

# The Emergency Department Arrival Mode and Its Relations to ED Management and 30-Day Mortality in Acute Heart Failure: An Ancillary Analysis From The EURODEM Study

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# Abstract

**Background:** Acute heart failure patients are often encountered in emergency departments from 11% to 57 % using emergency medical services. Our aim was to evaluate the association of emergency department arrival mode with acute heart failure patients' emergency department management and short-term outcomes.

**Methods:** This was a sub-analysis of the European EURODEM study. Data on patients presenting with dyspnoea were collected prospectively from 66 European emergency departments. Patients with emergency department diagnosis of acute heart failure were categorized into two groups: those using emergency medical services and those self-presenting (non-emergency medical service patients). The independent association between emergency medical services use and 30-day mortality was evaluated with logistic regression.

**Results:** Of the 500 acute heart failure patients, 309 (61.8 %) arrived at emergency department by emergency medical services. They were older (median age 80 vs. 75 years,  $p < 0.001$ ) and had more dementia (18.7 % vs. 7.2 %,  $p < 0.001$ ). On admission, emergency medical service patients had more often confusion (43 (14.2 %) vs. 4 (2.1 %),  $p < 0.001$ ) and higher respiratory rate (24/min vs. 21/min,  $p = 0.014$ ; respiratory rate  $> 30$ /min in 17.1 % patients vs. 7.5 %,  $p = 0.005$ ). The only difference in emergency department management appeared in the use of ventilatory support: 78.3 % of emergency medical services patients vs. 67.5% of non-emergency medical services patients received oxygen,  $p = 0.007$ , non-invasive ventilation was administered to 12.5 % of emergency medical service patients vs. 4.2% non-emergency medical service patients,  $p = 0.002$ . Emergency medical service patients were more often hospitalized (82.4 % vs. 65.9 %,  $p < 0.001$ ). The use of emergency medical services was an independent predictor of 30-day mortality (OR=2.96, 95% CI 1.27-6.92,  $p = 0.012$ )

**Conclusion:** Most acute heart failure patients arrive at emergency department by emergency medical services. These patients suffer from more severe respiratory distress and receive more often ventilatory support. Emergency medical service use is an independent predictor of 30-day mortality.

## Background

Acute heart failure (AHF) is a life-threatening condition encountered in emergency departments (ED) worldwide. The proportion of AHF patients arriving at the ED by EMS (emergency medical services) varies from 11% to 57 %<sup>1-7</sup>.

The main complaint of AHF is shortness of breath<sup>3,8</sup>. One of the main goals of AHF management (in addition to stabilisation of hemodynamic) is to relieve patients' symptoms and to reduce fluid overload. Intravenous (IV) diuretics and vasodilators are the mainstay of AHF management<sup>9</sup>. Registries show that approximately 80 % of AHF patients are treated with IV diuretics<sup>1, 10-15</sup>. However, less than half of AHF

patients receive IV vasodilators <sup>1, 10-14, 16</sup>. Non-invasive ventilation (NIV) is administered to 7-20 % of AHF patients <sup>1, 2, 11, 13, 14, 16, 17</sup>.

Earlier studies regarding AHF patients' EMS use have focused on clinical factors associated with the use and the prognostic effects of EMS <sup>4, 5</sup>. The aim of this study was to determine whether the arrival mode is associated with the administration of AHF treatments in ED, in addition to the patient outcomes.

## Methods

This study was a sub-analysis of the prospective, multinational EURODEM study <sup>18</sup>. Data was received from 66 European EDs: Belgium (n=3), Finland (n=5), France (n=5), Germany (n=5), Italy (n=1), the Netherlands (n=16), Romania (n=7), Spain (n=1), Turkey (n=7) and United Kingdom (n=16).

The EURODEM study included patients presenting to ED with shortness of breath, dyspnoea being one of the symptoms listed in the triage on ED admission. The data was collected in three 72-hour periods (February, May and October 2014) by local ED nurses or physicians. ED diagnoses were recorded. The physician made the ED diagnosis based on, patient history, clinical assessment, imaging, and laboratory tests. Patients with ED diagnosis of AHF were included to this analysis. The AHF patients were categorized based on their ED arrival mode: those arriving by EMS (EMS patients) and those self-presenting (non-EMS patients). The collected data included patient characteristics, initial assessment (clinical assessment and vital signs), laboratory tests, ED management, in-hospital outcomes, and 30-day mortality. The 30-day outcome was ascertained by a follow-up phone call. The study was performed in accordance with the Declaration of Helsinki. The approval of local ethics committee was received from all participating centres according to local requirements. In most participating centres patient consent for data collection was received.

