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Prospective assessment of integrating the existing emergency medical system with automated external defibrillators fully operated by volunteers and laypersons for out-of-hospital cardiac arrest: the Brescia Early Defibrillation Study (BEDS)

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KEYWORDS
Out-of-hospital cardiac arrest;
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Aims There are few data on the outcomes of cardiac arrest (CA) victims when the defibrillation capability of broad rural and urban territories is fully operated by volunteers and laypersons.
Methods and results In this study, we investigated whether a programme based on diffuse deployment of automated external defibrillators (AEDs) operated by 2186 trained volunteers and laypersons across the County of Brescia, Italy (area: 4826 km^2; population: 1 112 628), would safely and effectively impact the current survival among victims of out-of-hospital CA. Forty-nine AEDs were added to the former emergency medical system that uses manual EDs in the emergency department of 10 county hospitals and in five medically equipped ambulances. The primary endpoint was survival free of neurological impairment at 1-year follow-up. Data were analysed in 692 victims before and in 702 victims after the deployment of the AEDs. Survival increased from 0.9% (95% CI 0.4–1.8%) in the historical cohort to 3.0% (95% CI 1.7–4.3%) ($P = 0.0015$), despite similar intervals from dispatch to arrival at the site of collapse [median (quartile range): 7 (4) min vs. 6 (6) min]. Increase of survival was noted both in the urban [from 1.4% (95% CI 0.4–3.4 %) to 4.0% (95% CI 2.0–6.9 %), $P = 0.024$] and in the rural territory [from 0.5% (95% CI 0.1–1.6%) to 2.5% (95% CI 1.3–4.2%), $P = 0.013$]. The additional costs per quality-adjusted life year saved amounted to €39 388 (95% CI €16 731–49 329) during the start-up phase of the study and to €23 661 (95% CI €10 327–35 528) at steady state.
Conclusion Diffuse implementation of AEDs fully operated by trained volunteers and laypersons within a broad and unselected environment proved safe and was associated with a significantly higher long-term survival of CA victims.

Introduction

The use of automated external defibrillators (AEDs) by emergency medical technicians, firefighters, and policemen in the setting of out-of-hospital cardiac arrest (CA) has been introduced several years ago.[1–5] Integrating defibrillation by non-medical personnel within existing resuscitation programmes has met with conflicting results. Some studies suggest that the use of AEDs improves CA survival rates[6–8] and others show no or little improvement.[9–12]

The recent development in AED technology has enabled the potential use of these devices by law enforcement personnel and preliminary data collected in selected environments have shown that such use is safe and effective.[13–15] Recent reports focusing on early defibrillation attempted by trained and equipped volunteers within structured response systems have shown that public access defibrillation (PAD) using AED technology is safe and effective.[16] There are few data on the outcomes when the entire defibrillation capability of broad rural and urban territories is fully operated by volunteers and laypersons.[17,18]

Recently, the Italian government has promulgated a law which allows the use of AEDs by non-medical personnel

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across the country. Following this new legislation, we have conducted a study to evaluate whether a programme based on diffuse deployment of AEDs fully operated by a large number of trained volunteers and laypersons across the largest Italian county would increase the current survival among victims of out-of-hospital CA. The present manuscript reports the results of this study.

Methods

Study design

Diffuse deployment of AEDs operated by trained volunteers and laypersons was introduced across the County of Brescia, Italy, in January 2000. The county area is 4826 km^2 wide (1.6% of the Italian territory), comprises a population of 1 112 628 inhabitants (density: 234 inhabitants/km^2), and since 1992 has been served by an emergency medical service (EMS) system co-ordinated by one single dispatch centre. During 9 years preceding the beginning of the present study, the defibrillation capability of the EMS had consisted of manual defibrillators located in emergency departments of the 10 county hospitals and in five medically equipped ambulances. Before January 2000, the defibrillation programme across the county was exclusively operated by medical teams.

