Comparison of Nifekalant and Lidocaine for the Treatment of Shock-Refractory Ventricular Fibrillation

Yoshio Tahara, MD; Kazuo Kimura, MD; Masami Kosuge, MD; Toshiaki Ebina, MD;
Shinichi Sumita, MD; Kiyoshi Hibi, MD; Hideshi Toyama, MD;
Takayuki Kosuge, MD; Yoshihiro Moriwaki, MD; Noriyuki Suzuki, MD;
Mitsugi Sugiyama, MD; Satoshi Umemura, MD

Circulation Journal
Vol. 70 No. 4 April 2006
(Pages 442–446)

Circ J 2006; **70:** 442–446

Comparison of Nifekalant and Lidocaine for the Treatment of Shock-Refractory Ventricular Fibrillation

Yoshio Tahara, MD; Kazuo Kimura, MD*; Masami Kosuge, MD*; Toshiaki Ebina, MD*; Shinichi Sumita, MD*; Kiyoshi Hibi, MD*; Hideshi Toyama, MD; Takayuki Kosuge, MD; Yoshihiro Moriwaki, MD; Noriyuki Suzuki, MD; Mitsugi Sugiyama, MD; Satoshi Umemura, MD*

Background Although nifekalant is a class III antiarrhythmic agent without negative inotropic activity, its effect in patients with shock-refractory ventricular fibrillation remains unclear.

Methods and Results Patients who had an out-of-hospital cardiac arrest with ventricular fibrillation that persisted after 3 shocks from an external defibrillator, intravenous epinephrine, and another shock were retrospectively studied. The patients received lidocaine from January 1997 through June 2001 and nifekalant from July 2001 through December 2004. Short-term survival rates (survival to hospital admission and 24-h survival) were compared between the groups. The study group comprised 120 patients (mean age: 62±16 years): 55 received nifekalant and 65 received lidocaine. Age, sex, history of ischemic heart disease, whether arrest was witnessed or not and time to arrival at the hospital did not differ significantly between the groups. As compared with lidocaine, nifekalant was associated with significantly higher rates of survival to hospital admission (67% vs 37%, $p<0.001$) and 24-h survival (53% vs 31%, $p=0.01$). Multivariate analysis showed that treatment with nifekalant and early initiation of cardiopulmonary resuscitation were independent predictors of 24-h survival.

Conclusions As compared with lidocaine, nifekalant may improve short-term survival in patients with out-of-hospital cardiac arrest due to shock-refractory ventricular fibrillation. (*Circ J* 2006; **70:** 442–446)

Key Words: Antiarrhythmic agents; Cardiac arrest; Cardiopulmonary resuscitation; Emergency care; Ventricular fibrillation

In the United States of America, sudden death occurs in more than 400,000 adults each year. Ninety per cent of such deaths are attributed to heart disease. Ventricular fibrillation accounts for 80% of all cases of sudden cardiac arrest[1,2] In Japan, ventricular fibrillation is suspected to occur in 63% of all cases of cardiac arrest, but has been documented on the scene in only 15% of cases[3] This difference is attributed to a low rate of bystander cardiopulmonary resuscitation (CPR) and a long time interval from the onset of ventricular fibrillation to the initial recording of electrocardiograms (ECG) by emergency medical service (EMS) personnel. The rate of ventricular fibrillation documented on the scene will probably increase with improvements in EMS and health care systems.

Since publication of the American Heart Association (AHA) guidelines for CPR and emergency cardiac care in 2000, interest has focused on the role of CPR in the prevention of sudden death from cardiac arrest[4] Early detection of ventricular fibrillation and effective defibrillation have been acknowledged as important determinants of the rate of survival to hospital discharge. Patients in whom spontaneous circulation is restored using defibrillation promptly after the onset of ventricular fibrillation generally have a good prognosis, whereas those with persistent ventricular fibrillation have a poor prognosis[5–8] Adjunctive therapies that promote the return of spontaneous circulation in patients with ventricular fibrillation refractory to defibrillation are therefore needed.

The Amiodarone versus Lidocaine in Pre-hospital Ventricular Fibrillation Evaluation (ALIVE) trial compared amiodarone with lidocaine in patients with ventricular fibrillation persisting after shocks from an external defibrillator (shock-refractory ventricular fibrillation). The rate of survival to hospital admission was significantly higher in patients given intravenous amiodarone (22.8%) than in those given intravenous lidocaine (12.0%)[9] Intravenous amiodarone is recommended for antiarrhythmic therapy in patients with shock-refractory ventricular fibrillation by the 2000 AHA guidelines, but it is not approved in Japan.

Nifekalant is a class III antiarrhythmic agent according to the Vaughan Williams classification, similar to amiodarone. This drug has been developed and approved for clinical use in Japan. As compared with amiodarone, nifekalant is considered to have several advantages when used in patients who require CPR, such as lowering the threshold for ventricular defibrillation and having no effect or a mild positive inotropic effect on myocardial contractility[10] Several studies have reported that nifekalant is effective for the management of ventricular arrhythmias refractory to treatment with other drugs[11,12] Nifekalant is expected to be an effective adjunctive treatment for refractory ventricular fibrillation, but this remains to be confirmed clinically. We retrospectively compared intravenous nifekalant with intravenous lidocaine in patients who had refractory ventricular fibrillation with no return of spontaneous circulation after 3

(Received September 15, 2005; revised manuscript received January 17, 2006; accepted January 31, 2006)

*Division of Critical Care and Emergency Medicine, *Division of Cardiology, Yokohama City University Medical Center, Yokohama, Japan*
Mailing address: Kazuo Kimura, Yokohama City University Medical Center, 4-57 Urahune-cho, Minami-ku, Yokohama 232-0024, Japan.
E-mail: c-kimura@urahp.yokohama-cu.ac.jp

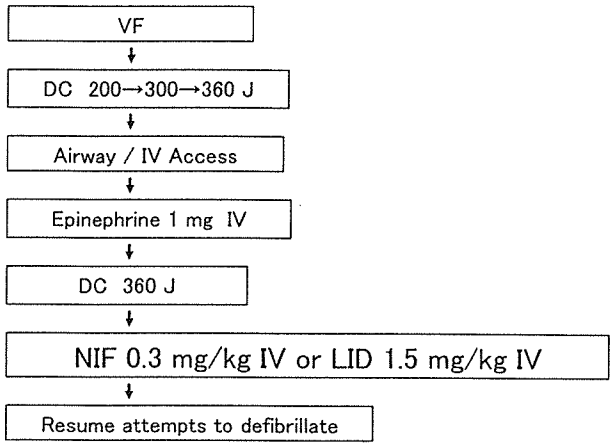

Fig 1. Nifekalant (2001-2004) vs Lidocaine (1997-2001): Observational Study. Patients were treated with nifekalant or lidocaine if they had out-of-hospital ventricular fibrillation resistant to 3 shocks, intravenous epinephrine, and further shock. The drugs were administered by hospital personnel after arrival. VF, ventricular fibrillation; DC, direct-current shock; IV, intravenous; NIF, nifekalant; LID, lidocaine.

shocks from an external defibrillator, as recommended by the 2000 AHA guidelines.

Methods

We studied patients who had out-of-hospital cardiac arrest with ventricular fibrillation and were transferred to our hospital from January 1997 through December 2004. In all patients, ventricular fibrillation persisted after 3 shocks from an external defibrillator used by emergency medical personnel, followed by an intravenous dose of epinephrine and another shock given by hospital personnel after arrival at the hospital. The mean age of the patients was 62±16 years. Of the patients, 80% were men.

Patients treated from January 1997 though June 2001 were given intravenous lidocaine. Those treated from July 2001 though December 2004 were given intravenous nifekalant. The rates of short-term survival (survival to hospital admission and 24-h survival), survival to hospital discharge and return to independent living or their former employment were compared between the groups. Treatment algorithms for ventricular fibrillation in the 2000 AHA guidelines recommend that patients with sudden cardiac arrest due to ventricular fibrillation initially receive 3 shocks from an external defibrillator. Patients who are not successfully resuscitated should be intubated for airway protection, and intravenous access should be established to permit drug administration. A 1-mg dose of epinephrine should be given intravenously, followed by another shock. Patients with persistent or recurrent ventricular fibrillation should be intravenously given antiarrhythmic agents (amiodarone, lidocaine, magnesium sulfate or procainamide), followed by one or more precordial shocks[3].

Fig 1 shows our protocol, which was similar to the 2000 AHA guidelines. Intravenous nifekalant (0.3 mg/kg) and intravenous lidocaine (1.5 mg/kg) were used as antiarrhythmic therapies. All patients received epinephrine and artificial ventilation in the hospital, and hospital personnel started intravenous infusion. Spontaneous circulation was not successfully restored by a single intravenous dose of nifekalant or lidocaine in any patient. If an additional shock failed to restore spontaneous circulation after a bolus of nifekalant or lidocaine, a continuous infusion of nifekalant ($0.4\,mg\cdot kg^{-1}\cdot h^{-1}$) or lidocaine ($1\,mg\cdot kg^{-1}\cdot h^{-1}$) was started; thereafter, shocks were delivered every minute. After hospital admission, a 12-lead ECG was recorded and corrected QT (QTc) intervals were evaluated to adjust the infusion dose.

Table 1 Clinical Characteristics of Patients and Course of Resuscitation Before Administration of Nifekalant or Lidocaine.

	NIF (N=55)	*LID (N=65)*	*p value*
Age (years)	*63±15*	*61±16*	*0.39*
Male sex (%)	*86*	*77*	*0.22*
Coronary artery disease (%)	*69*	*63*	*0.46*
Witnessed arrest (%)	*58*	*59*	*0.93*
CPR by bystander (%)	*42*	*39*	*0.70*
Time to CPR start (min)	*7±5*	*7±6*	*0.80*
Time to arrival at the hospital (min)	*26±8*	*27±10*	*0.88*
Time to study drug administration (min)	*34±7*	*35±9*	*0.79*
Total number of DC shocks	*9±4*	*10±4*	*0.92*
Total dose of epinephrine (mg)	*6±3*	*8±5*	*0.01*

NIF, nifekalant; LID, lidocaine; CPR, cardiopulmonary resuscitation; DC shock, direct-current shock.

Endpoints

The primary endpoints were the rates of survival to hospital admission and 24-h survival. Patients with resolution of ventricular fibrillation who had a transient but unsustained return of spontaneous circulation and died in the emergency room were not considered to have survived to hospital admission. The secondary endpoint was the rate of survival to hospital discharge. The most important goal of CPR was an absence of neurologic deficits during convalescence. The rates of return to independent living or former employment–that is, intact neurologic function–were also compared between the groups. The study protocol was approved by the Ethics Committee of Yokohama City University Medical Center.

Statistical Analysis

The results are expressed as means±SD, and p values were calculated with Student's t-test. Means (±SD) were compared between the groups with use of the chi-square test. A multivariate logistic regression analysis was used to identify clinical predictors of 24-h survival among the variables associated ($p<0.1$) on univariate analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. P values of less than 0.05 were considered to indicate statistical significance. All analyses were performed using SPSS 11J (SPSS Inc, Chicago).