For analyses, a systolic blood pressure (SBP) <100 mmHg was considered as 'hypotension' and SBP >140 mmHg as 'hypertension'. Respiratory distress was defined as respiratory rate (RR) > 30 breaths/min. The peripheral oxygen saturation (SpO<sub>2</sub>) was measured after 30-minute oxygenation. Categorical variables are reported as numbers and percentages (%) and continuous variables as medians with interquartile range (IQR). Between-group comparisons were performed with chi-square test for categorical variables and Mann-Whitney U test for continuous variables. For assessment of independent predictors of 30-day mortality, we used forward and backward selection of variables in logistic regression to calculate likelihood ratios, with significance <0.05 for inclusion and >0.1 for elimination. The variables in the selection process were based on clinical relevance and previous literature <sup>19, 20, 21, 22</sup>. To retain adequate sample size, variables with more than 10 % of missing data were excluded. Consequently, the following variables were tested in the selection models: age, gender, ED arrival mode, SBP, heart rate (HR), SpO<sub>2</sub>, sodium, potassium, confusion, a history of chronic obstructive pulmonary disease (COPD) and active cancer. Variables were retained in the final multivariable model if p-value was less than 0.05. IBM SPSS version 25 was used for statistical analysis. A p-value below 0.05 was considered statistically significant.

## Results

The EURODEM study included 2525 patients of which 507 had AHF as ED diagnosis. Data from the arrival mode was missing from seven patients, which were excluded from the analyses. The majority of AHF patients (n=309 (61.8%)) arrived at the ED by EMS. Compared to non-EMS patients, EMS patients were older (median age 80 (71-85) years vs. 75 (65-81) years,  $p<0.001$ ) and more often female (173 (56.4 %) vs. 80 (42.1%),  $p=0.002$ ) (Table 1).

A total of 290 (60.9 %) patient had a previous diagnosis of HF. No significant differences existed between the groups. EMS patients had more often dementia and a history of pulmonary embolism, whereas diabetes was more common in non-EMS patients. No other major differences in the prevalence of comorbidities were observed between the groups (Table 1). The median duration of dyspnoea before ED admission was 3 days in both groups (EMS 3 (1-7) days vs non-EMS 3 (2-10) days,  $p=0.002$ ) (Table 1).

On admission to ED, the median SBP of all AHF patients was 140 (120-159) mmHg. Only 27 (5.5 %) patients had SBP below 100 mmHg, whereas 243 (49.3 %) patients had SBP over 140 mmHg. The median HR of all AHF patients was 88 (75-110) beats per minute (bpm). No significant differences appeared in BP or HR levels between the groups. On admission, EMS patients were more tachypnoeic (RR 24 (19-30) breaths/min vs. 21 (18-26) breaths/min,  $p=0.014$ ). Forty-three (17.1 %) EMS patients had a RR higher than 30 breaths/min compared to 12 (7.5 %) non-EMS patients,  $p=0.005$ . The median SpO<sub>2</sub> after 30 min oxygenation was 94% in both groups. Of all AHF patients, 346 (71.8 %) were reported to have rales on lung auscultation; EMS patients more often (228 (76.8 %) vs. 118 (63.8 %),  $p=0.002$ ). Wheezing was also more common in the EMS group (62 (23.1%) vs. 25 (14.4%),  $p=0.024$ ) (Table 2).

Regarding laboratory tests, NT-proBNP was measured in 122 (24.4 %) AHF patients and BNP in 52 (10.4 %) patients. NT-proBNP was measured significantly more often in EMS patients (Figure 1) and the levels were significantly higher (median 5144 (1846-11205) pg/mL vs 2103 (688-5167) pg/mL,  $p=0.001$ ). The median pH of all AHF patients was 7.40 (7.34-7.45) (Table 2). EMS patients had significantly lower blood pH values (7.38 (7.32-7.44) vs 7.43 (7.37-7.46),  $p=0.002$ ) (Table 2).

