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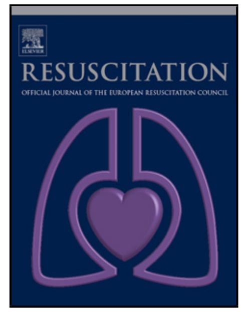

Title: New treatment bundles improve survival in Out of Hospital Cardiac Arrest patients: a historical comparison

Author: Leonello Avalli Tommaso Mauri Giuseppe Citerio Maurizio Migliari Anna Coppo Matteo Caresani Barbara Marcora Gianpiera Rossi Antonio Pesenti

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New treatment bundles improve survival in Out of Hospital Cardiac Arrest patients: a historical comparison

Leonello Avalli*, Tommaso Mauri§, Giuseppe Citerio*, Maurizio Migliari*, Anna Coppo*, Matteo Caresani$, Barbara Marcora*, Gianpiera Rossi*#, Antonio Pesenti*§#

Institutions* Dipartimento di Emergenza e Urgenza, Ospedale San Gerardo , Monza, Italy

§ Dipartimento di Scienze della Salute, Università Milano-Bicocca, Monza, Italy

Azienda Regionale Emergenza Urgenza, Regione Lombardia

$ AAT Monza Brianza

Corresponding author

Leonello Avalli MD
e-mail: l.avalli@hsgerardo.org
phone: 0039392334325 fax: 0039392334331
UOS Anestesia e Terapia Intensiva CCH
Ospedale S.Gerardo, via Pergolesi 33, Monza, Italia

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Abstract

Introduction. Before the introduction of the new international cardiac arrest treatment guidelines in 2005, patients with out-of-hospital cardiac arrest (OHCA) of cardiac origin in Northern Italy had very poor prognosis. Since 2006, a new bundle of care comprising use of automated external defibrillatiors (AEDs) and therapeutic hypothermia (TH) was started, while extracorporeal CPR program (ECPR) for selected refractory CA and dispatcher-assisted cardio-pulmonary resuscitation (CPR) was started in January 2010.

Objectives: We hypothesized that a program of bundled care might improve outcome of OHCA patients.

Methods: We analyzed data collected in the OHCA registry of the MB area between September 2007 and August 2011 and compared this with data from 2000 to 2003.

Results: Between 2007 and 2011, 1128 OHCAs occurred in the MB area, 745 received CPR and 461 of these had a CA of presumed cardiac origin. Of these, 125 (27%) achieved sustained ROSC, 60 (13%) survived to 1 month, of whom 51 (11%) were discharged from hospital with a good neurological outcome (CPC ≤2), and 9 with a poor neurological outcome *(*CPC >2)*.*

Compared with data from the 2000-2003 periods, survival increased from 6.1% to 13.01% ($p<0.0001$). In the 2007-2011 group, low-flow time and bystander CPR were independent markers of survival.

Conclusions: OHCA survival has improved in our region. An increased bystander CPR rate associated with dispatcher-assisted CPR was the most significant cause of increased survival, but duration of CA remains critical for patient outcome.

Introduction

Outcome from out-of-hospital cardiac arrest (OHCA) depends on a sequence of interventions called the “chain of survival” (1,2), which comprehends early access to the Emergency Medical System (EMS), early cardiopulmonary resuscitation (CPR), early defibrillation and appropriated and updated advanced care (3). Studies demonstrated that use of automated external defibrillators (AEDs) (4) coupled with widespread public access to AEDs (5), early bystander CPR (6-9), and advanced interventions such as therapeutic hypothermia (10,11), careful control of normocapnia (12,13) and normoxia (13-15), early referral to tertiary centers (16,17) and ECPR for selected refractory CA (18) might improve outcome. However, a recent study seriously questioned the utility of therapeutic hypothermia, while still stressing the utility of strict temperature control in the first 72 hours after OHCA (19). Additional factors correlated with survival include presence of witnesses, the underlying clinical condition of the patient and the presentation rhythm (20).