Entry criteria and collection of data

Included in the study were consecutive patients who, outside of the county hospitals, had been unconscious and unresponsive either suddenly or after a brief prodrome, had no palpable pulse, and had no spontaneous respiration. Excluded were patients who, in spite of signs of arrest, were <9 years of age, who had trauma, drug overdose, poisoning, drowning, exsanguination, electrocution, and asphyxia. For patient data collection, the Utstein definitions[19] were used, even though the recommended Utstein template was not fully adopted. The neurological function was tested using the scale of Cerebral Performing Category.[20] All patient data collected at the site of collapse, during hospitalization, and follow-up, were recorded on standardized forms and entered into a central database for analysis. The study had full research Ethics Committee approval.

Historical study phase

Between June 1997 and May 1999, the following parameters were collected throughout the county area to generate the working hypothesis for the prospective cohort: number of dispatched out-of-hospital CA, 692 (0.3 per year per 1000 inhabitants); number of outdoor CA, 100 (14.5%); time from call-to-arrival at the site of collapse by the first responder (partial response time), 7.4 ± 3.9 min; number of patients surviving free of neurological impairment at 1 year from collapse, 6 (0.9%). Two more parameters, not available in the historical cohort, were collected during a 'warm-up' pilot study phase performed during 6 months (between January and June 2000) preceding the beginning of the prospective study phase: the time between collapse and defibrillation option in the subgroup (110 of 176, 62.5%) of witnessed victims (total response time), 17.3 ± 13.6 min and the proportion of shockable rhythms at the time of ECG recording from the AEDs, 53 of 176 (30.1%). Victims of CA during this warm-up study phase were not included in the final analysis.

Prospective study phase

The prospective study phase began on 1 July 2000, after completion of a training and certification process involving 2186 volunteers and laypersons in the whole county. Training and certification also involved 152 paramedics of the emergency department in the various county hospitals. Forty-nine AEDs (one every 22 707 inhabitants) were added to the formerly available EMS. According to the probability of indoor and outdoor events, it was decided that ~85% of all AEDs would be operated by the new response system, whereas 15% would be available in key locations of public access areas. Therefore, 42 devices were given to ambulances or ambulatory services operated by associations of volunteers active throughout the county, of which nine within the urban territory (population: 194 697; area: 91 km^2; density: 2140 inhabitants/km^2) and 33 in the rural territory (population: 917 931; area: 4735 km^2; density: 194 inhabitants/km^2), whereas seven devices (three within the city limits and four in the countryside) were located in critical areas with high population flow for PAD. The rural territory comprised 37 communes with a population between 3264 and 53 118 (median 22 793) inhabitants.

Operational plan

Before January 2000, suspected reports of CAs to the dispatch centre resulted in activation of the nearest medically equipped ambulance, if available, or any of the 27 ambulances not provided with defibrillator capability for transportation to the nearest hospital. From January 2000, calls to the dispatch centre reporting a suspected CA resulted in activation of the nearest emergency system provided with mobile or fixed defibrillation capability as well as of a medically equipped ambulance.

Training and equipment of responders

The training programme was conducted by 14 qualified instructors during 5 h of theory and practical instruction, including training in basic life support. Certification for use of AEDs to all qualifying persons was under the medical responsibility of the director of the emergency medical department.

The devices used were Heartstart FR automated biphasic defibrillators (Philips Medical Systems, Heartstream Operation). All data recorded from the cards under device activation were downloaded for analysis.

Follow-up

All survivors of CA free of neurological impairment were followed by means of regular outpatient visits at months 1, 3, 6, and 12, and every 6 months thereafter. In the case of death, care was taken to draw the exact time and the circumstances leading to death by direct access to hospital files, when available, or by interviewing a witness or a close relative of the patient. Using this method, patients were followed during 58 ± 11 months (median 52 months) in the historical cohort and during 18 ± 13 months (median 16 months) in the prospective cohort.

Economic analysis

Economic data were collected prospectively as an integral part of the trial from the perspective of the government healthcare payer as a study endpoint. Resource use included purchase and updating of AEDs, costs of trainings, diagnostic procedures, cardiac surgical procedures, ICD implants, outpatient visits, rehabilitation, and re-hospitalization and was collected before discharge and at months 3, 6, 12, 18, and 24.[18] Hospital price weights were calculated for hospital resources according to the Italian patient-level itemized costing system[21,22] (Appendices 1 and 2). Costs of start were calculated during the first year of the study conduction (start-up phase), whereas costs of maintenance were calculated during each subsequent year (steady-state phase).