Figure 2 shows the frequency of AHF management in the ED. Intravenous diuretics were administered to 335 (68 %) AHF patients, whereas nitrate infusion was administered to 60 (13 %). The only significant difference in the use of ED management between the two groups appeared in ventilatory support, which was significantly more often provided to EMS patients: supplementary oxygen to 242 (78.3%) EMS patients vs. 129 (67.5 %) non-EMS patients ( $p=0.007$ ), and NIV to 38 (12.5 %) EMS patients vs. 8 (4.2%) non-EMS patients ( $p=0.002$ ). In univariate analysis lower SpO<sub>2</sub> ( $p<0.001$ ) and higher respiratory rate ( $p<0.001$ ) were associated to NIV use. Fourteen (2.8 %) patients received mechanical ventilation; no difference appeared between the patient groups (11 (3.6 %) EMS patients vs. 3 (1.6 %) non-EMS,  $p=0.191$ ). Patients reported to have confusion were intubated significantly more often compared to the rest of the AHF patients (10 (21.7 %) patients vs. 4 (0.9 %) patients,  $p<0.001$ ).

Seventy-six percent (n=365) of all AHF patients were hospitalized from the ED, EMS patients more frequently compared to non-EMS (238 (82.4%) vs. 120 (65.9),  $p<0.001$ ). The majority of all AHF patients (291 (58.2%)) were admitted to a ward, EMS patients more often (192 (62.1 %) EMS patients vs. 99 (51.8 %) non-EMS patients,  $p=0.013$ ) (Figure 3).

The median length of hospital stays (LOS) was 7 (2-12) days in both groups (EMS 7 (3-13) days vs. non-EMS 7 (1-11) days,  $p=0.058$ ). The all-cause in-hospital mortality was 6.6 % (33 patients); Twenty-seven (8.7 %) EMS patients and six (3.1 %) non-EMS patients died during hospitalization ( $p=0.014$ ). The 30-day mortality was significantly higher in the EMS group (40 (14.3 %) EMS patients vs. 9 (4.9 %) non-EMS patients,  $p<0.001$ ) (Figure 3). In addition, multivariable logistic regression showed that the arrival by EMS was an independent predictor of 30-day mortality (OR=2.96, 95% CI 1.27-6.92,  $p=0.012$ ). The other independent predictors were female gender (OR 0.46, 95% CI 0.23-0.93  $p=0.031$ ), active cancer (OR 3.44, 95% CI 1.14-10.41,  $p=0.029$ ), confusion (OR 6.45, 95% CI 2.76 -15.08,  $p<0.001$ ), and sodium level (OR 0.90, 95% CI 0.85-0.96,  $p=0.001$ ).

## Discussion

This study describes the association of ED arrival mode with AHF management in the ED and patient outcomes. Firstly, this study shows that in Europe the majority of AHF patients arrived at the ED by EMS. These patients were more likely to be older females with dementia than the patients self-presenting. Secondly, patients arriving at the ED by EMS suffered more often from respiratory distress, and consequently received more often ventilatory support. However, no other differences were observed in the administration frequencies of AHF treatments in the ED. Thirdly, EMS patients had worse short-term outcomes and the use of EMS was an independent predictor of 30-day mortality.

In the present study, the proportion of AHF patients using EMS is among the highest in the literature <sup>1-7,23</sup>. In line with the previous studies, older women were more prone to use EMS <sup>3-5</sup>. However, the comorbidities associated with the EMS use differed between these studies. In our study, EMS patients tended to have more dementia and a history of pulmonary embolism compared to non-EMS patients. In a Finnish study, EMS patients had more often cardiovascular disease and chronic kidney disease (CKD) <sup>3</sup>, in Spain cardiovascular diseases, CKD, COPD, and dementia were more prevalent <sup>4</sup>, and in North America the only more prevalent comorbidity was hypertension <sup>5</sup>. Most AHF patients had a history of HF. Contrary to some of the earlier studies no significant difference occurred between EMS and non-EMS patients <sup>3,5</sup>.

Although most initial parameters, such as SpO<sub>2</sub>, HR or BP, did not differ between the patient groups, EMS patients suffered more often from respiratory distress, had abnormal breath sounds, confusion, higher levels of NT-proBNP, and lower pH, reflecting more severe clinical presentation of AHF, especially pulmonary oedema <sup>24</sup>. As also reported earlier <sup>5</sup>, the EMS patients had shorter duration of symptoms before ED admission, which may also reflect the more severe clinical presentation.

Respiratory distress is one of the most common reasons for EMS use<sup>25</sup>, as also seen in our study. Due to more severe respiratory distress, EMS patients received more often ventilatory support compared to their counterparts. Although, the use of NIV in the EMS group was about the average compared to earlier studies<sup>1, 2, 11, 13, 14, 16, 17</sup>, it was fairly low in light of the ESC guidelines<sup>9</sup>. Naturally, the use of NIV and supplementary oxygen were associated to higher RR and lower SpO<sub>2</sub>. However, one fourth of all the AHF patients in our study had SpO<sub>2</sub> less than 90 % with supplementary oxygen, suggesting that NIV might have been indicated more often in both patient groups. Yet, 14 % of EMS patients were reported to have confusion, one of the contraindications for NIV use, which could partly explain the relatively low frequency of NIV use. Moreover, one fifth of all the patients reported to have confusion were intubated, which was significantly more often compared to the rest of the AHF patients.