Pushed by these results as presented by guidelines (21), over the last ten years, the public health administration of Lombardia (a highly populated northern Italian region) has invested to improve EMS care for OHCA patients. The prehospital phase of OHCA care was improved from the beginning of 2007, by equipping every ambulance with an AED. A program of dispatcher assisted CPR and the availability of public access AEDs (PAD) was started by June 2010. The hospital phase of OHCA care in the tertiary care referral center for the Monza and Brianza area within Lombardia (i.e. the San Gerardo Hospital), was improved with adoption of therapeutic hypothermia in January 2006, while E-CPR (extracorporeal cardiopulmonary resuscitation) was used for selected refractory OHCA patients from January 2010 (22). In 2000 and 2003, before the implementation of the abovementioned interventions, we performed two studies evaluating care and outcome in OHCA, in the same area. In those studies we monitored: ALS rescue , time to arrival on scene, bystander CPR, rate of defibrillation, ROSC on scene, total ROSC and survival at

1 month (23,24). The survival rate reported by those studies was around 5%, without increase of survival despite the increased number of CA rescued by Advanced Life Support (ALS) teams. The aim of this study is to evaluate whether the introduction of new treatment bundles, therapeutic hypothermia and ECPR improved the outcome of OHCA patients in the Monza and Brianza area when compared to historical controls (23,24).

Methods

Study design. We retrospectively analyzed data prospectively collected for administrative and statistical purposes in the OHCA registry of the Monza and Brianza area, an urban area within Lombardia with 441 000 inhabitants covered by a single emergency dispatch center. Data were collected in accordance with the Utstein Style (25).

All adult patients suffering from OHCA and rescued by EMS teams in the Monza and Brianza area from September 2007 to August 2011 were enrolled in this study. Exclusion criteria were: OHCA of non-cardiac origin (terminal neoplastic illness, trauma, primary respiratory arrest, drug overdose, upper airway obstruction and drowning) and OHCA not resuscitated for futility (i.e. obvious signs of death such as rigor mortis, hypostatic stains). All enrolled patients were submitted to CPR , those with ROSC were transported by EMS teams to the San Gerardo hospital and admitted to the Emegency Department. The remaining patients after 30 min of CPR without ROSC were declared expired in field. The patients with refractory CA but with ECPR criteria were transported to ED, connected to ECMO and subsequently admitted to the Intensive Care Unit (ICU).

Data collection. For each patient, we collected age, sex, past medical history, presence of witnesses, bystander-performed CPR before EMS arrival, time between call and EMS team arrival, time between call and first shock for patients with ventricular fibrillation or pulseless ventricular tachycardia (VF/VT), use of AED by EMS, indication to defibrillation by AED and first rhythm recorded, return of spontaneous circulation (ROSC) rate, no-flow time (defined as the time between loss of consciousness and start of EMS/ALS-performed CPR or time without flow even in the presence of lay CPR), low-flow time (defined as the time between start of EMS/ALS-performed CPR and ROSC) ALS team presence rate, defibrillation rate, therapeutic hypothermia rate, intra-aortic balloon counterpulsation (IABP) rate, hemofiltration (CVVH) rate, diagnostic cardiology rate and modality of revascularization, ICU and hospital length of stay, cerebral performance category (CPC) score at hospital discharge and survival at 1 month.

Outcome measurements. We compared the present study data with those collected in the 2 previous studies performed in the same area (23,24). The primary endpoints were 1 month survival and hospital discharge with minimal neurologic impairment (CPC≤2). The CPC values are: 1, good recovery; 2, moderate disability; 3, severe disability (minimally conscious state, severe motor deficit, aphasia and need for continuous help); 4, persistent vegetative state and 5, death or brain death. The secondary endpoints were the identification of factors influencing mortality.

Statistical analysis. Continuous variable are reported as mean ± standard deviation (SD) and categorical variables as numbers and percentage. Comparison between groups was performed using Student's T-test or Fisher's test and chi square test with 2x2 contingency tables. Backward multivariate logistic regressions were performed to identify factors independently associated with worse outcomes. A p value less than 0.05 was considered statistically significant. All statistical analyses were performed with the Statistical Package for Social Science version 20 for Windows (SPSS inc., Chicago, IL, USA).

Our Institutional Review Board approved the study and informed consent was waived due to the observational nature of the study.