Study endpoints

The primary study endpoint was comparative survival free of neurological impairment at 1-year follow-up in the prospective vs. the historical cohort. Secondary endpoints included: (i) comparative survival free of neurological impairment at 1-year follow-up in the prospective vs. the historical cohort within the urban territory; (ii) comparative survival free of neurological impairment at 1-year

follow-up in the prospective vs. the historical cohort within the rural territory; (iii) in the prospective cohort, survival free of neurological impairment at 1-year follow-up between CA victims receiving defibrillation option within 8 min and those receiving defibrillation option after 8 min from witnessed collapse;[23] and (iv) the cost-effectiveness of introducing the new AED programme.

Statistical analysis

On the basis of the assumption that the partial and total response times would not be longer than those from the historical and pilot study phase, respectively, we anticipated a 0.9% baseline survival rate free of neurological impairment at 1-year follow-up in the prospective study. We postulated that the introduction of 49 AEDs in the Brescia County would increase by 7.4 per year or more the number of CA victims surviving at 1-year follow-up free of neurological impairment. This figure was calculated based on a mean probability of 7.06 CA events per year collectable per device (i.e. 346 CA events per year in the historical group divided by 49 AEDs), a 30% probability of finding a shockable rhythm at the time of ECG recording by the device (as drawn from the pilot study phase), a 4.0% survival probability at discharge from hospital,[23,24] a 3.0% probability of survival at 1-year follow-up,[23] and an 80% device coverage capability for the total year time.

We estimated that the smallest number of patients required to establish a 95% confidence interval with a minimum width of 5% around a point of estimate of 5% would be 478 patients. To limit the influence that secular trends and unknown co-interventions may play when using an historical control, 112 patients were added in each group. Calculations were made based on a two-sided alpha level of 0.05 and a beta-error of 0.10. For analysis of the primary endpoint, statistical significance of two-sided tests was established at $P < 0.05$. Statistical analyses for secondary endpoints were descriptive and did not include any correction for the inflation of the Type I error due to multiple testing.

We also estimated the proportion of dispatched CA relative to the total number of sudden deaths in the County of Brescia certificated at the Central Statistical Office of the Lombardia Region.

Continuous data are reported as mean values $\pm$ 1 SD or medians, and values for categorical variables are presented as percentage. Comparisons between groups were made by unpaired *t*-test (for continuous variables) or χ^2 test (for categorical variables). Comparisons of time intervals with wide deviation from the normality assumption were made using non-parametric statistics (Mann–Whitney unpaired test). All tests for significance were two-tailed. Cumulative event rates were calculated by the Kaplan–Meier method, with the time to the first event as the outcome variable. The significance of the difference between groups was assessed with the log-rank test.

Results

A total of 702 patients were prospectively enrolled in the study between July 2000 and June 2002. Patients in this prospective cohort were similar to the 692 patients in the historical cohort (recruitment time frame, between June 1997 and May 1999) with regard to sex, proportion of outdoor events, witnessed events, and events in which basic life support was performed by the occasional witness (*Table 1*). In addition, the partial response time did not differ between the two cohorts. Patients in the prospective cohort were older than patients in the historical cohort.

All diagnostic and therapeutic interventions are outlined in *Table 2*. No differences were found in the prevalence of causes of CA and delivered therapies between the two cohorts.

Study endpoints

The 1-year survival free of neurological impairment increased from 0.9% (95% CI 0.4–1.8%) before to 3.0% (95%

Table 1 Characteristics of subjects with CA in the historical and prospective cohorts

