable neurological outcome after OHCA. Using data from the nationwide, prospective German Resuscitation Registry, we retrospectively analyzed 17,948 patients with a resuscitation attempt and a presumed cardiac or unknown cause of OHCA between 2013 and 2018. The consort flow-diagram for the study population is depicted in Figure S1. Patients with prehospital AH administration were matched in a 1:3 ratio with patients not treated with AH. The primary outcome was favorable neurological outcome at hospital discharge defined as cerebral performance category (CPC) 1 or 2. Secondary outcomes were return of spontaneous circulation (ROSC), ROSC at hospital admission, 24-h survival and survival to hospital discharge. Additional details can be found in the supplementary material.

In the matched cohort comprising 203 patients with and 609 patients without prehospital AH administration, baseline characteristics were comparable between groups (Table 1). Differences between the matched cohort and the full cohort are shown in Table S1. Prehospital AH administration was associated with favorable neurological outcome (OR 2.25 (1.31–3.87), $p=0.003$, Table S2). Patients with AH were more likely to gain ROSC (OR 2.22 (1.45–3.42), $p<0.001$, Table S3) despite similar ROSC after cardiac arrest (RACA) scores between groups [4]. Moreover, in AH patients, ROSC was more likely to be stable until hospital admission (OR 1.95 (1.26–3.00), $p=0.002$, Table S3). No difference was observed in survival at 24 h (OR 1.30 (0.77–2.17), $p=0.322$, Table S3), while AH was associated with increased survival to hospital discharge (OR 1.84 (1.09–3.09), $p=0.022$, Table S3). Sensitivity analysis with all 17,491 patients with known CPC status confirmed the robustness of our findings (Table S4). Subgroup analysis revealed a significant interaction with male sex and bystander CPR, variables predominantly seen in patients with AMI as the underlying cause of OHCA (Figure S2) [5].

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Table 1 Patient, EMS and inhospital treatment characteristics of the matched cohort

Characteristics	All patients (*N* = 812)	AH (*N* = 203)	noAH (*N* = 609)	*p* value
Age (mean ± SD)	68.1 ± 13.3	68.6 ± 12.3	68.0 ± 13.6	0.820
Age > 80 years (%)	18.7	18.7	18.7	1.000
Male sex (%)	71.3	67	72.7	0.117
Presumed cause of cardiac arrest (%)				
Cardiac or unknown cause	100	100	100	1.000
Pre-emergency status (%)				
Relevant preexisting illness	33	33	33	1.000
No or little preexisting illness	63.1	63.1	63.1	1.000
Unknown pre-emergency status	3.9	3.9	3.9	1.000
Place of collapse (%)				
Public space or doctor's office	22.7	22.7	22.7	1.000
Apartment	66.1	67	65.8	0.764
Initial ECG rhythm (%)				
VF/VT	48.3	48.3	48.3	1.000
Asystole	33.6	34.5	33.3	0.764
Time of no-flow (min:s), mean ± SD (*N*)				
Collapse to CPR	5:05 ± 6:18 (423)	4:39 ± 6:02 (131)	5:17 ± 6:24 (292)	0.329
Alarm to CPR	8:52 ± 08:32 (529)	9:05 ± 9:04 (161)	8:47 ± 8:17 (368)	0.943
Collapse witnessed (%)				
Witnessed by lay people	51.2	51.2	51.2	1.000
Witnessed by first responder	2	3	1.6	0.244
Witnessed by EMS	14.8	14.8	14.8	1.000
CPR to arrival of EMS (%)				
Bystander CPR	35	35	35	1.000
First responder CPR	4.6	4.9	4.4	0.771
CPR via telephone instruction	17.5	13.8	18.7	0.110
Intervals of EMS, mean ± SD (*N*)				
Alarm to arrival (min:s)	6:48 ± 3:56 (724)	6:45 ± 3:50 (184)	6:49 ± 3:58 (540)	0.952
Alarm to defib in VF/VT (min:s)	12:50 ± 10:31 (294)	12:40 ± 8:03 (83)	12:54 ± 11:22 (211)	0.198
Alarm to VP in asystole (min:s)	16:14 ± 9:27 (310)	15:59 ± 8:02 (88)	16:20 ± 09:58 (222)	0.857
Alarm to hospital admission (min:s)	60:54 ± 19:22 (535)	58:47 ± 17:58 (157)	60:46 ± 19:53 (378)	0.203
Measures taken by EMS (%)				
Vasopressors	85.2	85.2	85.2	1.000
Amiodarone	36	31.5	37.4	0.129
Intubation	64.5	64.5	64.5	1.000
RACA score	47.54 ± 17.21	47.48 ± 16.84	47.56 ± 17.35	0.952
ECG signs of ACS or diagnosed ACS (%)	18.2	18.2	18.2	1.000
Coronary angiography undertaken (%)	42.4	42.2	42.2	1.000
Mild hypothermia (%)	28.6	28.6	28.6	1.000

