Editorial

What should we consider when applying termination of resuscitation rules?

Jae Chol Yoon[1], Won Young Kim[2]

[1]Department of Emergency Medicine, Research Institute of Clinical Medicine of Chonbuk National University, Chonbuk National University Hospital, Jeonju, Korea; [2]Department of Emergency Medicine, Ulsan University College of Medicine, Asan Medical Center, Seoul, Korea

Correspondence to: Won Young Kim, MD, PhD. Department of Emergency Medicine, University of Ulsan College of Medicine, Asan Medical Center, 86, Asanbyeongwon-gil, Songpa-gu, Seoul 138-736, Korea. Email: wonpia73@naver.com.

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Historically, following full resuscitative efforts by emergency medical services (EMS), out-of-hospital cardiac arrest (OHCA) patients are transported to the hospital for continued resuscitation efforts at the emergency department. However, in patients in whom the chance of survival is deemed negligible, terminating resuscitation efforts in the field may be considered. In East Asia, EMS personnel are not legally permitted to terminate resuscitation, but field termination occurs in 40–60% and up to 40% of patients in Europe and the United States, respectively (1-4). The adoption of termination-of-resuscitation (TOR) rules may decrease the unnecessary consumption of valuable resources and number accidents during emergency transport (5).

The basic life support (BLS) TOR rule has 3 criteria, all of which must present before terminating resuscitative efforts: (I) arrest was not witnessed by EMS personnel; (II) no return of spontaneous circulation (ROSC) was observed in the field; and (III) no shocks were delivered. In a previous retrospective analysis of 700 OHCA patients with presumed cardiac etiology, applying the BLS TOR rules demonstrated 100% specificity and 100% positive predictive value (PPV) for identifying non-survivors (i.e., a patient with positive TOR can have resuscitation terminated in the field) (6). The advanced life support (ALS) TOR rules recommend considering the termination of resuscitation when the 3 BLS TOR criteria are met and no bystander cardiopulmonary resuscitation (CPR) was provided (7). The application of the BLS/ALS TOR rule was validated in North American and European sites, and the results consistently showed high specificity and PPV (8,9). Based on these studies, the 2015 American Heart Association (AHA) Guidelines Update for CPR and Emergency Cardiovascular Care (ECC) recommend that regional and local EMS authorities use the BLS TOR rule to develop protocols for terminating resuscitative efforts in adult victims of cardiac arrest in areas where ALS is not available or may be significantly delayed (10). However, the European Resuscitation Council (ERC) guidelines have challenged the TOR rules and argue that applying the TOR rules leads to an unexpected survival of 3.4% and 9%, respectively, this statement appears to be contradictory-please clarify in OHCA patients without sustained ROSC in the prehospital setting (11,12).

In a prospective multicenter observational study from Japan, Kashiura *et al.* assessed the validity of the BLS and ALS TOR rules for identifying neurologically unfavorable outcomes according to the causes of cardiac arrest (cardiac *vs.* non-cardiac) (13). This is the first report on the application of TOR rules to OHCA patients with a non-cardiac etiology, such as drug overdose, asphyxia, pulmonary embolism, incidental hypothermia, and aortic disease. These authors demonstrated that the BLS and ALS TOR rules demonstrate high specificity and PPV in OHCA patients with cardiac etiology (false-positive rates of 1.5% and 6.1% for BLS and ALS, respectively). However, both TOR rules demonstrated high false-positive rates (8.5% and 16.7% for BLS and ALS, respectively) when applied to patients with non-cardiac etiologies. Kashiura *et al.* thus suggested that the TOR rules should be cautiously applied to patients with OHCA of non-cardiac etiology. That study had several strengths, including the large sample size and that the efficacy of the TOR rule was validated in all patients who were transported to an emergency hospital (the EMS in the study area is legally obligated to transport OHCA patients to the hospital).

In contrast to other medical interventions, defining "no chance of survival" is very difficult in OHCA patients. It has been argued that survival rates of <1% still justify resuscitation efforts (11). The false-positive rate of 8.5% for OHCA patients with non-cardiac etiologies shows the need to modify or develop new TOR rules that are effective for OHCA patients with either cardiac or non-cardiac etiologies. This is an important consideration with the emergence of advanced technologies, such as targeted temperature management and extracorporeal CPR (ECPR) (14-16). It is often difficult to determine the etiology of cardiac arrest in prehospital settings, and, at the very least, EMS personnel should consider not applying the TOR rules to cases with presumably reversible etiologies. Moreover, the current AHA and ERC guidelines suggest that ECPR (including extracorporeal membrane oxygenation support for cardiac arrest patients undergoing CPR) should be considered as a rescue therapy when the initial ALS is unsuccessful and specific interventions should be facilitated (e.g., percutaneous coronary intervention, pulmonary thrombectomy) (14,16). It is challenging to continue to resuscitate a patient for transport and perform prolonged and high-quality CPR while on route to the hospital. The use of mechanical CPR devices may increase the feasibility of long-standing high-quality CPR in a moving vehicle. In considering the increased use of ECPR, EMS personnel should be trained to identify patients who have reversible causes and the TOR rule should not be implemented without modification.

One of the criteria for the TOR rule—whether or not a patient has demonstrated ROSC prior to transport—is another important area of consideration. The TOR rule does not specify a time limit for EMS to declare "no ROSC" despite resuscitation attempts, and due to this vagueness, it should specify protocols, algorithms, and results for OHCA patients in accordance with local EMS systems (8,9,17-19). The AHA guidelines made an addition of requiring 3 full rounds of CPR and automated external defibrillator analysis before EMS can declare "no ROSC" in the field (10). However, this time limit is approximately 6–8 min since 1 cycle of CPR takes 2 min, and this could be considered too short to observe ROSC before transporting OHCA patients. Actually, the diagnostic performance of the TOR rule for hospital mortality is still low, even when patients who received <6 min of CPR at the scene were excluded (19).

The period of resuscitative efforts that is adequate for determining ROSC in the field is therefore an important question. The 2000 position statement on TOR by the National Association of EMS Physicians (NAEMSP) recommends that the prehospital termination of resuscitation could be considered following full resuscitative efforts that include 20–30 min of treatment (20). The ERC guidelines recommended that an EMS team consider withholding resuscitative efforts if asystole is documented for >20 min despite ongoing ALS in the absence of a reversible cause (11). However, our study evaluated the relationship between downtime (i.e., the duration of resuscitation efforts) and neurologic outcomes, and we found that patients who received targeted temperature management demonstrated neurologically intact survival rates of 23% even when the downtime was >20 min (21). In addition, a large-scale multicenter study has evaluated these issues and patients with initial shockable rhythms or age <65 years were found to have a reasonable chance of neurologically intact survival, even with extraordinarily long downtimes (22). Another study assessed the relationship between resuscitation time and outcomes and suggested 48 minutes of shockable rhythms and 15 min of non-shockable rhythms as the optimal resuscitation duration, at which time the probability of survival fell to <1% (which can be defined as futile resuscitation) (23). However, the 2011 NAEMSP position statement on TOR states that no significant numerical value can be confidently recommended due to the lack of evidence (24). In other words, medical judgement is necessary and the TOR rules should be modified according to local EMS practices.

In summary, as advanced rescue therapies and specific circumstance-related interventions become more widely available and the success rate improves, it is important to consider the other predictors that contribute to survival when applying the TOR rule. At the very least, modifying the TOR rule to account for patient characteristics (e.g., the etiology of cardiac arrest, advanced age) and the optimal scene time before termination should be considered in order to prevent terminating resuscitation in patients who could potentially survive.

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Footnote

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