Characteristics	Historical cohort ($n = 692$)	Prospective, cohort ($n = 702$)	*P*-value
Age (years)	67.2 $\pm$ 14.9	69.4 $\pm$ 14.1	0.04
Male sex, *n* (%)	432 (62.9)	456 (65.1)	0.57
Outdoor event, *n* (%)	100 (14.5)	95 (13.5)	0.79
Witnessed event, *n* (%)	433 (62.6)	450 (64.1)	0.65
CPR administered before defibrillation option, *n* (%)	144 (20.8)	148 (21.1)	0.76
Interval in minutes from collapse to call to dispatch centre, median (quartile range)[a]	—[b]	2 (8)	—
Interval in minutes from dispatch to arrival at site of collapse (partial response time), median (quartile range)	7 (4)	6 (6)	0.88
Interval in minutes from collapse to first defibrillation option (total response time), median (quartile range)[a]	—[b]	13 (12)	—
Return of spontaneous circulation, *n* (%)	50 (7.2)	72 (10.2)	0.03
Survival to admission to a hospital department, *n* (%)	38 (5.5)	57 (8.1)	0.03
Survival to discharge from hospital, *n* (%)	10 (1.4)	31 (4.4)	0.04
Survival to discharge from hospital free of neurological impairment, *n* (%)	10 (1.4)	29 (4.1)	0.04
Survival free of neurological impairment at 1-year follow-up, *n* (%)	6 (0.9)	21 (3.0)	0.01

[a]Data refer to 450 out of 702 patients with witnessed CA.
[b]Data could not be calculated in the historical patient cohort.

Table 2 Diagnostic and therapeutic interventions in patients in the historical and prospective cohorts surviving at the time of the index event and categorized according to various phases of follow-up

	Historical cohort			Prospective cohort		
	In-hospital ($n = 38$)	At discharge ($n = 10$)	At 1-year FU[a] ($n = 6$)	In-hospital ($n = 57$)	At discharge ($n = 29$)	At 1-year FU[a] ($n = 21$)
Diagnosis (*n*)						
Acute myocardial infarction	16	4	3	23	12	7
Acute coronary ischaemia	7	3	1	12	7	6
CA without recognizable cause	15	3	2	21	10	8
Acute cerebral vascular disease	0	0	0	1	0	0
Therapy (*n*)						
Percutaneous revascularization	9	4	2	18	11	7
Surgical revascularization	2	2	1	5	5	4
Implantable defibrillator	3	3	2	9	9	8
Heart transplant	0	0	0	0	0	1
Medical treatment only	24	1	1	25	4	1

In-hospital indicates patients surviving to admission to a hospital department.
[a]FU denotes follow-up.

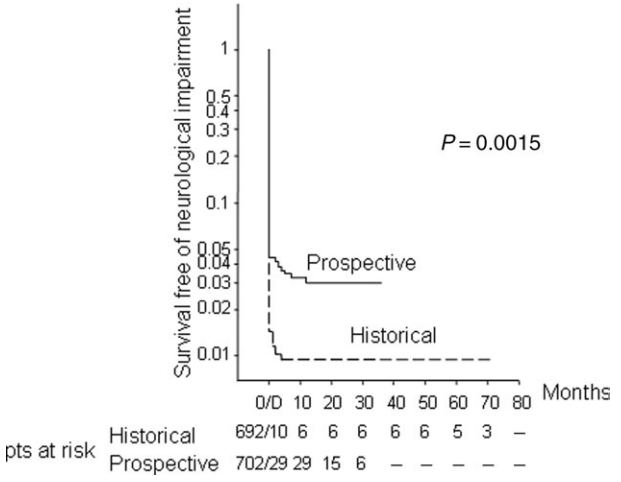

Figure 1 Kaplan–Meier estimates of the probability of survival free of neurological impairment in the historical and prospective cohorts. The probability of survival is reported using a logarithmic scale. D, patients at risk at discharge from hospital; pts, patients.

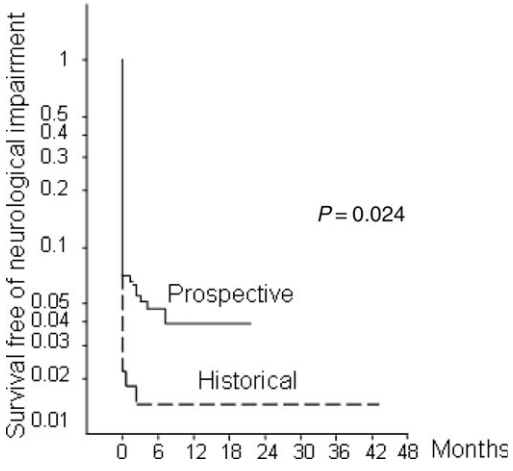

Figure 2 Kaplan–Meier estimates of the probability of survival free of neurological impairment in the historical and prospective cohorts, as analysed in the urban territory.