Results

During the 48-month study period, from September 2007 to August 2011, a total of 1128 OHCA events occurred in the area covered by the EMS teams of the Monza and Brianza area (Figure1). The mean age was 72±15 years and 60% were male. Time from call to EMS arrival on the scene was 9.2 ± 4.5 min. In 383 patients, resuscitation was not attempted for futility. 745 OHCA patients received resuscitation maneuvers, 461 of them with a presumed cardiac origin of CA, were enrolled in this study. 317 were transported to the hospital after achieving ROSC or during CPR. Among enrolled patients, OHCA was witnessed in 275 cases (60%), 124 (27%) received bystander CPR and 133 (29%) had VF or VT as first rhythm. 125 (27%) achieved sustained ROSC, 60 (13%) survived at 1 month and 51 of them (11%) were discharged from hospital with CPC ≤2, 9 with CPC >2. Of the 18 patients who had refractory OHCA and were connected to ECMO circuit during CPR, only one was discharged from hospital with CPC = 1 (22).

Table 1 shows different characteristics and survival rates between patients enrolled in this study and OHCA patients from the two previous studies (23,24). There was a significant increase in terms of age, Asystole/PEA rate, bystander CPR, defibrillation rate, ROSC on scene and total ROSC and an increase in 1 month survival from the previous studies. There was a significant reduction of witnessed CA, time of arrival to the scene and a decrease in rescue by ALS teams rate.

The EMS crews applied AED on 348 (75%) patients, while 222 (48%) were rescued by ALS and in 86 (19%) the first rhythm was analyzed first by the ALS crews. In total, 100% of patients were rescued with AED or by ALS. Data about the entire population studied are indicated in Table 2. There were significant differences between patients with sustained ROSC versus no-ROSC in terms of age, witnessed CA, bystander CPR, ALS rescue, presenting rhythm, call-to-first shock time and No-Flow time. (Table 2).

Data of patients admitted to the ICU are indicated in Table 3. There was a significant difference in favor of ICU survivors in terms of bystander CPR, No-Flow and Low-Flow time, but not in application of therapeutic hypothermia, ICU stay, hospital stay, 1 month survival and survival with CPC ≤ 2.

In the multivariate logistic regression analysis we could demonstrate that lack of witnesses, asystole/PEA at the first analysis, no bystander-initiated-CPR, and No-Flow time were independent predictors of no-ROSC and that no bystander-CPR and Low-Flow time were independent markers of mortality and of CPC >2 at hospital discharge (Tab.4)

Discussion

In this retrospective study, we analyzed the results from the area covered by a single dispatch center to EMS teams (Monza and Brianza area) before and after the introduction of advanced procedures for the treatment of OHCA. Data were recorded over four years and compared to historical controls from previous studies. The use of AED on all ambulances came on stream in late 2006, while the installation of PAD plus dispatcher-assisted CPR was introduced in 2010. Moreover, as mentioned above, therapeutic hypothermia and ECMO have become standard of care in the San Gerardo Hospital's ICUs respectively in 2006 and 2010. We observed an increase in in-hospital 1 month survival from 6,1 before 2003 (21,22) to 13% in 2007-2011. This increase was observed despite an increase in median age, an increase in asystole/PEA rate, a decrease in witnessed CA rate and a decrease in ALS rate. Other variables, such as bystander CPR and defibrillation rate otherwise increased. In several studies performed in recent years bystander CPR and the quality of CPR were identified as the major contributor to increased survival (7-9). In a recent study from South Korea (26) an implementation of dispatcher-assisted CPR program determined an increase in survival rate from 7.1% to

9.4% after two years. Similarly, we observed an increase in the number of patients who achieved sustained ROSC and 1 month survival after implementation of a dispatcher-assisted program. This is most likely due to an increase in bystander CPR rate before EMS arrival. The independent variables associated with no ROSC are the lack of witnesses, asystole/PEA, the percentage of bystander-CPR and the “no-flow” time. We also observed an increase in the number of patients rescued by ALS crew compared to 2000 but a substantial reduction of the same compared to 2003. The influence of these factors on the increase of patients who reached a sustained ROSC could be explained either by a reduction in the time of arrival on scene and/or by an early defibrillation administered by the BLS crew. We observed more that doubling of survival at one month with a vast majority of patients who reached a CPC score ≤ 2.