Since the clear majority of AHF patients present with congestion without hypoperfusion and hypotension<sup>9, 10, 26</sup>, vasodilators and diuretics are the mainstay of AHF management<sup>9</sup>. Although only 5 % of all AHF patients in our study were hypotensive and half hypertensive, only one patient out of eight received nitrate infusion. The underuse of vasodilators has been observed previously as well<sup>10, 11, 15</sup>. In contrast, diuretics were given to 70 % of patients. All in all, there is room for improvement in the ED management of AHF as also pointed out earlier<sup>4</sup>.

Finally, EMS patients were more often admitted to a ward and, in line with previous studies, had significantly higher in-hospital<sup>4, 7</sup> and 30-day mortality<sup>4, 5, 7, 27</sup>. Indeed, EMS patients seemed more fragile and severely ill<sup>3, 4</sup> and the same factors related to EMS use – female gender and confusion – were also observed among the independent predictors of 30-day mortality. Notably, confusion was a strong marker for increased risk of death as well, which warrants our attention to assess mental state not only in the most severe AHF, i.e. cardiogenic shock<sup>28</sup>, but in all AHF patients. Still, as also shown earlier<sup>5, 7, 27</sup> EMS use remained an independent predictor of 30-day mortality, which may be linked to patients' fragility and illness severity affected by unmeasured and unknown confounders, as well to patient preference. All in all, the selection of AHF patients for EMS transportation by dispatch centres and EMS seems reasonable in Europe.

## Limitations

Some limitations need to be addressed. First, we didn't have information about the criteria for EMS referral in different EMS regions. Second, our data did not include chest x-ray findings even though the clinician used imaging in decision making. Yet, the chest x-ray is known to have limited specificity and sensitivity<sup>9, 17</sup>. Third, the doses of AHF medications were not registered. Those might have differed between EMS and non-EMS patients due to difference in disease severity, but the overall use of AHF medications was similar. Fourth, there was a fair amount of missing data in some of the variables, especially in biochemistry, warranting caution in the interpretation of the results from the multivariable analyses.

## Conclusion

In conclusion, our study shows that the majority of AHF patients arrive at the ED by EMS. Older age, female gender, dementia, confusion, and especially respiratory distress seem to be the driving forces for EMS use. Apart from the more frequent use of respiratory support, the use of AHF treatments in the ED does not differ between EMS and non-EMS patients. EMS patients are more often admitted to a ward and the use of EMS is an independent predictor of 30-day mortality. More prospective research should be done in the pre-hospital phase to discover the reasons for differences in the outcomes between EMS and non-EMS patients.

## Abbreviations

AHF= acute heart failure

ED = emergency department

EMS= emergency medical services

IV = intravenous

NIV= non-invasive ventilation

SBP = systolic blood pressure

RR = respiratory rate

SpO<sub>2</sub>= peripheral oxygen saturation

IQR = inter quartile range

HR= heart rate

COPD= chronic obstructive pulmonary disease

LOS = length of hospital stay

CKD = chronic kidney disease

## Declarations

**Ethics approval and consent to participate:** The study was performed in accordance with the Declaration of Helsinki. Patient consent for data collection was received according to local policies.

**Consent for publication:** Not applicable

**Availability of data and materials:** The EURODEM database is not publicly available.

**Competing interests:** None to declare

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For the remaining authors none were declared.

**Authors contribution:** PH: analysis and interpretation of data, main author of the manuscript. TT: analysis and interpretation of data, critical revision of manuscript. CB: critical revision. RB: critical revision. JC: critical revision. MC: critical revision. LGC: critical revision. AG: critical revision. MK: critical revision. PLM: critical revision. ÒM: critical revision. JT: critical revision. OVM: critical revision. AP: critical revision. FV: critical revision. VPH: critical revision. SL: critical revision.

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EURODEM Study Group members are listed in the Supplemental Digital Content.