ACS acute coronary syndrome, *AH* aspirin and heparin have been given in the prehospital setting, *CPR* cardiopulmonary resuscitation, *defib* defibrillation, *ECG* electrocardiography, *EMS* emergency medical service (without first responder), *noAH* that no aspirin or heparin have been given in the prehospital setting, *RACA score* ROSC after cardiac arrest score, *VF/VT* ventricular fibrillation or ventricular tachycardia

In this registry, prehospital AH administration was associated with favorable neurological outcome, ROSC and survival to hospital discharge. Missing ICD-10 codes impede subgroup analysis stratified by definite diagnoses. However, existing interactions with male sex and bystander CPR in conjunction with published data support the hypothesis that our results are in line with our previous findings showing a benefit of AH administration especially in AMI patients [3, 5]. Further limitations are the low administration rate for AH, missing data on AH dosages and administration time, matching which resulted in the selection of patients with favorable conditions as well as the retrospective design. Our observational findings warrant a randomized clinical trial to assess the efficacy and safety of prehospital AH administration in patients with OHCA.

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-020-06075-6) contains supplementary material, which is available to authorized users.

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Compliance with ethical standards

Conflicts of interest

The authors declare that they have no conflict of interest.

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References

1. Gassler H, Fischer M, Wnent J, Seewald S, Helm M (2019) Outcome after pre-hospital cardiac arrest in accordance with underlying cause. Resuscitation 138:36–41. https://doi.org/10.1016/j.resuscitation.2019.02.039
2. Okubo M, Schmicker RH, Wallace DJ, Idris AH, Nichol G, Austin MA, Grunau B, Wittwer LK, Richmond N, Morrison LJ, Kurz MC, Cheskes S, Kudenchuk PJ, Zive DM, Aufderheide TP, Wang HE, Herren H, Vaillancourt C, Davis DP, Vilke GM, Scheuermeyer FX, Weisfeldt ML, Elmer J, Colella R, Callaway CW, Resuscitation Outcomes Consortium I (2018) Variation in survival after out-of-hospital cardiac arrest between emergency medical services agencies. JAMA Cardiol 3(10):989–999. https://doi.org/10.1001/jamacardio.2018.3037
3. Grabmaier U, Rizas KD, Berghof J, Huflaender Y, Wiegers C, Wakili R, Kaspar M, Angstwurm M, Massberg S, Weckbach LT, Brunner S (2018) Association between survival and non-selective prehospital aspirin and heparin administration in patients with out-of-hospital cardiac arrest: a propensity score-matched analysis. Intensive Care Med 44(4):537–539. https://doi.org/10.1007/s00134-018-5111-2
4. Grasner JT, Meybohm P, Lefering R, Wnent J, Bahr J, Messelken M, Jantzen T, Franz R, Scholz J, Schleppers A, Bottiger BW, Bein B, Fischer M, German Resuscitation Registry Study G (2011) ROSC after cardiac arrest—the RACA score to predict outcome after out-of-hospital cardiac arrest. Eur Heart J 32(13):1649–1656. https://doi.org/10.1093/eurheartj/ehr107
5. Kvakkestad KM, Sandvik L, Andersen GO, Sunde K, Halvorsen S (2018) Long-term survival in patients with acute myocardial infarction and out-of-hospital cardiac arrest: a prospective cohort study. Resuscitation 122:41–47. https://doi.org/10.1016/j.resuscitation.2017.11.047