From 4-Links to 5-Links of “Chain of Survival”

— Post-Resuscitation Care is Critical for Good Neurological Recovery —

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There are more than 100,000 cases per year of out-of-hospital cardiac arrest and that number is increasing year by year in Japan: 102,738 cases in 2005, 105,924 in 2006, and 109,461 in 2007.¹ Successful recovery from out-of-hospital cardiac arrest depends on rapid activation of the “Chain of Survival”, including early access to the ambulance system, early bystander cardiopulmonary resuscitation (CPR), early defibrillation and early advanced life support (ALS).² Of the 109,461 cases in Japan in 2007, 19,707 were witnessed and had a cardiac cause.¹ Only 1,195 cases (6.1%) survived with a certain level of neurological recovery 1 month after the collapse,¹ although patients with a cardiac arrest of cardiac origin that was witnessed were good candidates for return of spontaneous circulation (ROSC). ROSC is just the first step toward the goal of complete recovery from cardiac arrest, and post-resuscitation care seems to be critical for a good neurological outcome.

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Recently in Japan, we have got 2 major “arms” that have strong evidence for improved neurological outcomes after resuscitation. One is the automated external defibrillator (AED), and its use by a witness, or on-site defibrillation by emergency medical system personnel, is a key to early defibrillation, the second link of the “Chain of survival”. Hase et al reported that early ROSC using on-site defibrillation can provide better long-term neurological outcomes.³ According to a report from the Fire and Disaster Management Agency, a good neurological survival rate (35.5%) could be obtained 1 month after the collapse of a patient with an out-of-hospital cardiac arrest if the event was witnessed, the arrest was of cardiac origin and a bystander used an AED. In comparison, the rate for emergency medical system personnel was 18.5%.¹ It is certain that early ROSC, because of a bystander using an on-site AED, is one of the keys to good neurological recovery. To achieve early ROSC by early on-site defibrillation, it is very important to maintain “good” ventricular fibrillation (VF) that can respond to the DC shock. Minimum interruption of chest compression is reported to contribute to a higher rate of post-shock ROSC.⁴ High-quality bystander CPR is also a key to early ROSC, along with defibrillation. We have to popularize these early

steps of resuscitation. A simple resuscitation technique of chest-compression-only CPR could be a solution.⁵

Another “arm” is therapeutic hypothermia. Two randomized controlled trials published in 2002 demonstrated that mild hypothermia induced after resuscitation from cardiac arrest decreased mortality and improved neurological outcomes.^{6,7} In the European study, 55% of patients treated with hypothermia (33°C for 24 h) had a favorable outcome at 6 months, compared with 39% of those treated with standard care.⁶ In the Australian trial, 49% of patients who remained comatose after resuscitation from out-of-hospital cardiac arrest and who were treated with hypothermia (33°C for 12 h) were discharged home or to rehabilitation, compared with 24% of those treated with standard care.⁷ Subsequently, the International Liaison Committee on Resuscitation (ILCOR) endorsed the use of therapeutic hypothermia for patients with anoxic brain injury after out-of-hospital cardiac arrest, particularly when the initial cardiac arrest rhythm is VF.⁸ A meta-analysis showed that the number needed to treat was only 6.⁹ In Japan, therapeutic mild hypothermia has been used in some institutes. In 1998, Yanagawa et al reported a preliminary outcome study of mild therapeutic hypothermia for out-of-hospital cardiac arrest patients.¹⁰ They found that there was an improving tendency for fully recovery when treated with hypothermia (3/13) compared with standard care (1/15), although more complications such as pneumonia occurred among the hypothermia-treated patients. Nagao et al¹¹ reported mild hypothermia therapy for patients with out-of-hospital cardiac arrest who had not got ROSC on arrival at hospital. In that study, hypothermia was induced in 23 of 50 patients and 12 were discharged with good neurological recovery. They performed emergency cardiac catheterization in 39 of the 50, and reperfusion therapy by percutaneous coronary intervention (PCI) was done in 30 patients during cardiac arrest. PCI soon after or during CPR could explain the high ROSC rate, even in the patients without ROSC on hospital arrival. These reports were published before the international guideline for cardiopulmonary resuscitation and emergency cardiovascular care 2000. After the 2 randomized controlled trials published in 2002,^{6,7} and the ILCOR statement,⁸ guideline 2005 by the American Heart Association stated that unconscious adult patients with ROSC after out-of-hospital cardiac arrest should be cooled to 32–34°C for 12–24 h when the initial

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Figure. Five links of the “Adult Chain of Survival”. In the second link, “hands only” means continuous chest compression without a rescue breath. AED, automated external defibrillator; CPR, cardio-pulmonary resuscitation; ALS, advanced life support.

rhythm was VF (Class IIa), and that similar therapy may be beneficial for patients with out-of-hospital non-VF arrest or for those with in-hospital arrest (Class IIb).¹² Takeuchi et al started using therapeutic mild hypothermia after the issuing of guideline 2005 and reported its usefulness in treating patients with out-of-hospital cardiac arrest.¹³ Although theirs was not a randomized study, they showed that hypothermia was an independent predictor of neurological recovery. The very short time from collapse to ROSC, PCI after ROSC, and rapid induction of hypothermia were possible mechanisms of the high neurological recovery. Although we do not have enough human data concerning when to start hypothermia, an experimental study suggests that the sooner cooling is initiated, the better is the outcome.¹⁴ Takeuchi et al initiate hypothermia soon after arrival at the emergency center, using a rapid infusion of 1,000 ml of cold saline. Rapid infusion of 500–2,000 ml of 4°C saline is reported to be effective and safe in achieving a decrease in the esophageal temperature by around 1°C.¹⁵ This easy, rapid method of hypothermia induction can be done by emergency medical personnel and started before hospital. We may need to change some medical control systems, especially on-site fluid therapy for patients with out-of-hospital cardiac arrest.

Potential adverse effects of hypothermia include immunosuppression with increased infection risk, cold diuresis and hypovolemia, electrolyte disorders, insulin resistance, impaired drug clearance, cardiac arrhythmias, and mild coagulopathy. In 1998 Yanagawa reported increased incidence of pneumonia during hypothermia,⁹ but the study by Takeuchi did not show major adverse effects of hypothermia, except for recurrence of VF.¹³ Frequent blood testing and culturing of the sputum and blood are reported to be important in avoiding adverse effects.¹³

What should we cardiologists learn from the study by Takeuchi et al?¹³ We have to recognize that post-resuscitation care is very important for patients with cardiac arrest in order to obtain good neurological recovery. Immediate hypothermia and coronary intervention must be included in the post-resuscitation care, in addition to standard intensive care. Most of the resuscitated patients need to undergo cardiac catheterization followed by PCI, even when they were comatose, because acute coronary syndrome is the leading cause of out-of-hospital cardiac arrest. PCI soon after or during CPR can be another powerful “arm” of resuscitation. Cardiologists must take care of the body temperature of the patient during the catheterization procedure, similarly to hemodynamic changes. Now we have to consider the 5th link of “post resuscitation care” in addition to the 4 links of the “Chain of Survival” (Figure). AED have been provided at many places in Japan and a lot of people are learning CPR with AED operation, the initial 3 links of the “Chain of Survival”.¹ Health care professionals, especially cardiologists, should note the details of the last 2

links: ALS and post-resuscitation care (Figure).

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