Results

Of the 2,221 patients with out-of-hospital cardiac arrest treated at our hospital from January 1997 through December 2004, 12% of the patients had ventricular fibrillation and 120 (5%) met the inclusion criteria and were included in the study. Fifty-five patients received nifekalant, and 65 received lidocaine (Table 1). Age, sex, history of ischemic heart disease, whether the arrest was witnessed, whether a bystander initiated CPR, time to initiation of CPR, time to arrival at the hospital, time to study drug administration and

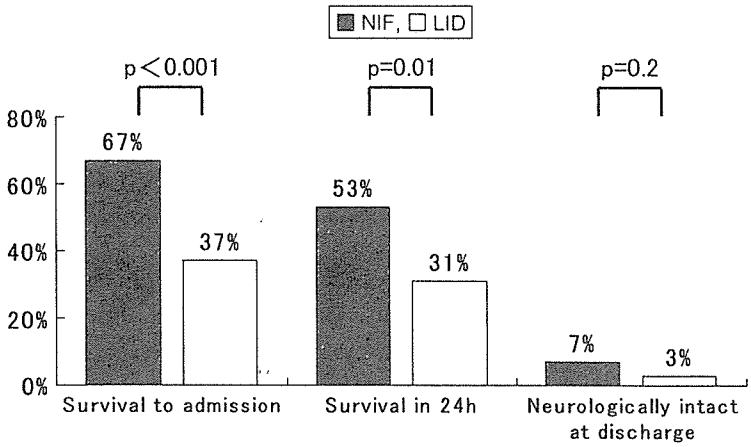

Fig 2. Effect of treatment with nifekalant or lidocaine on the rate of survival. Intravenous nifekalant was effective in increasing the rates of survival to hospital admission and 24-h survival. NIF, nifekalant; LID, lidocaine.

Table 2 Multivariate Predictors of 24-h Survival

Factor	*Odds ratio (95%CI)*	*p value*
Age (per additional year)	*0.98 (0.96–1.01)*	*0.21*
Sex (male vs female)	*2.11 (0.69–6.44)*	*0.19*
Witnessed arrest (yes vs no)	*1.42 (0.60–3.36)*	*0.43*
Time to CPR start <5 min (yes vs no)	*3.57 (1.43–8.94)*	*<0.01*
Time to drug administration (per additional min)	*0.97 (0.93–1.02)*	*0.25*
Treatment assignment (nifekalant vs lidocaine)	*3.16 (1.40–7.17)*	*<0.01*

CI, confidence interval; CPR, cardiopulmonary resuscitation.

the total number of shocks delivered did not differ significantly between the groups. The total dose of epinephrine was greater in patients given lidocaine than in those given nifekalant. Fig 2 shows the effects of nifekalant and lidocaine. As compared with patients given lidocaine, patients given nifekalant had significantly higher rates of survival to hospital admission (67% vs 37%, p<0.001) and 24-h survival (53% vs 31%, p=0.01). The rates of survival to hospital discharge (26% vs 22%, p=0.6) and intact neurologic function at discharge (7% vs 3%, p=0.2) were slightly but not significantly higher in patients given nifekalant than in those given lidocaine. At 24 h, survivors (n=49) differed significantly from non-survivors (n=71) with respect to age (58.8±15.7 years vs 63.5±15.5 years, p=0.09), being male (89% vs 75%, p=0.05), having the initial arrest witnessed (70% vs 51%, p=0.03), time to the start of CPR (<5 min) (53% vs 23%, p<0.01), time to arrival at the hospital (24.2±9.6 min vs 27.6±8.6 min, p=0.03), time to study drug administration (34.1±9.2 min vs 37.4±8.4 min, p=0.03) and whether nifekalant or lidocaine was administered (55% vs 33%, p=0.01)[13] Table 2 shows the results of multivariate analysis designed to identify baseline predictors of 24-h survival. The independent variables included in analysis were age, sex, treatment assignment (nifekalant or lidocaine), whether arrest was witnessed, time to CPR start (<5 min) and time to drug administration. Treatment with nifekalant (OR, 3.16; 95% CI, 1.40 to 7.17; p<0.01) and time to CPR start (<5 min) (OR, 3.57; 95% CI, 1.43 to 8.94; p<0.01) were found to be independent predictors of 24-h survival.

Discussion

In the present study of patients with cardiac arrest due to shock-refractory ventricular fibrillation, the rates of survival to hospital admission and 24-h survival were higher in patients given intravenous nifekalant than in those given intravenous lidocaine. Multivariate analysis showed nifekalant is an independent factor of 24-h survival. Our results suggest that nifekalant is therapeutically useful in patients undergoing defibrillation for ventricular fibrillation.

The optimal use of antiarrhythmic drugs for CPR remains poorly defined. The 2000 AHA guidelines recommend antiarrhythmic treatment with amiodarone, lidocaine and procainamide at the time of external defibrillation in patients with refractory ventricular fibrillation. The guidelines now classify amiodarone and procainamide as class IIb drugs ("acceptable and useful") and lidocaine as a class indeterminate drug ("no harm but no benefit").[4] Procainamide is currently listed as a class IIb drug for ventricular fibrillation unresponsive to other antiarrhythmic agents, but it is not considered a first-line drug. Lidocaine has conventionally been used to treat patients with out-of-hospital cardiac arrest due to refractory ventricular fibrillation. To our knowledge, however, no large clinical study has verified its effectiveness. The Amiodarone for Resuscitation After Out-of-hospital Cardiac Arrest due to Ventricular Fibrillation (ARREST) study, comparing amiodarone with placebo,[14] and the ALIVE study, comparing amiodarone with lidocaine, have focused attention on amiodarone as a potential drug of choice for the treatment of out-of-hospital cardiac arrest due to shock-refractory ventricular fibrillation.[9] However, amiodarone can cause adverse reactions such as hypotension and bradycardia.[15] These reactions are attributed to the fact that amiodarone is a multiple-channel blocker with complex pharmacologic properties, affecting β-adrenergic receptors, calcium channels, sodium channels, as well as potassium channels. Patients with out-of-hospital cardiac arrest due to shock-refractory ventricular fibrillation are likely to have cardiac dysfunction. Antiarrhythmic drugs with negative inotropic activity can negatively affect the outcome of CPR in such patients.

Nifekalant is a pure potassium-channel blocker effective for the management of out-of-hospital cardiac arrest due to shock-refractory ventricular fibrillation;[10] its advantages include no negative inotropic effects[16–18] and a lowering of the defibrillation threshold.[19–21] Even if adverse reactions develop, they are transient because nifekalant has a short

half-life.[10] In the present study, the period of continuous infusion of antiarrhythmic agents was 3 days on average. In patients with excessive QTc prolongation (>0.55), the infusion dose was reduced. Consequently, there were no side effects, including torsades de pointes and sinus arrest, during the study period. However, concurrent use of nifekalant and lidocaine should be avoided because interactions between these drugs can cause sinus-node suppression.[11] Ischemic myocardium during acute myocardial infarction is characterized by decreased intracellular ATP levels and opening of ATP-sensitive potassium channels, leading to non-uniform shortening of the action potential and refractory period, increasing the risk of reentry. Nifekalant blocks the delayed rectifier potassium (IKr) current and has strong antiarrhythmic activity against reentrant tachycardias. Its pharmacologic characteristics are considered particularly effective against ventricular arrhythmias occurring after the onset of acute myocardial infarction.[22]

In the present study, the rates of survival to hospital admission and 24-h survival were higher in patients given intravenous nifekalant than in those given intravenous lidocaine; however, the rate of survival to hospital discharge did not differ significantly between the groups. The lack of a difference in survival to discharge is most likely related to the time to the return of spontaneous circulation.[23] Differences in survival rates between the ALIVE study and the present study may be ascribed to differences between the rate of bystander initiated CPR (average 27% vs 40%) or differences in the underlying disease severity among patients with ventricular fibrillation.[9] Albeit such differences exist, the rate of survival to hospital admission was 1.9 times higher in the amiodarone group than in the lidocaine group in the ALIVE study, as compared with 1.8 times higher in the nifekalant group than in the lidocaine group in the present study. These results suggest that nifekalant and amiodarone are similarly effective.

Ventricular fibrillation becomes refractory to treatment with the passage of time; early detection of cardiac arrest due to ventricular fibrillation and early defibrillation are thus important determinants of outcome in patients with out-of-hospital cardiac arrest.[24] Furthermore, awareness of the importance of CPR should be widely disseminated among the general public.[25] In addition to CPR, improvement in survival with intact neurologic function among patients with cardiac arrest requires increased emphasis on cerebral-CPR after hospital admission. Improved patient care, including techniques for brain hypothermia, are essential.[26,27] More aggressive policies for resuscitation in conjunction with the use of intravenous nifekalant may contribute to higher rates of survival to hospital admission and survival with intact neurologic function.

Study Limitations

This was a retrospective study performed at a single center, not a randomized trial. Patients who had previously received lidocaine served as control. The baseline clinical characteristics of the 2 treatment groups were similar, except for a lower dose of epinephrine in the nifekalant group. This lower dose may be attributed to the fact that spontaneous circulation was regained without the need for additional epinephrine in a higher proportion of patients in the nifekalant group. In the lidocaine group, ventricular fibrillation most likely led to cardiac arrest during CPR in a substantial proportion of patients; additional epinephrine was therefore given and CPR continued. The difference in the dose of epinephrine suggests that nifekalant was more useful than lidocaine for the treatment of cardiac arrest due to ventricular fibrillation. However, lidocaine and nifekalant were used during different periods. Our outcomes may therefore have been affected by factors such as technical advances and improved medical care in addition to differences in drug efficacy. Another important limitation of the present study was that nifekalant was not compared with intravenous amiodarone, most commonly used for the management of shock-refractory ventricular fibrillation in Western countries but not available in Japan.

Conclusions

Our results show that nifekalant improves short-term survival; that is, the rates of survival to hospital admission and 24-h survival, as compared with lidocaine in patients with out-of-hospital cardiac arrest due to shock-refractory ventricular fibrillation. However, our findings are preliminary and must be confirmed by further clinical studies.

References

1. Zheng ZJ, Croft JB, Giles WH, Mensah GA. Sudden cardiac death in the United States, 1989 to 1998. *Circulation* 2001; **104:** 2158–2163.
2. Zipes DP, Wellens HJ. Sudden cardiac death. *Circulation* 1998; **98:** 2334–2351.
3. SOS-KANTO Committee. Incidence of ventricular fibrillation in patients with out-of-hospital cardiac arrest in Japan. *Circ J* 2005; **69:** 1157–1162.
4. Guidelines 2000 for cardiopulmonary resuscitation and emergency cardiovascular care: International consensus on science. *Circulation* 2000; **102**(Suppl I): I-142–I-157.
5. The Public Access Defibrillation Trial Investigators. Public-access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med* 2004; **351:** 637–646.
6. Bunch TJ, White RD, Gersh BJ, Meverden RA, Hodge DO, Ballman KV, et al. Long-term outcomes of out-of-hospital cardiac arrest after successful early defibrillation. *N Engl J Med* 2003; **348:** 2626–2633.
7. Still I, Nichol G, Wells G, Maio VD, Nesbitt L, Blackburn J, et al. Health-related quality of life is better for cardiac arrest survivors who received citizen cardiopulmonary resuscitation. *Circulation* 2003; **108:** 1939–1944.
8. Capucci A, Aschieri D, Piepoli MF, Bardy GH, Iconomu E, Arvedi M. Tripling survival from sudden cardiac arrest via early defibrillation without traditional education in cardiopulmonary resuscitation. *Circulation* 2002; **106:** 1065–1070.
9. Dorian P, Cass D, Schwartz B, Cooper R, Gelaznikas R, Barr A. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. *N Engl J Med* 2002; **346:** 884–890.
10. Nakaya H, Uemura H. Electropharmacology of nifekalant, a new class III antiarrhythmic drug. *Cardiovasc Drug Rev* 1998; **16:** 133–144.
11. Yoshioka K, Amino M, Morita S, Nakagawa Y, Usui K, Sugimoto A, et al. Can nifekalant hydrochloride be used as a first-line drug for cardiopulmonary arrest (CPA)? *Circ J* 2006; **70:** 21–27.
12. Katoh T, Mitamura H, Matsuda N, Takano T, Ogawa S, Kasanuki H. Emergency treatment with nifekalant, a novel class III anti-arrhythmic agent, for life-threatening refractory ventricular tachyarrhythmias. *Circ J* 2005; **69:** 1237–1243.
13. Cummins RO, Eisenberg MS, Hallstrom AP, Litwin PE. Survival of out-of-hospital cardiac arrest with early initiation of cardiopulmonary resuscitation. *Am J Emerg Med* 1985; **3:** 114–119.
14. Kudenchuk PJ, Cobb LA, Copass MK, Cummins RO, Doherty AM, Fahrenbruch CE, et al. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. *N Engl J Med* 1999; **341:** 871–878.
15. Sugiyama A, Satoh Y, Hashimoto K. Acute electropharmacological effects of intravenously administered amiodarone assessed in the invivo canine model. *Jpn J Pharmacol* 2001; **87:** 74–82.
16. Kondoh K, Hashimoto H, Nishiyama H, Umemura K, Ozaki T, Uematsu T, et al. Effects of MS-551, a new class III antiarrhythmic drug, on programmed stimulation-induced ventricular arrhythmias, electrophysiology, and hemodynamics in a canine myocardial infarction model. *J Cardiovasc Pharmacol* 1994; **23:** 674–680.