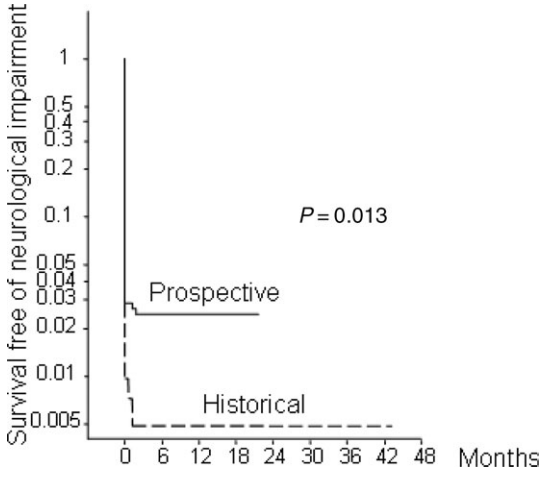

Figure 3 Kaplan–Meier estimates of the probability of survival free of neurological impairment in the historical and prospective cohorts, as analysed in the rural territory.

CI, 1.7–4.3%) ($P = 0.0015$) after the integration of the AED programme (*Figure 1*). Survivals to discharge free of neurological impairment in the two groups had been 1.4% (95% CI, 0.9–2.0%) and 4.1% (95% CI, 2.7–6.4%) (*Table 1*), respectively; during the first year of follow-up, four deaths (all cardiac deaths, one sudden) were observed in the 10 survivors at discharge of the historical cohort and seven (six cardiac deaths, one sudden) in the 29 survivors at discharge of the prospective cohort.

Increase of survival was noted both in the urban [from 1.4% (95% CI 0.4–3.4%) to 4.0% (95% CI 2.0–6.9%), $P = 0.024$] (*Figure 2*) and in the rural territory [from 0.5% (95% CI 0.1–1.6%) to 2.5% (95% CI 1.3–4.2%), $P = 0.013$] (*Figure 3*). Throughout the duration of the study, the yearly incidence of dispatched CAs was more than three times as high in the urban (0.7 per 1000 inhabitants) than it was in the rural territory (0.2 per 1000 inhabitants). Of interest, during the same time period, a significantly lower sudden death rate difference between the two environments (0.8 per 1000 per year and 0.6 per 1000 per year,

respectively, $P < 0.001$ vs. dispatched arrests) was reported to the Central Statistical Office data files of the Region Lombardia. Among dispatched CAs, the larger incidence of survivors in the urban when compared with the rural territory was associated with a larger proportion of witnessed events, a shorter total response time (*Table 3*), and a larger population per square kilometre covered per deployed device (*Table 4*). The number of additional survivors in the urban territory was three-fold larger (1.5 per 100 000) than in the rural territory (0.5 per 100 000) in front of a 16-fold smaller covered area per deployed device in the urban (7.6 km^2) when compared with the rural territory (127.9 km^2). Other meaningful demographic, geographic, and outcome characteristics are reported in *Table 4*.

Of the 26 victims of a witnessed CA surviving free of neurological impairment at discharge in the prospective cohort, 12 (46.1%) received defibrillation later than 8 min from collapse (13.1 $\pm$ 4.3 min). The 1-year survival in this group was 1.7% (95% CI 0.8–3.4%) when compared with 12.5% (95% CI 10.1–16.0%) in patients receiving defibrillation within 8 min from collapse ($P < 0.001$). Survivors in the group of patients receiving defibrillation after 8 min from collapse accounted for 30.6% (six of 19) of all survivors free of neurological impairment at 1-year follow-up (*Table 5*).