Surprisingly, there was no statistical difference between patients treated with therapeutic hypothermia and those treated only with fever control, This finding is influenced by the reduced numbers of cases and by the the fact that there might have been a bias in the decision to maintain therapeutic hypothermia in less severe patients such as those with very low time of CPR. Another explanation could be that in the presence of prolonged no-flow and low-flow times the application of hypothermia does not result in substantial advantages. In the recent RCT study by Nielsen and co-workers (19) no differences were found in survival between two ranges of temperature post CA, moving the attention on the control of temperature rather than on the beneficial effect of the hypothermia per se. The only variables in our study that are different from patient who survived CA after admission to ICU are bystander CPR rate, No-Flow and Low-Flow time. The independent variables associated with 1 month survival and with CPC ≤ 2 are bystander CPR and Low-Flow time. These findings seem to corroborate the possibility that an early CPR, possibly assisted by EMS dispatcher could reduce the duration of low vital organs and cerebral perfusion.

Study limitations: the main limitation of the study is the retrospective nature of the analysis, although the data were collected prospectively in the EMS register. There was not a central register for OHCA in the ICU's, but every data of hospitalization was recorded in a computerized database. The second limitation is that this is an historical comparison before and after the implementation of new guidelines on the treatment of CA, with a relatively small number of patients analysed. However, randomized studies on such bundles are very unlikely to be performed and before and after quality improvement studies have the value of returning a real life picture that may be nearer to everyday clinical practice.

Conclusions

The data reported in this study show that the determinants of increased survival in this historical period of time in victim of cardiac arrest of presumed cardiac origin were the increased bystander CPR rate and the duration of CA. In the urban area analysed it is difficult to further reduce the rescue time, while it is desirable to increase the numbers of CPR performed by bystanders with an extensive educational program associated with greater extent of AEDs available in the area.

Conflict of interest statement

None to declare.

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Table 1: Differences of treatments and survival rates of between patients enrolled in this study and OHCA patients from the two previous studies conducted in the same area

Table 2: Data on the entire population studied

Table 3: Multivariate logistic regression analysis for no-ROSC

Table 3: Data of patients admitted to the ICU

Table 4: Multivariate logistic regression analysis for no ROSC, 1 month death and Hospital discharge with CPC ≤ 2

Fig 1: Utsteyn Style diagram for out-of-hospital cardiac arrest patients in Monza Brianza area.

	2000 n=178	2003 n=174	2011 n=461	P 2011 vs 2000	P 2011 vs 2003
Age, years ± SD	70.2 ± 15	70.9 ± 15	73 ± 16	**0.021**	0.25
Males, n (%)	119 (67)	102 (59)	285 (62)	0.272	0.467
Witnessed CA, n (%)	129 (72)	147 (84)	276 (60)	**0.003**	**0.0001**
Asystole/PEA, n (%)	76 (47)	115 (66)	309 (67)	**0.0001**	0.850
Ventricular Fibrillation, Tachycardia, n (%)	40 (22)	46 (26)	133 (29)	0.112	0.621
Not revealed, n (%)	62 (35)	6 (3)	25 (5)	**0.0001**	0.31
Time of arriving on scene, min. ± SD	8.5 ± 3.5	10.1 ± 5.4	9.1 ± 4.5	0.075	**0.0375**
Bystander CPR, n (%)	27 (15)	38 (22)	124 (27)	**0.001**	0.220
ALS rescue, n (%)	45 (25)	159 (91)	222 (48)	**0.0001**	**0.0001**
Defibrillation rate, n (%)	37 (92)	44 (96)	133 (100)	**0.045**	0.427
ROSC on scene, n (%)	24 (13)	40 (24)	94 (21)	**0.052**	0.513
ROSC, n (%)	27 (15)	40 (24)	117 (26)	**0.005**	0.606
Outcome at 1 month, n (%)	10 (5.6)	6 (3.4)	60 (13.01)	**0.006**	**0.0002**