17. Sen L, Cui G, Sakaguchi Y, Singh BH. Electrophysiological effects of MS-551, a new class III agent: Comparison with dl-sotalol in dogs. *J Pharmacol Exp Ther* 1998; **285:** 687–694.
18. Takenaka K, Yasuda S, Miyazaki S, Kurita T, Sutani Y, Morii I, et al. Initial experience with nifekalant hydrochloride (MS-551), a novel class III antiarrhythmic agent, in patients with acute extensive infarction and severe ventricular dysfunction. *Jpn Circ J* 2001; **65:** 60–62.
19. Murakawa Y, Yamashita T, Kanese Y, Omata M. Can a class III antiarrhythmic drug improve electrical defibrillation efficacy during ventricular fibrillation? *J Am Coll Cardiol* 1997; **29:** 688–692.
20. Murakawa Y, Yamashita T, Kanese Y, Omata M. Do the effects of antiarrhythmic drugs on defibrillation efficacy vary among different shock waveforms? *Pacing Clin Electrophysiol* 1998; **21:** 1901–1908.
21. Murakawa Y, Yamashita T, Kanese Y, Omata M. Effect of a class III antiarrhythmic drug on the configuration of dose response curve for defibrillation. *Pacing Clin Electrophysiol* 1999; **22:** 479–486.
22. Wilde AA, Janse MJ. Electrophysiological effects of ATP sensitive potassium channel modulation: Implications for arrhythmogenesis. *Cardiovasc Res* 1994; **28:** 16–24.
23. Cummins RO, Eisenberg MS, Hallstrom AP, Litwin PE. Survival of out-of-hospital cardiac arrest with early initiation of cardiopulmonary resuscitation. *Am J Emerg Med* 1985; **3:** 114–119.
24. Larsen MP, Eisenberg MS, Cummins RO, Hallstrom AP. Predicting survival from out-of-hospital cardiac arrest: A graphic model. *Ann Emerg Med* 1993; **22:** 1652–1658.
25. Cummins RO, Ornato JP, Thies WH, Pepe PE. Improving survival from sudden cardiac arrest: The "chain of survival" concept: A statement for heart professionals from the Advanced Cardiac Life Support Subcommittee and the Emergency Cardiac Care Committee, American Heart Association. *Circulation* 1991; **83:** 1832–1847.
26. Nagao K, Hayashi N, Kanmatsuse K, Arima K, Ohtsuki J, Kikushima K, et al. Cardiopulmonary cerebral resuscitation using emergency cardiopulmonary bypass, coronary reperfusion therapy and mild hypothermia in patients with cardiac arrest outside the hospital. *J Am Coll Cardiol* 2000; **36:** 776–783.
27. Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med* 2002; **346:** 549–556.

Cardiopulmonary resuscitation by bystanders with chest compression only (SOS-KANTO): an observational study

SOS-KANTO study group

Lancet 2007; 369: 920–26
See **Comment** page 882

*Members listed at end of paper

Correspondence to:
Dr Ken Nagao, The SOS-KANTO Committee, Department of Emergency and Critical Care Medicine, Surugadai Nihon University Hospital, 1-8-13 Kanda Surugadai, Chiyoda-Ku, Tokyo, 101-8309, Japan
Kennagao@med.nihon-u.ac.jp

Summary

Background Mouth-to-mouth ventilation is a barrier to bystanders doing cardiopulmonary resuscitation (CPR), but few clinical studies have investigated the efficacy of bystander resuscitation by chest compressions without mouth-to-mouth ventilation (cardiac-only resuscitation).

Methods We did a prospective, multicentre, observational study of patients who had out-of-hospital cardiac arrest. On arrival at the scene, paramedics assessed the technique of bystander resuscitation. The primary endpoint was favourable neurological outcome 30 days after cardiac arrest.

Findings 4068 adult patients who had out-of-hospital cardiac arrest witnessed by bystanders were included; 439 (11%) received cardiac-only resuscitation from bystanders, 712 (18%) conventional CPR, and 2917 (72%) received no bystander CPR. Any resuscitation attempt was associated with a higher proportion having favourable neurological outcomes than no resuscitation (5·0% *vs* 2·2%, p<0·0001). Cardiac-only resuscitation resulted in a higher proportion of patients with favourable neurological outcomes than conventional CPR in patients with apnoea (6·2% *vs* 3·1%; p=0·0195), with shockable rhythm (19·4% *vs* 11·2%, p=0·041), and with resuscitation that started within 4 min of arrest (10·1% *vs* 5·1%, p=0·0221). However, there was no evidence for any benefit from the addition of mouth-to-mouth ventilation in any subgroup. The adjusted odds ratio for a favourable neurological outcome after cardiac-only resuscitation was 2·2 (95% CI 1·2–4·2) in patients who received any resuscitation from bystanders.

Interpretation Cardiac-only resuscitation by bystanders is the preferable approach to resuscitation for adult patients with witnessed out-of-hospital cardiac arrest, especially those with apnoea, shockable rhythm, or short periods of untreated arrest.

Introduction

Cardiopulmonary resuscitation (CPR) consisting of chest compression plus mouth-to-mouth ventilation done by bystanders is a major element in the so-called chain of survival for people with cardiac arrest.[1–4] Although bystander CPR improves likelihood of survival,[1–8] reports[9–14] have shown that bystander CPR was attempted for less than a-third of patients who had collapsed. Surveys have identified reluctance of bystanders to undertake mouth-to-mouth ventilation as a substantial barrier to CPR attempts.[10,15–17] This reluctance is partly caused by fear of transmission of infectious diseases. Despite the remote chance of such infection, fears about disease transmission are common in the present era of universal precautions.[10,15] Another barrier to bystanders attempting CPR is the complexity of the technique as presently taught.[18–20] In CPR guidelines, cardiac-only resuscitation by bystanders is recommended in dispatcher-assisted resuscitation or if a rescuer is unwilling or unable to do mouth-to-mouth ventilation.[2–4] However, this technique is not generally known, recommended, or taught to the public. Since few clinical studies have focused on the efficacy of cardiac-only resuscitation,[8,21,22] we sought to compare the outcomes for patients who underwent cardiac-only resuscitation or conventional CPR by bystanders. If cardiac-only resuscitation is as effective as conventional CPR by bystanders, rescuers might be more willing and able to provide this simple intervention than they are at present. Furthermore, clinical studies have established that interruptions to chest compressions during out-of-hospital cardiac arrest are common, even by trained emergency medical staff.[1,23,24] Studies suggest

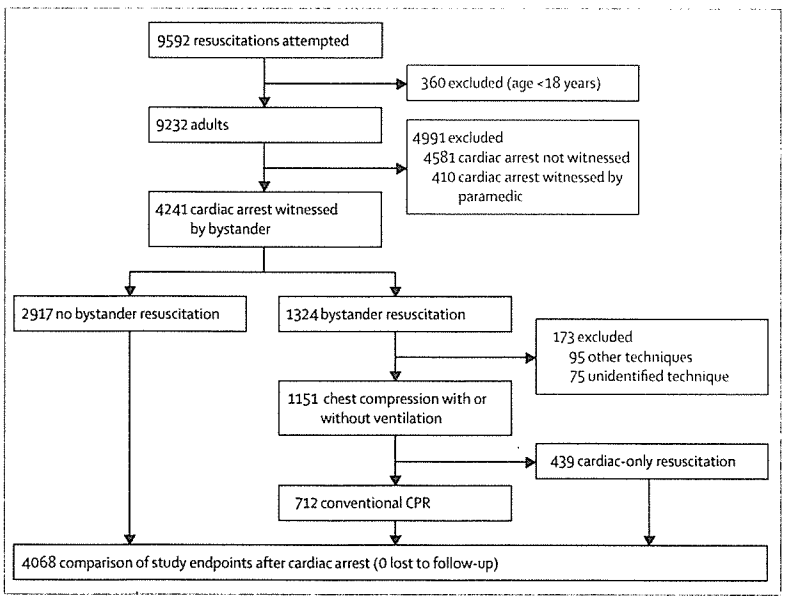

Figure 1: Study profile

that such interruptions can have lethal consequences.[25–27] Kern and colleagues[26] showed that cardiac-only resuscitation results in substantially better survival without neurological impairment 24 h after cardiac arrest than conventional CPR.

We therefore assessed the effect of cardiac-only resuscitation by bystanders on adults who had out-of-hospital cardiac arrest. We expected that cardiac-only resuscitation or conventional CPR would be better than no bystander intervention and that cardiac-only resuscitation would show similar neurological outcome to conventional CPR.

Methods

Participants

A survey of survivors of out-of-hospital cardiac arrest in the Kanto region of Japan (SOS-KANTO) was done by the Association for Acute Medicine of Kanto and included 58 emergency hospitals and emergency medical service units. Between Sept 1, 2002, and Dec 31, 2003, patients who had out-of-hospital cardiac arrest witnessed by bystanders and who were subsequently transported by paramedics to emergency hospitals participating in SOS-KANTO were included in the study. Exclusion criteria were: patients younger than 18 years of age; further cardiac arrest after the arrival of paramedics; documented terminal illness; presence of a do-not-resuscitate order; and bystander resuscitation without documented chest compressions.

Procedures

The study was a prospective, multicentre, observational trial that followed Utstein style reporting guidelines.[1] The study was approved by the SOS-KANTO Research Ethics Board, and the requirement for informed consent was waived according to Japanese government guidelines.[28] Paramedics observed the technique of bystander resuscitation and asked additional questions of bystanders to assess the characteristics of resuscitation.[1,2] The technique during bystander resuscitation was identified as cardiac-only resuscitation, conventional CPR, pulmonary-only resuscitation, unidentified resuscitation technique (including change of technique), or chest compression not documented. Chest compression rate and depth were not assessed. The person attempting bystander resuscitation was classified as a lay person with basic CPR training, a lay person assisted by a dispatcher, a lay person without either training or dispatcher assistance, or an off-duty health worker. All event times were measured by the dispatch centre clock, and times of collapse and first bystander resuscitation attempts were obtained from the bystanders. Cardiac arrest was defined as the cessation of cardiac mechanical activity, manifesting as unresponsiveness, apnoea (or gasping breathing), and absence of pulse. The arrest was presumed to be from a cardiac cause, unless it was known to have been caused by a non-cardiac cause including trauma, drowning, and asphyxia.[1]

Resuscitation attempts were documented by both paramedics and attending physicians according to Utstein style reporting guidelines.[1] Data for individual patients were entered into a database by SOS-KANTO members at each hospital and were independently cross-checked twice by different investigators. Original data were made available to the data and safety monitoring committee for independent scrutiny.