The costs of integrating the new defibrillation system into the community amounted to €1 017 514 for the start-up and €681 766 during the steady state. The additional costs per quality-adjusted life year saved amounted to €39 388 (95% CI €16 731–49 329) during the start-up phase of the study and to €23 661 (95% CI €10 327–35 528) during the steady state.

Other data pertaining to the prospective cohort only

In the prospective cohort, the total response time was 17.6 $\pm$ 14.7 min. The sensitivity and specificity of the AED detection algorithm was 100.0% for each during 1047 ECGs in the AED data card. No complications were reported related to the use of the AED.

Five (16.1%) of the survivors in the prospective cohort had been treated with AEDs in public access locations.

In patients (211) with ventricular fibrillation (VF) at the time of ECG recording, the 1-year survival free of neurological impairment was 10.0%.

Table 3 Characteristics of patients in the historical and prospective cohorts observed in the urban and in the rural territories

Characteristics	Historical cohort			Prospective cohort		
	Urban territory ($n = 279$)	Rural territory ($n = 413$)	*P*-value	Urban territory ($n = 255$)	Rural territory ($n = 447$)	*P*-value
Age (years)	68.1 $\pm$ 13.9	66.6 $\pm$ 15.5	0.97	70.7 $\pm$ 13.9	68.7 $\pm$ 14.3	0.78
Male sex *n* (%)	179 (64.4)	253 (61.9)	0.66	159 (62.8)	297 (66.4)	0.62
Outdoor event *n* (%)	45 (16.1)	55 (13.3)	0.87	35 (13.7)	60 (13.4)	0.55
Witnessed event *n* (%)	187 (67.0)	246 (59.6)	0.04	185 (72.5)	265 (59.3)	0.02
CPR administered before defibrillation option, *n* (%)	45 (16.1)	99 (24.0)	0.01	45 (17.6)	103 (23.0)	0.65
Interval in minutes from collapse to call to dispatch centre, median (quartile range)[a]	—[b]	—[b]	—	2 (4)	4 (9)	0.74
Interval in minutes from dispatch to arrival at site of collapse (partial response time), median (quartile range)	7 (5)	7 (5)	0.63	7 (5)	6 (5)	0.61
Interval in minutes from collapse to first defibrillation option (total response time), median (quartile range)[a]	—[b]	—[b]	—	12 (9)	15 (14)	0.01
Return of spontaneous circulation, *n* (%)	21 (7.5)	29 (7.0)	0.85	31 (12.2)	41 (9.2)	0.53
Survival to admission to a hospital department, *n* (%)	23 (8.2)	15 (3.6)	0.01	29 (11.4)	28 (6.3)	0.02
Survival to discharge from hospital, *n* (%)	6 (2.2)	4 (1.0)	0.54	18 (7.1)	13 (2.9)	0.01
Survival to discharge from hospital free of neurological impairment, *n* (%)	6 (2.2)	4 (1.0)	0.66	16 (6.3)	13 (2.9)	0.01
Survival free of neurological impairment at 1-year follow-up, *n* (%)	4 (1.4)	2 (0.5)	0.73	10 (4.0)	11 (2.5)	0.62

[a]Data refer to 450 out of 702 patients with witnessed CA.
[b]Data could not be calculated in the historical patient cohort.

Table 4 Demographic, geographic, and outcome characteristics observed in the urban, in the rural, and in the whole territory of the Brescia County in relation with the device deployment capability

	Population (no. of inhabitants)	Area (km^2)	Density (no. of inhabitants per km^2)	Yearly incidence of dispatched arrests per 1000 inhabitants	Baseline (historical) no. of survivors per year per 100 000 inhabitants	No. of deployed devices	Mean covered area per device (km^2)	No. of inhabitants covered per device	Additional no. of survivors per year per 100 000 inhabitants	Additional lives saved per year per deployed device	No. of devices needed to save one additional life per year
Urban territory	194 697	91	2140	0.7	1.0	12	7.6	16 264	1.5	0.25	4.0
Rural territory	917 931	4735	194	0.2	0.1	37	127.9	24 813	0.5	0.12	8.3
Total	1 112 628	4826	234	0.3	0.3	49	98.5	23 049	0.7	0.15	6.7

Outcome data refer to survival free of neurological impairment at 1 year from CA.