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# Tables

<b>Table 1. Patient characteristics</b>							
	<b>All, n=500</b>		<b>EMS, n=309</b>		<b>Non-EMS, n=191</b>		<b>p-value</b>
		missing (n)		missing (n)		missing (n)	
<b>Demographics</b>							
Age, years	78 (69-84)		80 (71-85)		75 (65-81)		<0.001
Duration of symptoms (days)	3 (1-7)		3 (1-7)		3 (2-10)		0.002
Gender (male) n (%)	244 (49.1)		134 (43.6)		110 (57.9)		0.002
<b>Comorbidities, n (%)</b>							
Previous heart failure	290 (60.9)		180 (61.6)		110 (59.8)		0.685
Diabetes	188 (38.2)		100 (32.8)		88 (47.1)		0.002
Hypertension	348 (71.0)		225 (73.8)		123 (66.5)		0.085
Prior atrial fibrillation	175 (35.7)		110 (36.3)		65 (34.8)		0.729
COPD	128 (27.6)		82 (28.8)		46 (25.8)		0.493
Smoker	79 (17.9)	61 (12.2)	49 (18.4)	43 (13.9)	30 (17.0)	15 (7.9)	0.712
Asthma	32 (6.8)		19 (6.5)		13 (7.3)		0.725
Ischemic heart disease	197 (41.6)		120 (41.1)		77 (42.5)		0.757
Dyslipidaemia	168 (35.8)		93 (32.5)		75 (41.0)		0.062
Renal impairment	119 (25.2)		80 (27.4)		39 (21.7)		0.164
Valvular disease	86 (18.1)		57 (19.5)		29 (15.9)		0.333
Anaemia	76 (16.3)		47 (16.4)		29 (16.2)		0.947

Active cancer	30 (6.5)	17 (6.0)	13 (7.3)	0.572
Prior PE	21 (4.3)	19 (6.3)	2 (1.1)	0.007
Obesity	117 (24.9)	75 (25.8)	42 (23.5)	0.574
Dementia	67 (14.3)	54 (18.7)	13 (7.2)	0.001

The values are given either as number (%) or median (interquartile range)

COPD= chronic obstructive pulmonary embolism

PE = pulmonary embolism

<b>Table 2. Clinical characteristics on admission</b>							
	<b>All AHF, n=500</b>		<b>EMS- patients, n=309</b>		<b>Non-EMS- patients, n=191</b>		<b>p-value</b>
<b>Vital signs</b>		Missing (n)		Missing(n)		Missing (n)	
SBP<100 mmHg, n (%)	27 (5.5)		18 (5.9)		9 (4.8)		0.597
SBP>140 mmHg, n (%)	243 (49.3)		146 (47.9)		97 (51.6)		0.421
SBP (mmHg)	140 (120-159)		140 (120-156)		143 (122-162)		0.285
DBP (mmHg)	80 (66-91)		80 (66-92)		80 (67-90)		0.801
Heart rate (bpm)	88 (75-110)		90 (75-110)		85 (75-104)		0.115
Heart rate >100 bpm, n (%)	160 (32.5)		111 (36.4)		49 (26.2)		0.019
Hear rate >120 bpm, n (%)	52 (10.6)		38 (12.5)		14 (7.5)		0.082
Respiratory rate, (per min)	22 (18-28)		24 (19-30)		21 (18-26)		0.014
Respiratory rate >30/min, n (%)	55 (13.3)	89 (17.8)	43 (17.1)	58 (18.8)	12 (7.5)	30 (15.7)	0.005
SpO <sub>2</sub> (%) with supplementary O <sub>2</sub>	94 (90-97)		94 (90-97)		94 (89-96)		0.569
SpO <sub>2</sub> < 90% with supplementary O <sub>2</sub> , n (%)	118 (24.5)		71 (23.7)		47 (25.8)		0.607
Temperature (°C)	36.5 (36.0-36.9)		36.5 (36.0-37.0)		36.5 (36.0-36.8)		0.262
<b>Clinical signs, n (%)</b>							
Rales on auscultation	346 (71.8)		228 (76.8)		118 (63.8)		0.002
Wheezing on	87 (19.7)	58	62	41 (13.2)	25	17 (8.9)	0.024