Study endpoints

The primary endpoint was favourable neurological outcome 30 days after cardiac arrest, defined as a Glasgow-Pittsburgh cerebral-performance category of

	Any bystander resuscitation	No bystander resuscitation	p value
Age (years)	68 (55–80)	68 (57–78)	0·8450
Male sex	778/1151 (68%)	2022/2917 (69%)	0·2848
Cardiac cause	806/1151 (70%)	1836/2917 (63%)	<0·0001
Location of cardiac arrest			<0·0001
Home or other residence	598/1138 (53%)	1790/2879 (62%)	
Public, indoors	413/1138 (36%)	623/2879 (22%)	
Public, outdoors	127/1138 (11%)	466/2879 (16%)	
First physical findings at arrival of EMS			
Gasping breathing	123/1151 (11%)	166/2917 (6%)	<0·0001
Pupilometer (mm*)	5·0 (5·0–6·0)	6·0 (5·0–6·0)	0·0002
Initial cardiac rhythm			<0·0001
VF/pulseless VT	329/1151 (29%)	549/2917 (19%)	
PEA	239/1151 (21%)	755/2917 (26%)	
Asystole	584/1151 (51%)	1613/2917 (55%)	
Treatment			
Defibrillatory shock	440/1151 (38%)	839/2917 (29%)	<0·0001
Tracheal intubation	1119/1151 (97%)	2804/2917 (96%)	0·0901
Epinephrine	1047/1151 (91%)	2681/2917 (92%)	0·3266
Hypothermia	28/1151 (2%)	48/2917 (2%)	0·0949
Medical history			
Coronary heart disease	122/1118 (11%)	287/2838 (10%)	0·4570
Hypertension	178/1118 (16%)	424/2838 (15%)	0·4392
Heart failure	35/1118 (3%)	106/2838 (4%)	0·3588
Diabetes	139/1118 (12%)	332/2838 (12%)	0·5207
Time (min)			
From collapse to call receipt†	3·0 (1·0–5·0)	3·0 (1·0–5·0)	0·6396
From call receipt to first AED analysis	10·0 (8·0–12·0)	10·0 (8·0–12·0)	0·4422
From first AED analysis to departure from scene‡	14·0 (10·0–17·0)	14·0 (10·0–18·0)	0·8066
From departure to arrival at hospital§	10·0 (6·0–13·0)	10·0 (6·0–13·0)	0·7415

Data are median (IQR) or numerator/total number (%). Calculations based on available data. AED=automated external defibrillator. CPR=cardiopulmonary resuscitation. EMS=emergency medical services. PEA=pulseless electrical activity. VF=ventricular fibrillation. VT=ventricular tachycardia. *The pupil was measured by EMS workers using one patient's checklist card with pupillometer rulers, and was recorded for 1080 patients in the any resuscitation group and for 2764 in the no bystander resuscitation group. †Time recorded for 850 patients in the any resuscitation group and for 2046 in the no bystander resuscitation group. ‡Time recorded for 1125 in the any resuscitation group and for 2861 in the no bystander resuscitation group. §Time recorded for 1073 in the any resuscitation group and for 2716 in the no bystander resuscitation group.

Table 1: **Baseline characteristics of the patients**

	Cardiac-only resuscitation	Conventional CPR	p value
Age (years)	69 (55-80)	68 (55-80)	0·3002
Male sex	316/439 (72%)	462/712 (65%)	0·0125
Cardiac cause	305/439 (69%)	501/712 (70%)	0·7491
Location of cardiac arrest			0·0063
Home or other residence	253/432 (59%)	345/706 (49%)	
Public, indoors	136/432 (31%)	277/706 (40%)	
Public, outdoors	43/432 (10%)	84/706 (12%)	
First physical findings at arrival of EMS			
Gasping breathing	50/439 (11%)	73/712 (10%)	0·5443
Pupilometer (mm*)	5·0 (5·0-6·0)	5·0 (5·0-6·0)	0·7251
Initial cardiac rhythm			0·9116
VF/pulseless VT	124/439 (28%)	205/712 (29%)	
PEA	94/439 (21%)	145/712 (20%)	
Asystole	221/439 (50%)	362/712 (51%)	
Treatment			
Defibrillatory shock	173/439 (39%)	267/712 (38%)	0·5177
Tracheal intubation	424/439 (97%)	695/712 (98%)	0·3022
Epinephrine	397/439 (90%)	650/712 (91%)	0·6213
Hypothermia	10/439 (2%)	18/712 (3%)	0·7890
Medical history			
Coronary heart disease	52/429 (12%)	70/689 (10%)	0·3063
Hypertension	60/429 (14%)	118/689 (17%)	0·1628
Heart failure	12/429 (3%)	23/689 (3%)	0·6135
Diabetes	52/429 (12%)	81/689 (12%)	0·3848
Performer of bystander resuscitation			<0·0001
Off-duty medical staff	97/439 (22%)	350/712 (49%)	
Lay person with CPR training	70/439 (16%)	128/712 (18%)	
Lay person with dispatcher-assisted resuscitation	139/439 (32%)	133/712 (19%)	
Lay person with no training or assisted resuscitation	133/439 (30%)	101/712 (14%)	
Time (min)			
From collapse to first bystander resuscitation attempt†	4·0 (2·0-5·0)	4·0 (2·0-5·0)	0·8080
From first bystander resuscitation attempt to first AED analysis	9·0 (8·0-11·0)	9·0 (7·0-11·0)	0·3846
From first AED analysis to departure from scene‡	14·0 (10·0-18·0)	14·0 (11·0-18·0)	0·7379
From departure to arrival at hospital§	10·0 (6·0-13·0)	10·0 (6·0-13·0)	0·8020

Data are median (IQR) or numerator/total number (%). Calculations based on available data.
AED=automated external defibrillator. CPR=cardiopulmonary resuscitation. EMS=emergency medical services. PEA=pulseless electrical activity. VF=ventricular fibrillation. VT=ventricular tachycardia. *The pupil was measured by EMS workers using one patient's checklist card with pupillometer rulers, and was recorded for 421 patients in the cardiac-only resuscitation group, and for 659 in the conventional CPR group. †The time was recorded for 323 patients in the cardiac-only resuscitation group, and for 527 in the conventional CPR group. ‡The time was recorded for 436 in the cardiac-only resuscitation group, and for 689 in the conventional CPR group. §The time was recorded for 414 in the cardiac-only resuscitation group, and for 659 in the conventional CPR group.

Table 2: **Baseline characteristics of the patients receiving bystander CPR**

1 (good performance) or 2 (moderate disability) on a five-category scale.[12] The other categories of 3 (severe disability), 4 (vegetative state), and 5 (death) were regarded as unfavourable neurological outcome.[12] The secondary endpoint was survival 30 days after cardiac arrest, defined as a Glasgow-Pittsburgh cerebral-performance category of 1, 2, 3, or 4. The neurological outcome was defined by physicians who were unaware of the patient's bystander resuscitation group.

Statistical analysis

An estimate of the number of patients needed to test our hypothesis was derived from analyses of three previous large-scale studies in Japan.[13-16] The calculation was based on a two-fold improvement in favourable neurological outcomes from a baseline outcome of 1·6, and a 1:1:6 ratio of patients who had bystander-witnessed cardiac arrest and received cardiac-only resuscitation versus conventional CPR versus no resuscitation. The minimum sample size for comparison of favourable neurological outcome at 30 days was estimated to be 400 patients for each bystander resuscitation group, and 1120 patients for the no bystander resuscitation group on the basis of a two-sided α value of 0·05 and a β error of 0·10. Baseline characteristics were compared by use of the χ^2 test for categorical variables and the Mann-Whitney U test for continuous variables, as appropriate. Odds ratios and their 95% CI were calculated for the study endpoints. A multiple logistic-regression analysis was done for independent predictors of resuscitation, including age, cause of cardiac arrest, technique of bystander resuscitation, resuscitation-related time intervals, and initial recorded cardiac rhythm.[12] The non-linear regression analysis with logarithm was used to illustrate the relation between favourable neurological outcome 30 days after cardiac arrest and the time between first bystander resuscitation attempts and first use of automated external defibrillator (AED) in patients receiving bystander CPR with ventricular fibrillation or ventricular tachycardia as an initial cardiac rhythm.

Role of the funding source

The sponsors had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data and had final responsibility for the decision to submit for publication.

Results

9592 patients received advanced life support by paramedics and were transported to emergency hospitals during the study. Of those, 5464 patients were not eligible. The SOS-KANTO study therefore included 4068 adult patients who had bystander-witnessed cardiac arrest out of hospital; 1151 (28%) received bystander resuscitation, including 439 (11%) who received cardiac-only resuscitation and 712 (18%) who received conventional CPR, and 2917 (72%) did not receive any bystander resuscitation. No patient was lost to follow-up for study endpoints at 30 days after cardiac arrest (figure 1).

At baseline, significant differences (table 1) were seen between the any resuscitation group and the no bystander resuscitation group for cause of cardiac arrest, location where the cardiac arrest happened, proportion with gasping breathing and pupillometer reading at arrival of emergency medical services, initial recorded cardiac rhythm, and the need for defibrillation by emergency

	Cardiac-only resuscitation	Conventional CPR	No bystander resuscitation	Any resuscitation versus no bystander resuscitation	Cardiac-only resuscitation versus no bystander resuscitation	Cardiac-only resuscitation versus conventional CPR
All patients	27/439 (6%)	30/712 (4%)	63/2917 (2%)	2·4 (1·6–3·4)	3·0 (1·9–4·7)	1·5 (0·9–2·5)
Cause						
Cardiac	26/305 (9%)	27/501 (5%)	54/1836 (3%)	2·3 (1·6–3·4)	3·1 (1·9–5·0)	1·6 (0·9–2·9)
Non-cardiac	1/134 (0·7%)	3/211 (1%)	9/1081 (0·8%)	1·4 (0·4–4·6)	0·9 (0·1–7·1)	0·5 (0·1–5·1)
Findings at arrival of EMS						
Apnoea (no gasping)	24/389 (6%)	20/639 (3%)	55/2751 (2%)	2·2 (1·5–3·3)	3·2 (2·0–5·3)	2·0 (1·1–3·7)
Gasping breath	3/50 (6%)	10/73 (14%)	8/166 (5%)	2·3 (0·9–5·8)	1·3 (0·3–4·9)	0·4 (0·1–1·5)
VF/pulseless VT	24/124 (19%)	23/205 (11%)	45/549 (8%)	1·9 (1·2–2·9)	2·7 (1·6–4·6)	1·9 (1·0–3·5)
PEA	1/94 (1%)	3/145 (2%)	8/755 (1%)	1·6 (0·5–5·3)	1·0 (0·1–8·2)	0·5 (0·1–5·0)
Asystole	2/221 (0·9%)	4/362 (1%)	10/1613 (0·6%)	1·7 (0·60–4·6)	1·5 (0·3–6·7)	0·8 (0·1–4·5)
Time from EMS call to first AED analysis						
≤10 min	22/286 (8%)	22/403 (5%)	52/1801 (3%)	2·3 (1·5–3·5)	2·8 (1·7–4·7)	1·4 (0·8–2·7)
>10 min	5/153 (3%)	8/309 (3%)	11/1116 (1%)	2·9 (1·3–6·5)	3·4 (1·1–9·9)	1·3 (0·4–4·0)
Time from collapse to first bystander resuscitation attempt						
≤4 min	23/227 (10%)	18/351 (5%)				2·1 (1·1–4·0)
>4 min	2/96 (2%)	4/176 (2%)				0·9 (0·2–5·1)
Time from first bystander resuscitation attempt to first AED analysis						
≤9 min	20/210 (10%)	18/295 (6%)				1·6 (0·8–3·1)
>9 min	5/113 (4%)	4/232 (2%)				2·6 (0·7–10·0)
Performer of CPR						
Lay person	23/342 (7%)	19/362 (5%)				1·3 (0·7–2·4)
Off-duty medical worker	4/97 (4%)	11/350 (3%)				1·3 (0·4–4·3)

Data are numerator/total number or odds ration (95% CI). AED=automated external defibrillator. CPR=cardiopulmonary resuscitation. EMS=emergency medical services. PEA= pulseless electrical activity. VF=ventricular fibrillation. VT=ventricular tachycardia.