Discussion

Main findings

In the present study, augmentation of the current EMS system with an emergency layperson-integrated service (ELPIS) system proved safe and was associated with a significantly higher long-term survival of CA victims. In fact, when challenged against the most recent historical outcome data within the same territory, the 0.9% overall 1-year survival free of neurological impairment recorded between June 1997 and May 1999 significantly increased to 3.0% during the initial study period, between July 2000 and June 2002. This improvement was recorded despite similar intervals from dispatch to first defibrillation option in the two periods.

When analysed in the different territories, overall survival was significantly larger in the city when compared with the countryside and was associated with a shorter total response time and a larger number of deployed devices per population density. Opposite to the absolute values, a relatively more prominent outcome benefit was observed in the rural than in the urban territory.

An unprecedented finding relates to the more than three times higher incidence of dispatched out-of-hospital CAs in the urban (0.7 per 1000 per year) than in the rural territory (0.2 per 1000 per year). This difference appears to be mainly due to a lower access to dispatch (either due to higher incidence of unwitnessed events or, possibly, due to a lower tendency to dispatch of witnesses) by members of the rural community when compared with members in the urban community. Such observation is substantiated by a similar incidence of sudden death events recorded in the two territories (0.8 per 1000 per year in the urban territory; 0.6 per 1000 per year in the rural territory) during the same time period according to the Central Statistical Office data files of the Region Lombardia.

Finally, the introduction of the ELPIS system in the Brescia county proved cost-effective[25,26] both during the start-up phase of the study and after achievement of the steady state.

Clinical implications

The results of the Brescia Early Defibrillation Study (BEDS) are mainly applicable to territories, such as Italy or less developed areas, that have been suffering or are suffering legislative, logistic, or budget constraints in the use of AEDs. Nevertheless, some of the observations from this study may also have implications in the context of more structured programmes. In fact, it is possible that integration of ELPIS may help to improve outcome in some selected environments reporting unsatisfactory benefit from current EMS systems[9–12,27–29] and further increase survival in other selected environments already showing a better outcome than in the present study.[6–8,23,24,30–34]

The 4.1% overall survival rate at discharge (6.3% in the urban territory) observed in BEDS (*Tables 1 and 2*) is far from satisfactory, but not different from that reported in some studies performed in more structured and selected environments using EMS systems supported by paramedics.[9–12,25–27] A major determinant for this low outcome is likely represented by a total response time exceeding 17 min from collapse which does not reflect the common standards reported in more structured environments; however, this figure represents a useful reference for less

Table 5 Characteristics of subjects (450/702) with witnessed CA in the prospective cohort receiving a defibrillation within 8 min and after 8 min from collapse

Characteristics	Defibrillation		*P*-value
	Within 8 min ($n = 104$)	After 8 min ($n = 346$)	
Age (year)	70.8 ± 15.3	70.2 ± 13.1	0.65
Male sex, *n* (%)	62 (59.6)	226 (65.3)	0.73
Outdoor event, *n* (%)	27 (26.0)	44 (12.7)	0.01
CPR administered before defibrillation option, *N* (%)	34 (32.7)	82 (23.7)	0.56
Interval in minutes from collapse to call to dispatch centre, median (quartile range)[a]	1 (1)	4 (9)	<0.001
Interval in minutes from dispatch to arrival at site of collapse (partial response time), median (quartile range)	4 (4)	8 (6)	<0.001
Interval in minutes from collapse to first defibrillation option (total response time), median (quartile range)[a]	7 (4)	17 (13)	<0.001
Return of spontaneous circulation, *n* (%)	32 (30.8)	27 (7.8)	<0.001
Survival to admission to a hospital department, *n* (%)	24 (23.1)	22 (6.4)	<0.001
Survival to discharge from hospital, *n* (%)	14 (13.5)	13 (3.8)	<0.001
Survival to discharge from hospital free of neurological impairment, *n* (%)	14 (13.5)	12 (3.5)	<0.001
Survival free of neurological impairment at 1-year follow-up, *n* (%)	13 (12.5)	6 (1.7)	<0.001

[a]Data refer to 450 out of 702 patients with witnessed CA.

developed EMS systems and offers consistent hope for future improvement in the response time within the investigated territory.