auscultation		(11.6)	(23.1)		(14.4)		
Peripheral oedema	273 (56.2)		173 (58.1)		100 (53.2)		0.293
Jugular vein distension	110 (25.1)	62 (12.4)	72 (27.4)	46 (14.9)	38 (21.7)	16 (8.4)	0.181
Confusion	47 (9.6)		43 (14.2)		4 (2.1)		<0.001
<b>Laboratory parameters</b>							
NT-proBNP (pg/mL)	3661(1328-10377)	381 (76.2)	5144 (1846-11205)	223 (72.2)	2103 (688-5167)	155 (81.2)	0.001
Creatinine (µmol/L)	101 (78-136)		107 (77-137)		94 (80-131)		0.751
Sodium (mmol/L)	138 (136-141)		138 (135-141)		138 (136-141)		0.476
Potassium (mmol/L)	4.3 (4.0-4.8)		4.3 (4.0-4.8)		4.3 (3.9-4.7)		0.243
CRP (mg/dL)	10 (4-30)		13 (5-41)		8 (3-20)		0.003
pH	7.40 (7.34-7.45)		7.38 (7.32-7.44)		7.43 (7.37-7.46)		0.001
PaCO <sub>2</sub> (mmHg)	38.0 (31.6-45.5)		39.2 (31.5-46.0)		36.0 (32.0-43.1)		0.296
White cell count (10 <sup>9</sup> /L)	9.0 (7.0-11.5)		9.0 (7.0-13)		8.8 (6.8-10.2)		0.070
Haemoglobin (g/dL)	12.3 (10.7-13.9)		12.2 (10.6-13.7)		12.3 (10.7-14.0)		0.626
Haemoglobin <100 g/L, n (%)	58 (12.9)	51 (10.2)	38 (13.8)	33 (10.7)	20 (11.6)	18 (9.4)	0.497

The values are given either as number (%) or median (interquartile range)