Table 3: **Patients with a favourable neurological outcome at 30 days after cardiac arrest**

medical workers. Generally, the two groups that received bystander resuscitation had similar baseline characteristics (table 2). However, higher proportions in the cardiac-only resuscitation group than in the conventional group were male, more patients had cardiac arrest at home, and more were treated by lay people. The group who had any resuscitation attempt had significantly higher frequencies of favourable neurological outcome at 30 days than the no bystander resuscitation group in the whole cohort (5% [57/1151 *vs* 2% [63/2917]; p<0·0001) and in the subgroups of patients with cardiac causes (7% [53/806] *vs* 3% [54/1836]; p<0·0001), with apnoea (4% [44/1028] *vs* 2% [55/2751]; p<0·0001], with ventricular fibrillation or tachycardia as initial cardiac rhythm (14% [47/329] *vs* 8% [45/549]; p=0·0044), and with both of the times between call to emergency medical services and first AED analysis (for interval ≤10 min; 6% [44/689] *vs* 3% [52/1801]; p<0·0001: for interval >10 min; 3% [13/462] *vs* 1% [11/1116]; p=0·0069). The cardiac-only resuscitation group also had significantly higher frequencies of favourable neurological outcome at 30 days than the no bystander resuscitation group in those categories. Although the frequency of favourable neurological outcome at 30 days did not differ between the cardiac-only resuscitation group and the conventional CPR group for the whole cohort (p=0·1459, table 3), cardiac-only resuscitation resulted in a higher proportion of patients with favourable neurological outcomes than conventional CPR in the subgroups of patients with apnoea (p=0·0195), with ventricular fibrillation or tachycardia as initial cardiac rhythm (p=0·041), and with

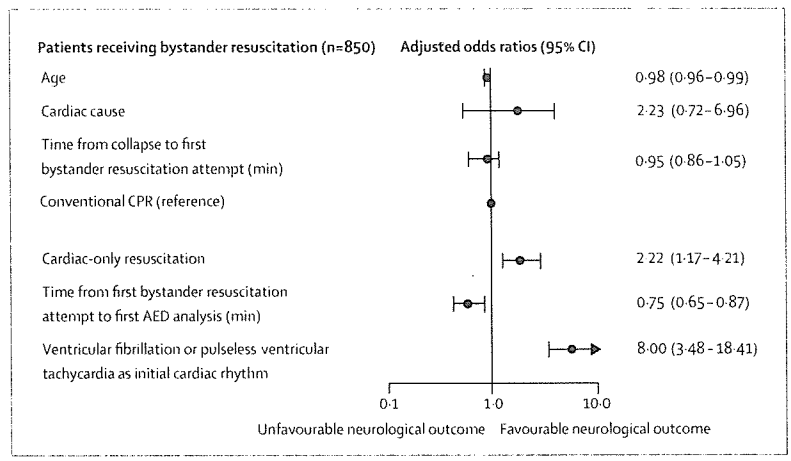

Figure 2: **Adjusted odds ratios for primary endpoint associated with selected factors in patients receiving bystander resuscitation whose bystander resuscitation-related time intervals were known**

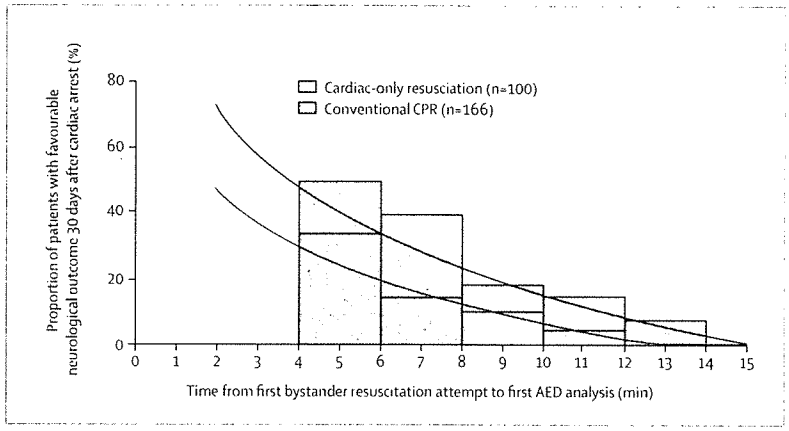

Figure 3: **Relation between primary endpoint and time from first bystander resuscitation attempts to first AED analysis in patients who received bystander resuscitation with ventricular fibrillation or pulseless ventricular tachycardia**

Each curve shows predicted frequency of favourable neurological outcome at 30 days by the non-linear regression analysis with logarithm (vertical axis shows predicted frequency of favourable neurological outcome, and predicted frequency of 1 is equivalent to 100%). Each box represents the actual frequencies of favourable neurological outcome at 30 days for each bystander resuscitation group every 2 min. p=0·0086 for comparison of cardiac-only resuscitation group with conventional CPR group.

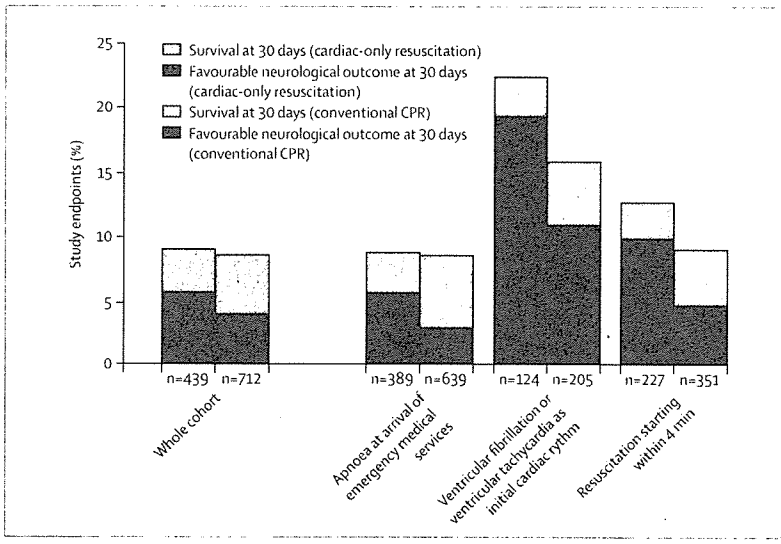

Figure 4: **Frequencies of study endpoints between the cardiac-only resuscitation group and the conventional CPR group in all patients and in subgroups of patients**

resuscitation starting within 4 min of collapse (p=0·0221). However, the bystander resuscitation groups had similar frequencies of favourable neurological outcome at 30 days in the subgroups of patients who received bystander resuscitation from a lay person or from a medically trained person. Additionally, there was no evidence for any benefit from the addition of mouth-to-mouth ventilation in any subgroup of patients who received bystander resuscitation.

Multiple logistic-regression analysis (figure 2) showed that cardiac-only resuscitation resulted in higher proportions of favourable neurological outcome than conventional CPR (p=0·0144), and other independent predictors of favourable outcome were age, time between first bystander resuscitation attempt and first AED analysis, and ventricular fibrillation or tachycardia as initial cardiac rhythm. When sex and gasping breathing were included in the analysis, the results did not change.

Figure 3 shows the relation between favourable neurological outcome at 30 days and the time between first bystander resuscitation attempt and first AED analysis (ie, the duration of bystander resuscitation) in patients with ventricular fibrillation or tachycardia. Cardiac-only resuscitation resulted in higher proportions of favourable neurological outcome than conventional CPR (22% [22/100] vs 10% [17/166], the odds ratio, 2·5; 95% CI, 1·2–4·9; p=0·0086], and likelihood of a favourable neurological outcome decreased in both bystander resuscitation groups for every 1 min increment in time from first resuscitation attempt to first AED analysis (p=0·0105 for the cardiac-only rescuscitation and p=0·0003 for conventional CPR). When the time from collapse to first AED analysis was used instead, the results were unchanged.

The proportions of people who were alive at 30 days differed from those who had favourable neurological outcome at 30 days (figure 4). In all subgroups of patients, the proportions surviving at 30 days showed no differences between the two bystander resuscitation groups, and these two groups also had similar frequencies of survival until hospital admission.

Discussion

This report shows that bystander cardiac-only resuscitation is equivalent or superior to conventional bystander CPR in adult patients with witnessed out-of-hospital cardiac arrest, in terms of neurological benefit. Not only the any resuscitation group, but also the cardiac-only resuscitation group had higher proportions of favourable neurological outcome than the no bystander resuscitation group for the whole cohort, and cardiac-only resuscitation resulted in better outcome than conventional CPR in some important subgroups of patients. These subgroups included patients with apnoea (about 90% of patients in this study), and those with shockable cardiac rhythm or short periods of untreated arrest (CPR that started within 4 min of arrest). These patients had the greatest chance of survival (table 3, figures 3 and 4). After adjustment for resuscitation, cardiac-only resuscitation was an independent predictor of favourable neurological outcome in patients who received bystander resuscitation (figure 2). Furthermore, there was no evidence for any benefit from the addition of mouth-to-mouth ventilation in any subgroup of patients (table 3, figures 2, 3, and 4).

Some experts have expressed concern that the absence of assisted ventilation with chest compressions might result in lower survival and worse neurological outcomes in survivors of cardiac arrest.[14] Several clinical studies have

shown that cardiac-only resuscitation is at least as effective as chest compression with mouth-to-mouth ventilation.[8,21,22] In this study, however, cardiac-only resuscitation resulted in better or similar neurological outcome than conventional CPR. Moreover, the proportion of patients surviving, including those surviving until hospital admission, showed no differences between the cardiac-only resuscitation group and the conventional CPR group in any subgroup of patients. The number of patients who received bystander cardiac-only resuscitation was higher in this study (n=439) than in previous ones (n=273,[21] 241,[22] and 41[8]). We suggest that the large number of patients provided adequate power to attribute better neurological outcome to cardiac-only resuscitation, and there was no evidence of increased numbers of survivors with neurologically unfavourable outcomes in the group who had cardiac-only resuscitation compared with conventional CPR.

Several mechanisms might account for the efficacy of cardiac-only resuscitation. If the airway is open, gasping breathing and passive chest recoil provide some air exchange.[15,29–33] Measured minute ventilation and arterial oxygenation decrease after 4–10 min of resuscitation irrespective of attempts at ventilation.[15,26,30] Several studies suggest that ventilation is not essential during the initial 12 min of resuscitation with untreated arrest intervals of less than 6 min,[15,25,30,31] and that gasping breathing is associated with a better outcome.[15,29,31,33] In this study, most patients who had bystander resuscitation had an untreated arrest interval of less than 6 min and a duration of bystander resuscitation of less than 12 min, and the two bystander resuscitation groups had similar time intervals and had similar proportions of patients with gasping breath.

Another reason for the efficacy of cardiac-only resuscitation could be that mouth-to-mouth ventilation has several potential disadvantages. These disadvantages include gastric insufflations and importantly, less cycle time spent on effective compressions.[3–4,15,19,23–28,34] Time spent on mouth-to-mouth ventilation takes precious time away from chest compressions that support cerebral and coronary perfusion.[4,15,19,23–28] Intrathoracic pressure drops after each pause for mouth-to-mouth ventilation, and several chest compressions have to be done before previous rates of cerebral and coronary perfusion are re-established.[3,4,26] In this study, the quality of chest compressions might not have been as good in the cardiac-only resuscitation group as in the conventional resuscitation group, because the proportion of patients treated by people with no first-aid training, with or without dispatcher-assistance, was higher in the cardiac-only group (272/439, 62% *vs* 234/712, 33%). Also, the proportion treated by medically trained individuals was lower in the cardiac-only group than in the conventional CPR group (97/439, 22% *vs* 350/712, 49%) However, there would be less interruption of chest compressions in the cardiac-only resuscitation group. We suggest that interruption of chest compressions was the main reason why conventional CPR did not result in better neurological outcome than cardiac-only resuscitation.