In BEDS, 77% of witnessed CA victims received a defibrillation option later than 8 min from collapse. This figure does not reflect the optimal standards for early defibrillation programmes requiring at least 90% of victims to be reached within 8 min;[23] however, it should be noted that in our study patients receiving defibrillation later than 8 min from collapse contributed for about one-third to 1-year survival free of neurological impairment. This finding outlines the need for strenuous resuscitation efforts also in patients receiving a late defibrillation option with current technology and to re-evaluate the optimal standards for early defibrillation programmes.

Study limitations

There are several limitations in the present study that need to be discussed. First, the absence of control of co-interventions makes it possible that other effects between undetected parameters and those in the analysis are present. We recognize that using a prospectively designed hypothesis based on the outcome expected according to the data collected in the same environment before introduction of the new system does not completely counter-balance this limit; still, this method is more rigorous than direct comparisons as applied in most prior studies.[9–12,24,30–32,34]

Secondly, in the historical cohort, we were unable to collect some relevant data for comparative analysis with the prospective cohort. They include the interval from collapse to call to dispatch centre, the total response time, and the incidence of shockable rhythms at the time of defibrillation option. However, lack of these data appears counter-balanced by the similar distribution in the two cohorts of other relevant data such as partial response time, proportion of outdoor and witnessed events, and cardiopulmonary resuscitation (CPR) administered before defibrillation.

Thirdly, most of the outcome data in this study are evaluated in the general population of CA victims and not in victims of VF. We intentionally focused on CA victims, because evaluation of VF victims only would lead to underestimate the costs of integrating the ELPIS in the current EMS system.

Fourthly, implementation of promising pre-hospital therapies, such as amiodarone,[35] or in-hospital therapies, such as hypothermia,[36] during the prospective study phase was not considered. On one hand, the use of pre-hospital iv amiodarone was prevented due to (i) evidence of increased survival to hospital admission, but not to hospital discharge[35] and (ii) the presence of law constraints preventing administration of iv therapy by non-medical personnel. On the other hand, hypothermia was not considered, because evidence of its potential impact on clinical outcome became available late during conduction of the study.[36] Anyhow, pre-hospital and in-hospital therapies did not differ in the historical and prospective study cohorts except for the use of AEDs operated by volunteers and laypersons in the latter group.

Finally, the outcome figures of this study reflect the current limits within the selected territory of both the number of AEDs available and the total response time. On

the basis of the results of this study, efforts are currently undertaken to provide consistent improvement of both factors, and consequent results are under evaluation.

Conclusions

The data of the present study provide a reference picture of the safety and potential efficacy of a community programme based on a county-wide AED supported emergency system fully operated by trained volunteers and laypersons. The results of this effort show that significant improvements in the long-term survival of out-of-hospital CA victims can be expected and provide a reference model to evaluate the estimated benefit of ELPIS in unselected environments.

Conflict of interest: none declared.

Appendix 1

List of costs for the acquisition and activation of the AEDs in the BEDS trial. Costs are presented in Euros (€).

Parameter	Unitary cost	Number of units	Total cost
AED			
Start-up	3411	49	167 139
Steady state	—	—	—
Training courses			
Start-up	50	183	9150
Steady state	50	183	9150
Device batteries			
Start-up	147	150	22 050
Steady state		150	22 050
Device patches			
Start-up	30	700	21 000
Steady state		700	21 000
ECG-VC-card			
Start-up	271	50	13 550
Steady state	271	50	13 550

Appendix 2

Disease-related group (DRG) costs calculated according to the Italian patient-level itemized costing system. Costs are presented in Euros (€).

DRG condition	Unitary cost
Acute myocardial infarction	3503
Circulatory CA	1362
Percutaneous transluminal angioplasty	4831
Percutaneous transluminal angioplasty plus stenting	6338
Coronary artery bypass surgery	15 855
Chronic implant of automatic defibrillator	20 820
Heart transplantation	38 666
Hospitalization in intensive care unit	543 per day
Rehabilitation	237 per day

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