SBP= systolic blood pressure

DBP=diastolic blood pressure

SpO<sub>2</sub> = peripheral oxygen saturation

## Figures

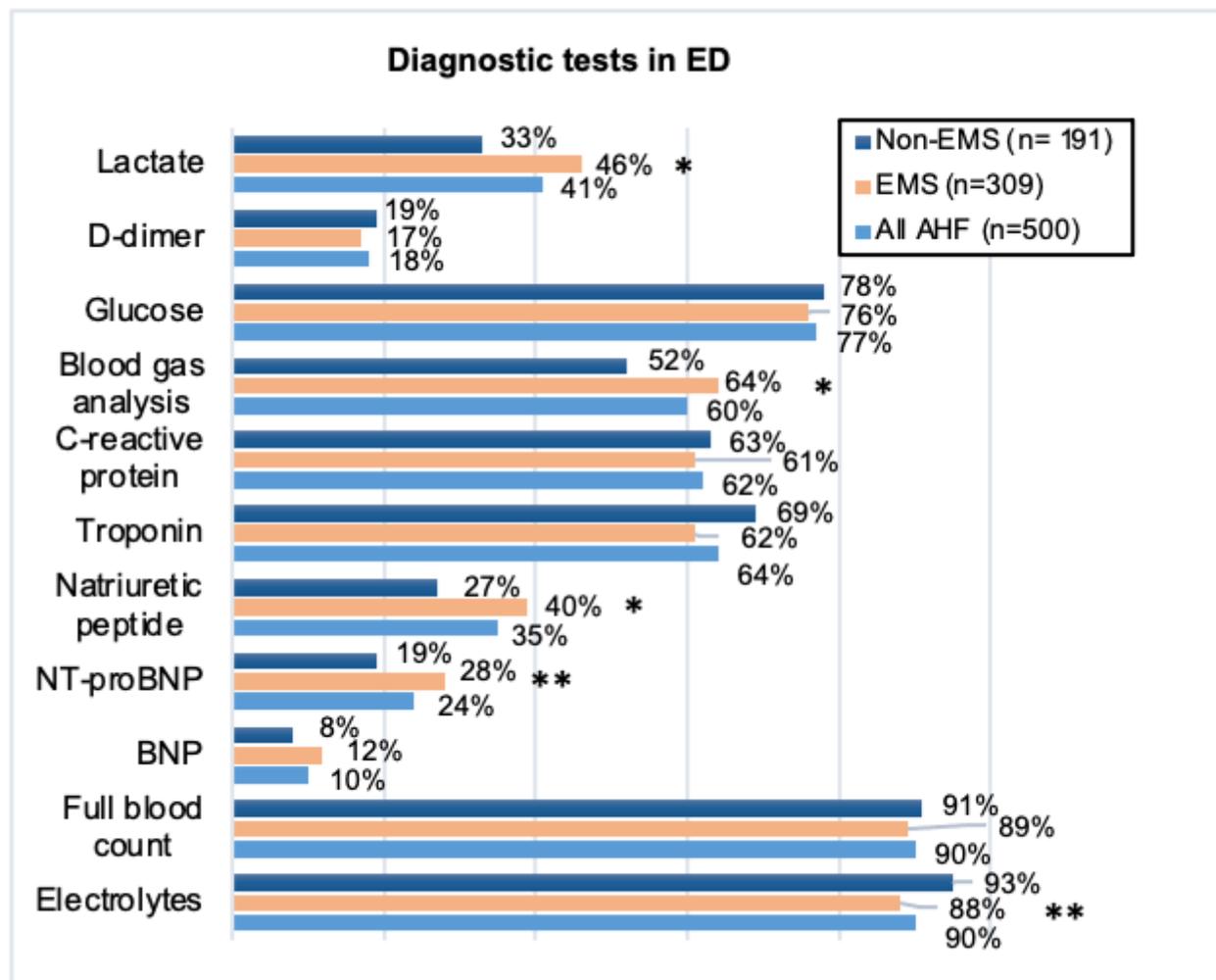


Figure 1

The frequency of diagnostic tests on admission to emergency department \* p <0.01 \*\* p <0.05 P-values are for comparison between EMS and non-EMS patients