There are several limitations to our study. It was neither a randomised controlled trial nor a population-based study. However, the overall survival and patients' characteristics in this study were similar to those of population-based studies from similar large metropolitan areas—Osaka, Japan,[13] and New York, USA[35] Although the total number of patients was large, there were few patients with arrest caused by asphyxia, drowning, or traumatic brain injury. The quality of bystander resuscitation was not assessed, and resuscitation-related event times were known for only 70% of the study population. Additionally, post-resuscitation care could not be standardised. Recent studies[14,36–38] have shown that therapeutic hypothermia can result in better outcomes for patients with out-of-hospital ventricular fibrillation. In this study, few patients were treated by induction of hypothermia, and the proportions given this treatment were similar in the two bystander resuscitation groups.

On the basis of these findings, we conclude that bystander cardiac-only resuscitation is the preferred approach to resuscitation for adult patients with witnessed out-of-hospital cardiac arrest especially those with apnoea, shockable cardiac rhythm, or short periods of untreated arrest.

SOS-KANTO study group

Nihon University Surugadai Hospital, Tokyo, Japan (Ken Nagao MD, Kimio Kikushima MD); Teikyo University Hospital, Tokyo, Japan (Tetsuya Sakamoto MD); Kawaguchi Municipal Medical Center, Saitama, Japan (Kazuhide Koseki MD); Toho University Oomori Hospital, Tokyo, Japan (Masaki Igarashi MD); St Luke's International Hospital, Tokyo, Japan (Shinichi Ishimatsu MD); Saitama Medical School Hospital, Saitama, Japan (Akira Sato MD); Keio University Hospital, Tokyo, Japan (Shingo Hori MD); Showa University Fugigaoka Hospital, Tokyo, Japan (Shigeru Kanesaka MD); Tokyo Metropolitan Bokutoh Hospital, Tokyo, Japan (Yuichi Hamabe MD); National Defense Medical College, Saitama, Japan Daizo Saito MD); and Kimitsu Chuo Hospital, Chiba, Japan (Shinya Kitamura MD).

Contributors

K Nagao and T Sakamoto as principal investigators, participated in idea formation, study design and completion, data collection, data management, data analyses, interpretation of results and revision of the report, and contributed to the final report. K Nagao obtained funding. K Kikushima, K Koseki, M Igarashi, S Ishimatsu, A Sato, S Hori, S Kanesaka, Y Hamabe, D Saito, and S Kitamura participated in study idea formation, study designand completion, data collection, data management, and interpretation of the results. K Nagao, T Sakamoto, K Kikushima, and D Saito did the statistical analysis. All authors approved the final version.

Participating investigators and co-ordinators—Akiko Nonaka, Atsushi Katsumi, Atsushi Sakurai, Hiroaki Suzuki, Hiroshi Imai, Hiroshi Miyauchi, Hiroyasu Suga, Jozi Tomioka, Kazutaka Imai, Kazuya Kiyota, Ken Arima, Kitoji Takuhiro, Kiyoshi Matsuda, Kohei Takahashi, Masafumi Naito, Masaharu Yagi, Masato Honma, Masaru Sasaki, Masaru Suzuki, Minoru Nakano, Naohiko Fugiyoshi, Naoki Kozima, Naoshige Harada, Noriyoshi Ohashi, Noriyuki Suzuki, Ryutaro Moriwaki, Ryoji Takahashi, Satoru Kikuchi, Seichi Noda, Shigeto Oda, Shohei Imaki, Tadashi Fugikawa, Takaaki Kikuno, Takashi Kamohara, Takayuki Suda, Tatsuo Ishii, Tokuzi Irabu, Tomohito Sadahiro, Toshiaki Ikeda, Toshiharu Tanaka, Toshihiko Obayashi, Toshiro Ogawa, Yasuyuki Miyahara, Yoshihide Nakagawa, Yoshiki Tokuyasu, Yoshio Tawara, Yoshiyuki Haga, Yoshiyuki Minowa, Yukio Tanaka, Zyunichi Sasaki, and Zyunmei Fudouzi.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

We thank all the bystanders who undertook basic resuscitation and the paramedics, emergency medical technicians, nurses, and physicians who participated in the SOS-KANTO study. This study was supported by a grant from the Laerdal Foundation of Acute Medicine, Norway and a research grant for Cardiovascular Disease (14c-7) from the Ministry from Health, Labour and Welfare, Japan

References

1 Cummins RO, Chamberlain DA, Abramson NS, et al. Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the Utstein Style: a statement for health professionals from a task force of the American Heart Association, the European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the Australian Resuscitation Council. *Circulation* 1991; **84:** 960–75.

2 American Heart Association in collaboration with International Liaison Committee on Resuscitation. Guidelines 2000 for cardiopulmonary resuscitation and emergency cardiovascular care: international consensus on science. *Circulation* 2000; **102** (suppl I): II–384.

3 International Liaison Committee on Resuscitation. 2005 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. *Circulation* 2005; **112:** I–136.

4 American Heart Association. 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2005; **102:** IV1–205.

5 Herlitz J, Ekstrom L, Wennerblom B, Axelsson A, Bang A, Holmberg S. Effect of bystander initiated cardiopulmonary resuscitation on ventricular fibrillation and witnessed cardiac arrest outside hospital. *Br Heart J* 1994; **72:** 408–12.

6 Gallagher EJ, Lombardi G, Gennis P. Effectiveness of bystander cardiopulmonary resuscitation and survival following out-of-hospital cardiac arrest. *JAMA* 1995; **274:** 1922–25.

7 Holmberg M, Holmberg S, Herlitz J; Swedish Cardiac Arrest Registry. Factors modifying the effect of bystander cardiopulmonary resuscitation on survival in out-of-hospital cardiac arrest patients in Sweden. *Eur Heart J* 2001; **22:** 511–19.

8 Waalewijn RA, Tijssen JGP, Koster RW. Bystander initiated actions in out-of-hospital cardiopulmonary resuscitation: results from the Amsterdam Resuscitation Study (ARREST). *Resuscitation* 2001; **50:** 273–79.

9 Stiell IG, Wells GA, Field B, et al. Advanced cardiac life support in out-of-hospital cardiac arrest. *N Engl J Med* 2004; **351:** 647–56.

10 Ewy GA. Cardiopulmonary resuscitation-strengthening the links in the chain of survival. *N Engl J Med* 2000; **342:** 1599–61.

11 Wenzel V, Krismer AC, Arntz HR, et al. A comparison of vasopression and epinephrine for out-of-hospital cardiac resuscitation. *N Engl J Med* 2004; **305:** 105–13.

12 Mashiko K, Otsuka T, Shimazaki S, et al. An outcome study of out-of-hospital cardiac arrest using the Utstein template—a Japanese experience. *Resuscitation* 2002; **55:** 241–6.

13 Iwami T, Hiraide A, Nakanishi N, et al. Age and sex analysis of out-of-hospital cardiac arrest, Japan. *Resuscitation* 2003; **57:** 145–52.

14 SOS-KANTO committee. Survey of survivors after cardiac arrest in the kanto area: SOS-KANTO, the result of initial totaling. *KANTO J Jpn Assoc Acute Med* 2003; **24:** 10–16 (in Japanese).

15 Becker LB, Berg RA, Pepe PE, et al. A reappraisal of mouth-to-mouth ventilation during bystander-initiated cardiopulmonary resuscitation: a statement for healthcare professionals from the ventilation working group of the basic life support and pediatric life support subcommittees, American Heart Association. *Circulation* 1997; **96:** 2102–12.

16 Ornato JP, Hallagan LF, McMahan SB, Peeples EH, Rostafinski AG. Attitudes of BCLS instructors about mouth-to-mouth resuscitation during the AIDS epidemic. *Ann Emerg Med* 1990; **19:** 151–56.

17 Brenner BE, Kauffman J. Reluctance of internists and medical nurses to perform mouth-to-mouth resuscitation. *Arch Intern Med* 1993; **153:** 1763–69.

18 Braslow A, Brennan RT, Newman MM, Bircher NG, Batcheller AM, Kaye W. CPR training without an instructor: development and evaluation of a video self-instructional system for effective performance of cardiopulmonary resuscitation. *Resuscitation* 1997; **34:** 207–20.

19 Assar D, Chamberlain D, Colquhoun M, et al. Randomized controlled trials of staged teaching for basic life support. 1: Skill acquisition at bronze stage. *Resuscitation* 2000; **45:** 7–15.

20 Chamberlain D, Smith A, Colquhoun M, Handley AJ, Kern KB, Wodllard M. Randomized controlled trials of staged teaching for basic life support 2. Comparison of CPR performance and skill retention using either staged instruction or conventional training. *Resuscitation* 2001; **50:** 27–37.

21 Van Hoeyweghen RJ, Bossaert LL, Mullie A, et al; Belgian Cerebral Resuscitation Study Group. Quality and efficiency of bystander CPR. *Resuscitation* 1993; **26:** 47–52.

22 Hallstrom A, Cobb L, Johnson E, Copass M. Cardiopulmonary resuscitation by chest compression alone or with mouth-to-mouth ventilation. *N Engl J Med* 2000; **342:** 1546–53.

23 Wik L, Kramer-Johansen J, Myklebust H, et al. Quality of cardiopulmonary resuscitation during out-of-hospital cardiac arrest. *JAMA* 2005; **293:** 299–304.

24 Valenzuela TD, Kern KB, Clark LL, et al. Interruptions of chest compressions during emergency medical systems resuscitation. *Circulation* 2005; **112:** 1259–65.

25 Berg RA, Kern KB, Sanders AB, Otto CW, Hilwig RW, Ewy GA. Bystander cardiopulmonary resuscitation: is ventilation necessary? *Circulation* 1993; **88:** 1907–15.

26 Kern KB, Hilwig W, Berg RB, Sinders AB, Ewy GA. Importance of continuous chest compression during cardiopulmonary resuscitation. Improved outcome during a simulated single lay-rescuer scenario. *Circulation* 2002; **105:** 645–49.

27 Yu T, Weil MH, Tang W, et al. Adverse outcomes of interrupted precordial compression during automated defibrillation. *Circulation* 2002; **106:** 368–72.

28 The guideline of ethics for the epidemiological survey. The Ministry of Health, Labor and Welfare in Japan Web site. Available at: http://www.mhlw.go.jp/general/seido/kousei/i-kenkyu/index.html#2 (accessed Mar 6, 2007).

29 Chandra NC, Gruben KG, Tsitlik JE, et al. Observations of ventilation during resuscitation in a canine model. *Circulation* 1994; **90:** 3070–75.

30 Noc M, Weil MH, Tang W, Turner T, Fukui M. Mechanical ventilation may not be essential for initial cardiopulmonary resuscitation. *Chest* 1995; **108:** 821–27.

31 Berg RA, Kern KB, Hilwig RW, et al. Assisted ventilation does not improve outcome in a porcine model of single-rescuer bystander cardiopulmonary resuscitation. *Circulation* 1997; **95:** 1635–41.

32 Idris AH, Banner MJ, Wenzel V, Fuerst RS, Becker LB, Melker RJ. Ventilation caused by external chest compression is unable to sustain effective gas exchange during CPR: a comparison with mechanical ventilation. *Resuscitation* 1994; **28:** 143–50.

33 Clark JJ, Larsen MP, Culley LL, Graves JR, Eisenberg MS. Incidence of agonal respirations in sudden cardiac arrest. *Ann Emerg Med* 1992; **21:** 1464–67.

34 Sanders AB, Ewy GA. Cardiopulmonary resuscitation in the real world: when will the guidelines get the message? *JAMA* 2005; **293:** 363–65.

35 Richmond N, Silverman R, Kusick M, Foltin G, Vlahov D. Survival from out-of-hospital cardiac arrest in New York City: 10 years later. *Circulation* 2004; **110:** III–455 (abstract).

36 Nagao K, Hayashi N, Kanmatsuse K, et al. Cardiopulmonary cerebral resuscitation using emergency cardiopulmonary bypass, coronary reperfusion therapy and mild hypothermia in patients with cardiac arrest outside the hospital. *J Am Coll Cardiol* 2000; **36:** 776–83.