Tab 1

OHCA of Cardiac Origin n=461	OHCA ROSC n=117	OHCA no ROSC n=344	p value
Age, yrs ± SD	66.6 ± 13.0	76.4 ± 14,8	**0.0001**
Male, n (%)	76 (65)	203 (59)	0,274
Witnessed, n (%)	102 (87)	183 (53)	**0.0001**
Bystander CPR, n (%)	60 (51)	65 (19)	**0.0001**
PAD, n (%)	2 (2)	4 (1)	0,646
AED, n (%)	94 (80)	254 (74)	0,172
ALS rescue, n (%)	76 (65)	146 (42)	**0.001**
Presenting rhythms FV/TV, n (%)	79 (67)	54 (16)	**0.0001**
Call/first shock, min ± SD (when indicated)	5.9 ± 4.7	9.5 ± 3.9	**0.0001**
No-Flow time, min ± SD	4.9 ± 5.4	11.1 ± 4.9	**0.0001**

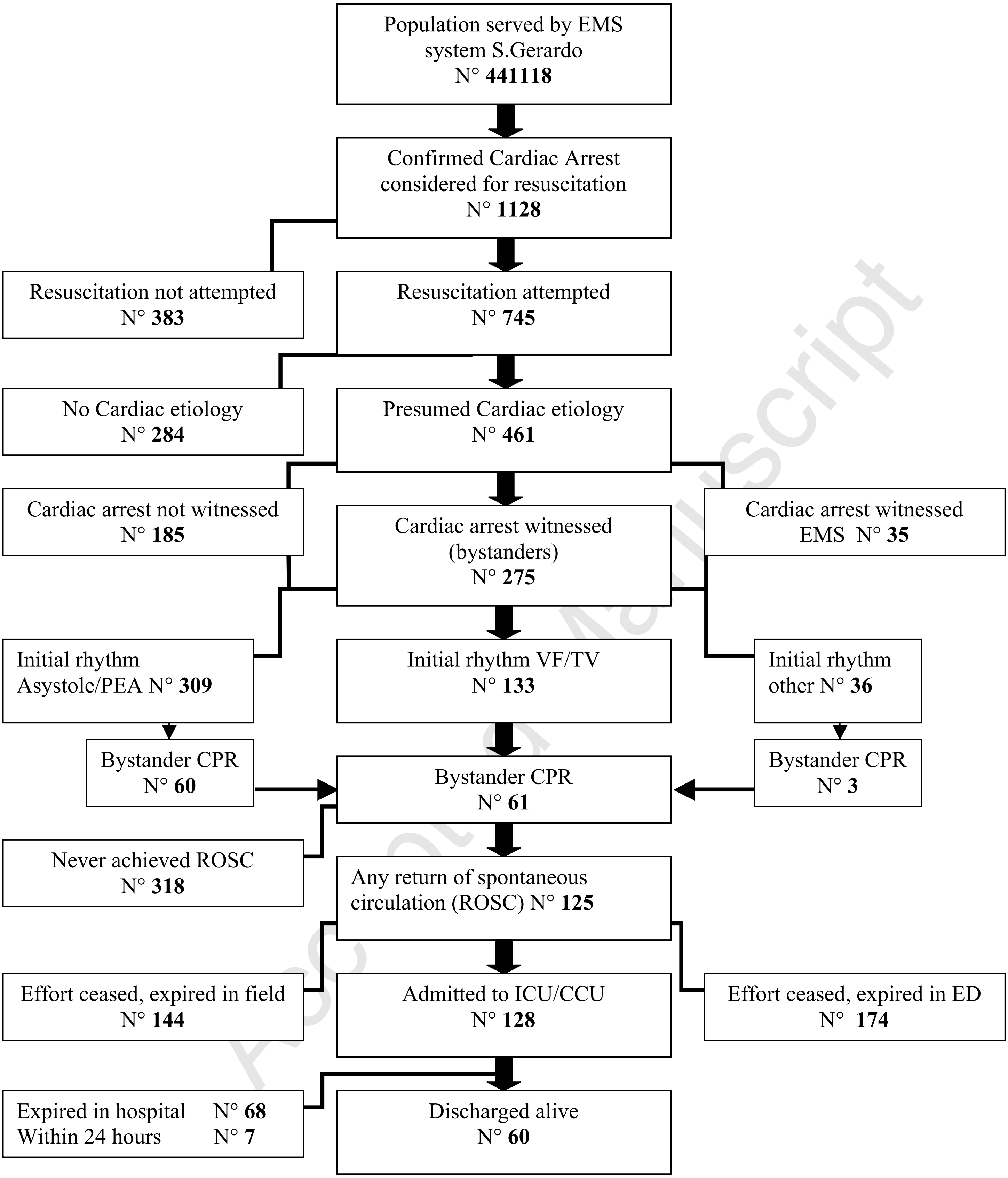
Tab2

Patients ICU admitted	OHCA +ROSC 28th days Survived n = 60	OHCA Dead n = 68	p value
Age, yrs ± SD	64.0 ± 15	65.5 ± 12	0.538
Male, n (%)	43 (71)	52 (76)	0.243
Witnessed, n (%)	56 (93)	55 (81)	0.065
Bystander CPR, n (%)	39 (65)	23 (34)	**0.0007**
AED, n(%)	49 (83)	50 (73)	0.297
ALS rescue, n(%)	41 (68)	46 (68)	1.000
No-flow time, min ± SD	5.1 ± 4.1	8.5 ± 5.7	**0.0005**
Low-flow time, min ± SD	15.5 ± 15.3	38.9 ± 29.5	**0.0001**
Presenting rhythms FV/TV, n (%)	46 (77)	42 (62)	0.086
Hypothermia	41 (68)	58 (85)	**0.033**
Diagnostic and therapeutic manoeuvres, n (%)			
Emergency Coronary Angiography	41 (68)	43 (63)	0.580
Primary PCI	26 (43)	33 (48)	0.597
Coronary Artery Bypass Grafting	9 (15)	3 (4)	0.065
ICU stay, days ± SD	9.4 ± 8.1	5.4 ± 8	**0.049**
Hospital stay, days ± SD	22.9 ± 13.4	5.8 ± 9.3	**0.0001**
1 month survival, n (%)	60 (100)	2 (3)	**0.0001**