## Management in ED

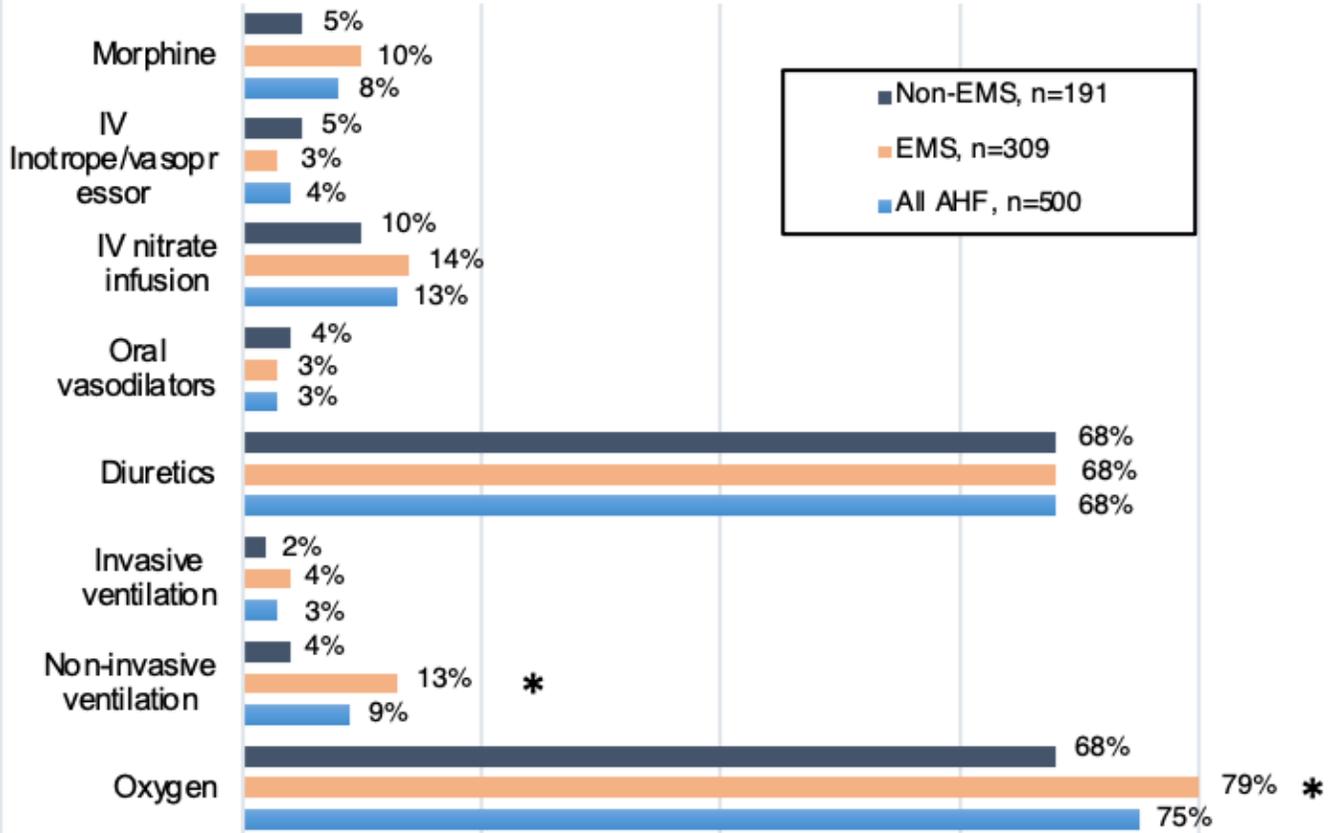
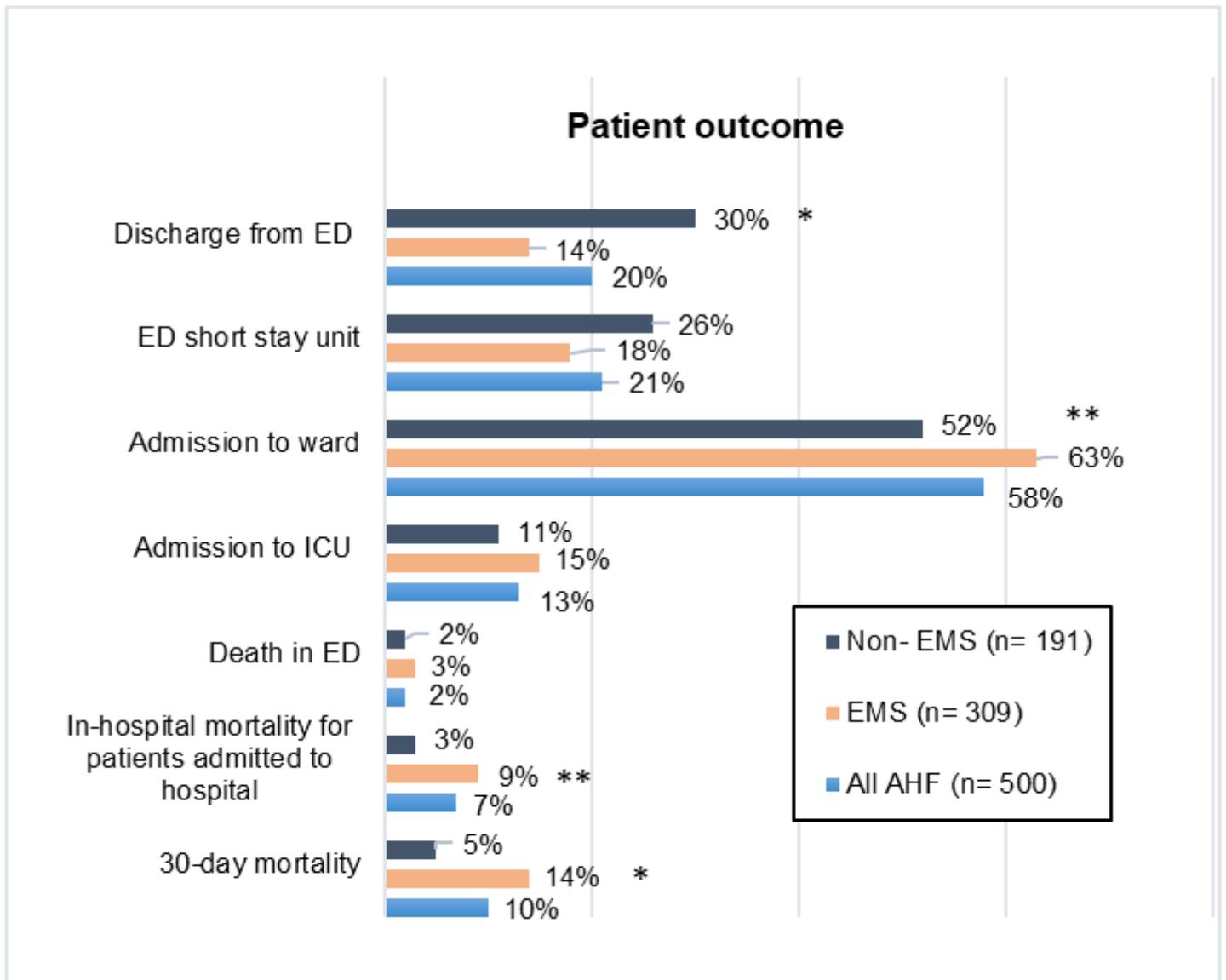


Figure 2

Acute heart failure management on admission to emergency department \*  $p < 0.01$  P-values are for comparison between EMS and non-EMS patients



**Figure 3**

Patient outcomes ICU = intensive care unit, ED= emergency department \* p <0.001 \*\* p <0.05 P-values are for comparison between EMS and non-EMS patients

## Supplementary Files

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- [EURODEMstudygroupmembers.docx](#)