37 The Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcomes after cardiac arrest. *N Engl J Med* 2002; **346:** 549–56. (Erratum. *N Engl J Med 2002*; **346:** 1756).

38 Berrard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med* 2002; **346:** 557–63.

ACLS 2005 ガイドラインで何が変わったのか 7
蘇生後の治療

長尾 建

ながお けん：駿河台日本大学病院 救命救急センター

● はじめに

2000年に報告された心肺蘇生法（cardiopulmonary resuscitation：CPR）と救急心血管治療の国際ガイドラインでは，心停止心拍再開後のresuscitative hypothermiaは多施設無作為比較臨床試験がなかったことから，その効果は未確定とした[1]。しかし，2005年に改変された国際ガイドラインでは，かかるresuscitative hypothermiaをClass II a（有用・有益・有効性が高い）として支持した[2,3]。

● Resuscitative hypothermia 2002 多施設無作為比較試験

2002年，N Engl J Medに院外心停止心拍再開後の患者に対する無作為比較試験が二つ報告された[4,5]。一つはヨーロッパの5ヵ国9センターが参加した多施設無作為比較試験であった。深部体温（膀胱温）をモニタリングし，24時間・32～34℃に冷却した低体温施行群137例と非冷却群（正常体温）138例に割付けた。そして6ヵ月以内の良好な神経学的転帰を比較した。低体温施行例の良好な転帰は55%，正常体温施行例のそれは39%で，有意に32～34℃・24時間の冷却が神経学的転帰を改善したとした[4]。

もう一つはオーストラリアの4病院が参加した多施設無作為比較試験であった。深部体温を鼓膜温または膀胱温で，最終的には肺動脈血液温をモニタリングし，12時間・33℃に冷却した低体温施行群43例と正常体温群34例に割付けた。そして，退院または転院時の良好な神経学的転帰を比較した。低体温施行例の良好な転帰は49%，正常体温施行例のそれは26%で，有意に33℃・12時間の冷却が神経学的転帰を改善したとした[5]。

● ILCOR の therapeutic hypothermia 勧告 2003

上記二つの多施設無作為比較試験成績をもとに，2003年ILCORは下記のごとくのresuscitative hypothermiaを勧告した[6]。

①初回心電図リズムが心室細動（ventricular fibrillation：VF）の院外心停止で心拍再開後も昏睡状態にある成人患者は，32～34℃・12～24時間の冷却をすべきである。

②かかる低体温治療は，院外VF以外の無脈性電気活動や心静止，または院内心停止後に心拍が再開した患者にも有益かもしれない。

● 国際 CPR ガイドライン 2005

以上のことから，2005AHAガイドラインでは前項の①はclass II a，②はclass II bとした[1]。

1 Resuscitative hypothermia の患者選択規準

表1にヨーロッパ試験，オーストラリア試験，および自施設の院外心停止例に対するresuscitative hypothermiaの患者導入規準と除外規準を示す[7]。これらの患者選択規準の多く

表 1　Resuscitative hypothermia の患者選択規準
ヨーロッパ試験 vs オーストラリア試験 vs 自験例（文献 7 より引用）

	ヨーロッパ試験	オーストラリア試験	自験例
導入規準			
年齢（歳）	18～75	男＞18，女＞50	18～74
目撃された心停止	Yes		Yes
VF または無脈性 VT	Yes	Yes	Yes
心臓性心停止	Yes	Yes	Yes
CPR 開始までの時間（分）	5～15		≤15
心拍再開までの時間（分）	＜60		
心拍再開後昏睡状態	Yes	Yes	Yes
除外規準			
心拍再開後ショック状態	Yes	Yes	Yes
低酸素血症	Yes		
妊娠	Yes	Yes	Yes

は一致している。すなわち成人，心原性 VF，心拍再開後に循環動態は改善するも昏睡状態にある患者である。一方，異なる規準としては，目撃者の有無，高齢者（76 歳以上），救急隊による CPR 開始までの時間，心拍再開までに要した時間があげられる。

したがって 2005AHA ガイドラインでは，resuscitative hypothermia 患者導入規準のよい適応として，初回心電図が VF の院外心停止で心拍再開後も昏睡状態にある成人患者とした。さらに，有益かもしれない適応患者として，院外非 VF，院内心停止後に心拍が再開した例とした[1]。

では，この適応規準を満たす院外心停止の患者は，わが国ではどのくらいいるのだろうか。SOS-KANTO，ウツタイン大阪プロジェクトでは総院外心停止の 5%程度と推測される[8,9]。

2005 年，低酸素・虚血性脳症の新生児に対する低体温療法の無作為比較試験が報告された[10]。33.5℃，72 時間の低体温療法は中等症～重症の低酸素・虚血性脳症の死亡，脳障害を軽減したとした。したがって，新生児にも有用であると思われる。

2　Resuscitative hypothermia の冷却手法

ヨーロッパ試験では，病院到着後に体表面をクーリングブランケットと必要に応じてアイスパックを用いて冷却する手法を用いた[4]。オーストラリア試験では，救急車内で心拍再開直後からアイスパックで冷却を開始し，病院到着後，全身（頭部，頸部，躯幹，四肢）の体表面をアイスパックで冷却した[5]。体表面冷却法とは別の冷却手法として，4℃ に冷却した輸液を 1～2L 急速に静脈内投与する手法[11]，血液を体外循環で冷却する手法（自施設では，現在持続的血液透析回路に組みこんで静脈血を冷却する KTEK-3）[7,12]，血管内に冷却カテーテルを挿入して血液を冷却する手法などが報告されている[6,13]。

2005AHA ガイドラインでは，体表面冷却法が簡便であるとしたが，目標深部体温到達までに時間を要するとした（ヨーロッパ試験では平均 8 時間）[3]。さらに，正確な深部体温保持には熟練を要する。自施設では現在，収容直後から，4℃ 細胞外液輸液を 1～2L（体重により調整）を急速ボーラス投与し，引き続き KTEK-3 を用いた体外式血液直接冷却手法を用い，迅速かつ正確な深部体温管理を簡便に実施している[14]。この体外式血液直接冷却手法の有用性は，ヨーロッパ試験の Holzer らも報告している[15]。

3　Resuscitative hypothermia の開始時期，目標深部体温，持続時間

冷却開始時期は早期であればあるほど，その有効性は高いと考えられている[2,3,6]。しかし，その冷却開始時期の限界点，また目標深部体温

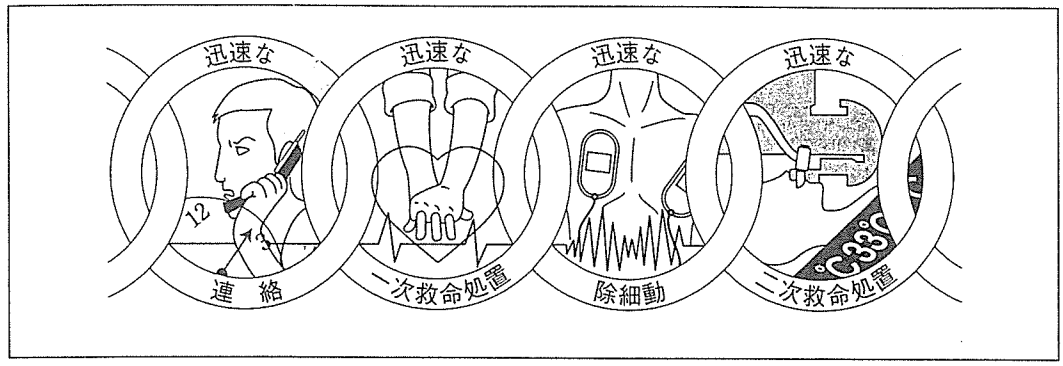

図 1　救命の連鎖（The chain of survival）
文献 19 より引用

到達までの時間の限界点は，さらに至適目標深部体温は 32～34℃が最適なのか，その冷却持続時間は，心停止時間（心拍再開までの時間）で異なるのか否かなどの検証は十分でなく，今後の課題としている[2,3,6]。自施設では，心停止から心拍再開までの時間により 3 分類し，その効果を検証している。わが国でも，かかる課題に対する多施設共同無作為比較試験を実施したい。

4　Resuscitative hypothermia の有害事象

ヨーロッパ試験では，hypothermia 関連の有害事象出現率は，正常体温施行例と有意差を示さなかったとした（低体温施行例 vs 正常体温例：すべての出血；26%vs19%，血小板輸血；1%vs0%，肺炎；37%vs29%，敗血症；13%vs7%，膵炎；1%vs1%，腎不全；10%vs10%，人工透析；4%vs4%，肺水腫；7%vs4%，痙攣発作；7%vs8%，重症不整脈；36%vs32%）[4]。オーストラリア試験でも 2 群間で有害事象出現率に有意差を認めなかったとした。しかし，低体温施行例は正常体温例に比し，冷却期間中の心係数は低値，体血管抵抗と血糖値が有意に高値であったと報告した[5]。

2005AHA ガイドラインでは，凝固障害，重症不整脈，高血糖を指摘している[3]。

5　血糖管理の必要性

2005 ILCOR, AHA ガイドラインでは，resuscitative hypothermia 施行例を含め，蘇生後の血糖（正常範囲内）管理の必要性を報告した[2,3]。これは，蘇生後の高血糖が神経学的転帰と関連している研究があるとしたためであった[16]。また 2001 年，蘇生後患者ではないが，重症患者の血糖管理がその院内死亡率を減少させた報告があったためであった[17]。しかし，その血糖管理の至適値はどのくらいか，今後の研究課題とした。

自施設では，心原性ショック時の収容時血糖値がその転帰に関与し，そのカットオフ値は 166 mg/dL であったことを報告した[18]。

● おわりに

院外心停止患者の転帰を最大限に引き上げるには，おのおのの国，地域で the Chain of Survival（迅速な通報，迅速な一次救命処置，迅速な除細動，迅速な二次救命処置）をウツタイン様式を用いて検証し，その弱点を明らかにし，救急医療体制を再構築していくことである。

図 1 にわが国の社会に適した the Chain of Survival の内容を，おのおのの鎖の中に示した。

迅速な携帯電話による 119 番通報，迅速な市民による心臓マッサージのみ CPR，迅速な AED を用いた電気的除細動，迅速な hypothermia の導入が，わが国の救急医療に大きく貢献すると考えている[19]。

文献

1) The American Heart Association in Collaboration with the International Liaison Committee on Resuscitation. Circulation 2000；102：I-1-384.
2) 2005 International Consensus on Cardiopulmonary Resuscitation（CPR）and Emergency Cardiovascular Care（ECC）Science with Treatment Recommendations. Circulation 2005；112：III-I-136.
3) 2005 American Heart Association Guidelines for

Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2005；112：IV-6-211.
4) The Hypothermia after Cardiac Arrest Study Group. N Engl J Med 2002；346：549-56.
5) Bernard SA, Gray TW, Buist MD, et al. N Engl J Med 2002；346：557-63.
6) Nolan JP, Morley PT, Vanden Hoek TL, et al. Circulation 2003；108：118-21.
7) Nagao K, Hayashi N, Kanmatsuse K, et al. Hayashi N, Bullock R, Dietrich DW, et al, editors. Hypothermia for Acute Brain Damage. Tokyo, Berlin, Heidelberg, New York：Springer-Verlag；2004. p. 278-86.
8) SOS-KANTO Committee. Circ J 2005；69：1157-62.
9) Hayashi Y, Hiraide A, Morita H, et al. Resuscitation 2004；63：161-6.
10) Shankaran S, Laptook AR, Ehrenkranz RA, et al. N Engl J Med 2005；353：1574-84.
11) Bernard S, Buist M, Monteiro O, et al. Resuscitation 2003；56：9-13.
12) Nagao K, Hayashi N, Kanmatsuse K, et al. J Am Coll Cardiol 2000；36：776-83.
13) Schmutzhard E, Engelhardt K, Beer R, et al. Crit Care Med 2002；30：2481-8.
14) 長尾建，上松瀬勝男．日本循環器学会専門医誌 2004；12：285-93.
15) Holzer M, Behringer W, Janata A, et al. Crit Care Med 2005；33：1346-50.
16) Langhelle A, Tyvold SS, Lexow K, et al. Resuscitation 2003；56：247-63.
17) van den Berghe G, Wouters P, Weekers F, et al. N Engl J Med 2001；345：1359-67.
18) Tada K, Nagao K, Hayashi N, et al. Circ J 2006；70：1064-9.
19) 長尾建，林成之，上松瀬勝男．日内会誌 2004；93：300-5.