Hospital discharge with CPC ≤ 2, n (%)	51 (85)	0 (0)	**0.0001**
Use of IABP, n (%)	9 (15)	19 (28)	0.089
Use of CVVH, n (%)	0 (0)	3 (4)	0.247

Tab3

No ROSC n=461	**p**	**OR**	**95% CI inf**	**95% CI sup**	**1 month death n=128**	**p**	**OR**	**95% CI inf**	**95% CI sup**	**Hospital discharge with CPC ≤ 2**	**p**	**OR**	**95% CI inf**	**95% CI sup**
Age	0.346					0.358					0,239			
No Bystander CPR	**0.040**	2.001	1.033	3.876		**0.052**	2.899	0.990	8.486		**0,003**	4.587	1,687	12.473
No witnessed CA	**0.050**	2.338	0.999	5.472		0.523					0,428			
Asystole/PEA	**0.0001**	7.766	4.076	14.797		0.069					0,177			
No-Flow Time	**0.0001**	1.224	1.134	1.322		0.075					0,158			
Low-Flow time	na	na	na	na		**0.0001**	1,069	1,039	1,001		**0,0001**	1,053	1,026	1,080

Tab 4


Population served by EMS system S.Gerardo N° 441118
Confirmed Cardiac Arrest considered for resuscitation N° 1128
Resuscitation not attempted N° 383
Resuscitation attempted N° 745
No Cardiac etiology N° 284
Presumed Cardiac etiology N° 461
Cardiac arrest not witnessed N° 185
Cardiac arrest witnessed (bystanders) N° 275
Cardiac arrest witnessed EMS N° 35
Initial rhythm Asystole/PEA N° 309
Initial rhythm VF/TV N° 133
Initial rhythm other N° 36
Bystander CPR N° 60
Bystander CPR N° 61
Bystander CPR N° 3
Never achieved ROSC N° 318
Any return of spontaneous circulation (ROSC) N° 125
Effort ceased, expired in field N° 144
Admitted to ICU/CCU N° 128
Effort ceased, expired in ED N° 174
Expired in hospital N° 68
Within 24 hours N° 7
Discharged alive N° 60