

In-hospital cardiac arrest

Max Harry Weil, MD, PhD; Michael Fries, MD

To review the current management of in-hospital cardiac arrest and to identify variables that influence outcomes, OLDMEDLINE from 1950 to 1966 and MEDLINE from 1966 to March 2005 were searched using the keywords *cardiopulmonary resuscitation, cardiac arrest, in hospital, and adult*. Secondary sources were derived from review publications and personal communications by one of the authors. There is no secure evidence that the ultimate outcomes after cardiopulmonary resuscitation in settings of in-hospital cardiac arrest have improved in the >40 yrs that followed the landmark report by Kouwenhoven, Jude, and Knickerbocker, which launched the modern era of cardiopulmonary resuscitation. A paucity of objective measurements preclude secure protocols for sequencing of interventions and, even more, when to initiate and discontinue cardiopulmonary resuscitation. The preparedness of both physicians and nursing professionals to

implement the published guidelines has itself been questioned. Whereas early access defibrillation with automated external defibrillators may be of benefit in out-of-hospital settings, there has as yet been no secure evidence that automated external defibrillators have had a favorable impact on in-hospital cardiopulmonary resuscitation when used on infrequent occasions by first responders. This contrasts with the much greater success of advanced life support providers and especially when electrical defibrillation is promptly performed by expertly trained personnel after onset of cardiac arrest. Outcomes are therefore improved in critical care settings and especially in coronary care units in which patients are continuously monitored. (Crit Care Med 2005; 33:2825–2830)

KEY WORDS: in-hospital cardiac arrest; cardiopulmonary resuscitation; automated external defibrillators

Modern cardiopulmonary resuscitation (CPR) is based on two major principles, namely closed-chest cardiac massage to restore threshold blood flows, especially to the heart and the brain, and artificial ventilation through an unobstructed airway to maintain vital gas exchange. Both techniques were pioneered in the 1950s. Breathing was pioneered by Safar (1) and chest compression by Kouwenhoven (2) and their coworkers. Since then, our knowledge of the pathophysiology of cardiac arrest and resuscitation has greatly expanded based on both experimental and clinical research. Workers in the field have become increasingly aware of the very small time window between onset of cardiac arrest and irreversibility of cellular injury and especially so in the heart and brain. Accordingly, the American Heart Association has highlighted the “chain of survival” to

guide the priority of interventions for basic life support. The usefulness of the chain of survival concept is now supported by persuasive evidence of earlier and more appropriately sequenced interventions with greater survival, including early arrival of professional rescuers, early CPR, and early defibrillation (3–5).

Professional rescuers in hospitals are now provided with an expanded resource of therapeutic options, both devices and drugs. Nevertheless, these again have not objectively improved overall survival rates (6–9). The expectations of the lay public are otherwise. Electronic media and especially current “emergency room” television dramas on comprehensively monitored simulated victims persuade the onlooker that CPR is almost inevitably life restoring and therefore there is expectation of successful outcomes (10, 11). To the contrary, in-hospital cardiac arrest (IHCA) at the end stage of disease and especially in nonmonitored patients in conventional medical/surgical units has a low probability of survival. Given this discrepancy on the one hand and the commitment of large human and material resources, we examined the options of staffing and facilities by which survival from in-hospital cardiac arrest may be further improved.

SURVIVAL AFTER IN-HOSPITAL CARDIAC ARREST

In 1987, McGrath (12) reviewed the literature after more than a quarter century of in-hospital CPR. Based on a total of almost 13,000 patients, McGrath (12) found no evidence that survival had increased over that interval. The overall survival rate remained at approximately 14%. Surprisingly, more advanced methods and instrumentation including automated rhythm analyses did little to improve outcomes, the proven value of electrical defibrillation notwithstanding. There may have been some improvement in postresuscitation survival in the years that followed (13–15). However, the extent to which this represented liberalized definitions of cardiac arrest under the umbrella of respiratory arrest, more uniform documentation and reporting, and more restrictive in-hospital CPR intervention with expanded numbers of “do not attempt resuscitation” (DNAR) orders is not apparent. The desirability of more uniform reporting by a diversity of institutions was recognized and implemented by the consensus that brought forth the Utstein template (16, 17). In the year 2000, the American Heart Association launched a large-scale registry of IHCA, the national registry of CPR (NRCPR). By 2003, the database included 207 participating hospitals and doc-

From the Weil Institute of Critical Care Medicine, Rancho Mirage, CA (MHW, MF); the Keck School of Medicine of the University of Southern California, Los Angeles, CA (MHW); and the Department of Anesthesiology, University Hospital Aachen, Aachen, Germany (MF).

The authors have no financial interests to disclose.
Copyright © 2005 by the Society of Critical Care Medicine and Lippincott Williams & Wilkins

DOI: 10.1097/01.CCM.0000191265.20007.9D

umented 14,720 cardiac arrests over a period of 2.5 yrs (18). This was a welcome initiative and has great promise of yielding more objective data on outcomes in relationship to underlying disease states and current interventions.

Nevertheless, at the time of this writing, in-hospital cardiac arrest still yields only an overall survival of 17% (18) suggesting the possibility that there may be moderate improvement. These outcome statistics are supported by data published from Canada (19), Australia (20) and Italy (21). It is noteworthy that although the overall survival rate is low, neurologic recovery in survivors is reasonably good. Almost 60% have good cerebral performance at the time of hospital discharge (18).