トピックス

III. トピックス
2. SOS関東
(Survey of Survivors after Out-of-hospital Cardiac Arrest in the Kanto area)
—日本救急医学会関東地方会院外心停止多施設共同研究—

長尾　建

要　旨

関東地方の院外心停止患者に対する救急医療体制を把握し，その構築に寄与することを目的に，国際的集計手法（ウツタイン様式）を用いた多施設前向き観察臨床研究（SOS-KANTO）を開始した．この分析では院外心臓性心停止患者の約60%が虚脱直後心室細動であり，bystander CPRはこの心室細動を長引かせ，生存率を向上させた．しかし，bystander CPR施行率は低値で，簡単な心臓マッサージのみCPRの普及が必要であると結論した．〔日内会誌　95：2476～2483，2006〕

Key words：心臓マッサージ，心室細動，心肺蘇生法

はじめに

2004年の我が国の救急車出場件数は5,031,464件で，このうち医療機関に94%が搬送されていた(総務省消防庁，http://www.fdma.go.jp/neuter/topics/fieldList6_1.html)．その内訳は急病が58.7%，交通事故が13.3%，一般負傷が12.9%，その他が15.1%であった．院外心停止患者は94,920人[東京ではその約1割の9,307人(東京消防庁：救急活動の実態　平成16年)]で，この発生数は高齢者人口の増加に伴い増加し，数年後には10万人(東京では1万人)に達すると推察される．

2000年AHA/ILCORはevidence based medicine（EBM）に基づく心肺蘇生（cardiopulmonary resuscitation；CPR）と救急心血管治療のための国際ガイドライン2000（Circulation 102；I-1-384，2000）[1]を報告し，昨年11月にはその後のEBMを追加し，改訂版国際CPRガイドライン2005（Circulation 112：III-1-136，IV-1-211，2005）を報告した．

これらの国際ガイドラインでは，院外心停止患者に対する救急医療体制の検証に，国際的な定義と用語を使用したウツタイン様式[1]を用いた記録が必要であるとした．

21世紀初頭，我が国でウツタイン様式を用いた院外心停止患者の大規模集計は，救命救急センター効果検証委員会(全国10施設の救命救急センターに搬送された2,290例の分析)報告とウツタイン大阪プロジェクト（大阪府全域で発生した救急隊員が関わった全例の分析，毎年約5,000例，Resuscitation 53：121–125，2002，57：145–152，2003）報告があった．

しかし，関東地方を対象とした院外心停止患

ながお　けん：駿河台日本大学病院救命救急センター，SOS-KANTO Study Group

者に対するウツタイン様式を用いた大規模集計はなかった．そこで，救急医学会関東地方会において，ウツタイン様式による記録法を統一(表)し，2002年9月1日からその調査を開始した[2]．

なお，この日本救急医学会関東地方会院外心停止多施設共同研究の名称を，SOS-KANTO (Survey of Survivors after Cardiac Arrest in the Kanto Area) とした．

1．The Chain of Survival（救命の連鎖）

成人の院外心停止患者の生還を可能にする最も重要な救急医療体制は，chain of survival (迅速な119番通報，迅速な一次救命処置，迅速な電気的除細動，迅速な二次救命処置）の円滑な連動である(図1)．国際ガイドライン2005で変更された主なchain of survivalのトピックスは，本稿II，ガイドライン2005を参照して頂きたい．

2．SOS-KANTO集計成績

2006年7月までに，SOS-KANTO研究班として，連結不可能　匿名化手法を用い集計し，その初期集計[2]，中間集計[3]を日本救急医学会関東地方会雑誌で，総説の一部として，日本内科学会雑誌(93：300–305，2004)，日本循環器学会専門医誌(11：31–38，2004，12：285–293，2004)などでも報告した．さらに，原著論文としてCirculation Journalに，また現在投稿中の論文(Lancet, in press）もある．

以下に，SOS-KANTO集計の概要を示す．

1）院外心室細動(ventricular fibrillation；VF)出現率

我が国では，欧米と異なり院外VF患者が少ないと言われていた．しかし，その検証は十分ではないと考え，かかる点を中間集計7,138例を用いて分析した．この結果，救急隊現場到着時，心臓性心停止患者(全体の院外心停止患者の58%を占める)の初回心電図記録がVF/無脈性心室頻拍(ventricular tachycardia，VT)であった割合は16.2%であった．これは欧米のVF/VT出現率より，はるかに低値であった．しかし，ウツタイン様式を用いた研究論文を比較すると，欧米とSOS-KANTOでは大きな3つの違いがあることが判明した．①我が国と欧米では救急隊が現場でCPRを開始する規準が違う．すなわち，院外心停止患者に対して救急隊が現場でCPRを開始し病院に搬送する割合は，関東では93%，世界最高水準にあるシアトルでは約50%であった．このことは，VF出現率（初回VF患者数/CPR実施全患者数）の算出に大きな影響を与えることが判明した．②迅速な一次救命処置であるbystander CPR実施率が違う．関東のbystander CPR施行率は，シアトルの約半分の25%であった．③迅速な電気的除細動に関与する初回心電図記録までの時間が違う．SOS-KANTO研究では119番通報から初回心電図記録(救急隊員による)までの時間は平均11.1分，シアトルでは4分であった．(SOS-KANTO研究ではbystander CPRの実施はVF出現率を増加させるも，虚脱からの時間が長くなればなる程，その出現率は減少することを証明した．)．そこで，目撃者の居た心臓性院外心停止患者2,244例を用い，虚脱から初回心電図記録までの時間とVF出現率を検証した．この成績を図2に示す．

関東のVF出現率は，欧米より10%低値であったが，虚脱直後にはVFは約60%を占めることが判明した．

自動体外式除細動器（automated external defibrillators；AED)の設置場所に関する検証は十分ではなかったが，心停止の発症場所とVFの関連を分析した．VF出現率が20%以上であった場所は，公共の場（浴場を除く，職場，道路，その他）であった．一方，一般の家は低値で8%であった[3]．

図3に市民がAEDを用いて電気的除細動を試みる訓練と標準的CPR（心臓マッサージ＋口対口人工呼吸)の訓練を受けた場合と，標準的CPR

表

●．所轄警察　　署　連絡　○済　○未

救急隊員の皆様へ　お忙しいところ誠に恐縮ですが，下記 1 ～ 15 までの御記入をお願い申しあげます．
尚，CPA で某医に搬送し心拍再開後に転送した傷病者については記載する必要ありません．
傷病者氏名＿＿＿＿＿＿＿＿○をチェックし下線空欄を埋めてください．時刻は 24 時間表示です．

救急医学会関東地方会　病院外心肺停止患者記録（SOS-KANTO trial）2002.9.1-

●．発生状況　　救急隊名＿＿＿＿＿＿＿＿隊長名＿＿＿＿＿＿＿＿

1．覚知年月日　20　　年　　月　　日
2．傷病者　　年齢　　歳（推定　　歳）　男・女
3．発生場所：　一般の家（○風呂　○トイレ　○その他）　○道路　○職場　公共の場（○浴場　○その他）
　○救急車内　医療機関内（○一次　○二次　○三次施設）　○その他
4．普段生活：　○機能良好　○中等度障害　○重度障害　○植物状態　○不明

●．救急活動

5．出動状況　119 番覚知時刻：　　時　　分
　出場時刻：　　時　　分
　現着時刻：　　時　　分
　傷病者接触時刻：　　時　　分

定義
心肺停止：脈無し（5 秒以上），意識無し，呼吸無し
心停止：脈無し，意識無し，あえぎ様呼吸あり
呼吸停止：脈あり，意識無し，呼吸無し
心拍再開：触知できる脈拍の回復

6．傷病者　　接触時：○心肺停止　○心停止のみ　○呼吸停止のみ
　接触後：○心肺停止　○心停止のみ　○呼吸停止のみ：　停止時刻　　時　　分
7．搬送状況　現場出発：　　時　　分　病院到着：　　時　　分　初療室入室：　　時　　分
　搬送中心拍再開：○あり（　　時　　分）　○なし　○一時再開（　　時　　分）
　搬送中自発呼吸：○あり　○なし　○一時出現
8．目撃者の有無　○なし　○あり　目撃（倒れたところを見た，または聞いた）時刻：　　時　　分頃
　目撃者：○一般人（○家族や知人　○通行人　○その他）
　○医療関係者（○救急隊　○消防隊　○看護師　○医師　○その他）
　発症状況：○突然　○徐々に　○不明
9．バイスタンダー CPR　○なし（救急隊到着後の CPR も含む）　○あり　開始時刻：　　時　　分頃
　施行者：　○一般人（○ CPR の研修あり　○研修なし口頭指導あり　○研修なし口頭指導なし）
　○医療関係者（○救急隊　○消防隊　○看護師　○医師　○その他）
　内容：気道確保　○あり　○なし　人工呼吸　○あり　○なし　心臓マッサージ　○あり　○なし
　AED（全自動除細動器）　○あり　○なし　口腔内異物の除去　○あり　○なし
　効果：心拍再開　○あり　○なし　自発呼吸　○あり　○なし
10．接触時の状態　意識：JCS＿＿＿＿　呼吸：○なし　○あり　初回 SpO_2：　　%
　脈拍：○なし　○あり　血圧：○測定不能　○測定可能　　/　　mmHg
　瞳孔：右　　mm×左　　mm　対光反射：○迅速　○鈍い　○消失
11．心電図モニター　○装着可能　開始時刻：　　時　　分　○装着不可
　初回波形：○ VF　○無脈性 VT　○無脈性電気的活動（PEA）　○心静止　○その他
　搬送中の変化：○あり（全ての変化をチェック　○ VF　○無脈性 VT　○ PEA　○心静止）　○なし
12．救命行為　○ CPR なし　○ CPR あり　開始時刻：　　時　　分
13．特定行為　指示要請時刻：　　時　　分　指示覚知時刻：　　時　　分　○要請せず
　指示を受けた場所　○現場　○救急車内　○その他
　除細動　○適応あり除細動を実施：開始時刻　　時　　分　計　　回実施（○単相性　○二相性）
　指示なし除細動　○あり　○なし　効果：○心拍再開　○適応外波形に変化　○変化せず
　○適応あるも施行できず：○連絡中適応外波形に変化　○機器不調　○家族拒否
　○適応なし：○心拍再開　○適応外波形　○その他
　気道確保　○用手的のみ：○下顎挙上法　○頭部後屈あご先挙上法
　○器具使用：○経鼻・経口エアウェイ　○ラリンゲアルマスクエアウェイ
　○食道閉鎖式エアウェイ（コンビ，WB チューブなど）
　○気管挿管（医師による）
　○器具使用中断（嘔吐などで）
　デマンドを用いた人工呼吸：○使用　○使用せず（バックマスクを使用）
　静脈路確保：○確保できた　○確保できず　○施行せず
　異物による気道閉鎖の解除：○施行した　○施行せず　○適応無し
14．編成：　救命士：○なし　○一人　○二人以上
　○連携あり（○救急隊　○ポンプ隊　○ドクターカー　○ヘリコプター）○なし
15．心停止の推定：
　○外因性：○交通外傷　○墜落転落　○一般負傷　○熱傷　○絞首　○溺水　○窒息　○中毒　○その他
　○内因性：主な前駆症状　○あり（○頭痛　○胸痛　○背部痛　○呼吸困難　○その他）○なし　○不明
　○不詳：内因性，外因症の判断が困難