INCIDENCE OF VENTRICULAR FIBRILLATION

We anticipated that not unlike out-of-hospital cardiac arrest, ventricular fibrillation (VF) would be the predominant initial rhythm. Yet the NRCPR found that VF is the initial rhythm in only 25% of documented cardiac arrests (18). This contrasts with a higher incidence of out-of-hospital VF. For reasons that are not as yet apparent, however, there is also a declining incidence in VF in the out-of-hospital setting (22). Since a diversity of patients with a higher proportion of non-cardiac patients were included in the NRCPR, the likelihood is that noncardiac patients at the end stage of disease are more likely to present with apnea followed by bradycardia, pulseless electrical activity, or asystole. This especially applies to circulatory shock states and terminal respiratory failure. Changes in pharmacologic management of arrhythmias and the impact of implantable pacemakers and defibrillators have also been cited as a potential explanation for decreases in the incidence of VF in out-of-hospital populations (22), and we suspect that these interventions also play a role in the lower incidence of VF in IHCA cardiac arrests.

DETERMINANTS OF OUTCOMES

Age, rhythm, concurrent heart and blood vessel diseases and their complications, hospital location, and whether the patient is monitored together with non-cardiac underlying disease states and their complications and especially neuro-

logic, respiratory, and renal impairment negatively affect outcomes of in-hospital cardiac arrest. Most important, survival is contingent on whether cardiac arrest is witnessed and the time of day at which the event occurs (18–21, 23–27). Nevertheless, controversy remains as to whether the age of the patient, the non-intensive care unit location, and the presence of neoplastic disease are individual predictors of poor outcomes (28–30).

In the absence of a DNAR directive and without prior knowledge of underlying mechanism, the professional provider who responds to the “cardiac arrest” call is first confronted by the decision of whether CPR is appropriate for that individual or whether there is a clear mandate to withhold CPR. In the United States, the policy is to start CPR unless it is specifically documented that such violates the patient’s wishes or those of surrogates who mandate otherwise. DNAR orders are also a source of confusion and often controversy among professional providers, who confront both legal and ethical dilemmas in implementing such orders (31). In a retrospective review of >1,000 instances in which resuscitation efforts were withheld, the majority of such patients had been designated DNAR. As anticipated, these patients were significantly older or in poor overall physical health (32). Yet, there is no consensus that decisions on proceeding with CPR should be based either on age or solely on a DNAR order. In the absence of a DNAR order, the ultimate decision would still defer to reasonable medical judgment. There should be valid indications for this medical intervention (33). The personal wishes of the individual patient who makes an informed decision before requiring life support interventions must be respected and appropriately updated (34). Yet to attempt resuscitation on a brain-dead patient or when death is an expected terminal event of a noncurable disease fails to meet the test of valid medical indication (35).

EARLY DEFIBRILLATION IN HOSPITALS

The value of early defibrillation of shockable rhythms in the out-of-hospital setting is beyond dispute. Its life-saving value in the hands of first responders is well documented (4, 36). The Public Access Defibrillation Study, in which minimally trained, volunteer rescuers provided for early defibrillation with

automated external defibrillators (AEDs) (5, 37) in the out-of-hospital setting, was associated with more favorable outcomes. There is also some optimism that such may have application to in-hospital practice. In the United States, hospitals have typically organized CPR teams of trained professionals who respond to hospital-wide calls for resuscitation (18). However, even these expert professional teams who are provided with appropriate mobile resuscitation equipment and supplies have not measurably affected survival rates from in-hospital cardiac arrest. Nevertheless, there is great variability in the professional training, experience, and capability of the rescuers. Even more important, the response time of the team members and their access to equipment and supplies often account for substantial delay. This has provided incentive on the part of the local ward staff to initiate CPR before arrival of the team, including the use of AEDs. AEDs are assumed to be a special asset for infrequent first responders who may not be competent in electrocardiogram rhythm interpretation or defibrillator settings, who are then provided with capability to perform defibrillation, guided by voice prompts of the AEDs. As late as 10 yrs ago, in Europe, only 20% of hospitals had formal teams that responded to hospital-wide codes (38), and in the absence or in case of delayed arrival of such teams, health care providers including physicians who have theoretical but little practical knowledge of both CPR and electrical defibrillation may therefore be empowered by AED-guided CPR (31, 39, 40).

QUALIFICATIONS OF IN-HOSPITAL RESCUERS

Physicians from acute care specialties including anesthesiology (41) often have rather little knowledge and experience in recognizing and treating cardiac arrest outside of the operating room (42–47). Nursing staffs on general medical surgical services in contrast to specialist nurses serving in acute care units in which patients are continuously monitored have a special burden. They may be the first to respond but are the least prepared in comparison with well-trained critical care unit and emergency department nurses. Nonspecialized nursing personnel cannot as a rule expeditiously perform the complex tasks of CPR, even in mock scenarios on a manikin (47). Accordingly, effective CPR is rarely begun

before the arrival of experienced providers in the in-hospital setting (48, 49). Finally, it is the frequency of use that determines performance. A majority of occasional providers have poor retention of CPR skills, including physicians, a reality that is no different from that documented for volunteer, nonprofessional rescuers (46, 50). This is a reality even though only minimal AED training is required. According to Beckers et al. (51), only 15 mins are required to acquire skills to effectively operate an AED.

GUIDELINES FOR ADVANCED LIFE SUPPORT

A closely related issue already cited is that professional emergency physician teams in a teaching hospital setting typically do not abide by protocols of published international guidelines; equally important, there is inconsistent performance (52, 53). Admittedly the guidelines are largely a consensus based on limited data and subject to changes. Yet, guidelines are presented with the anticipation that they represent a consensus of the best medical opinion at the time of their publication. Nevertheless, the interventions mandated by the guidelines also allow that the professional judgment of the individual physician takes precedence. For instance, Aufderheide and coworkers (54, 55) pinpointed the adverse effects of hyperventilation by professional rescuers when they complied with the guidelines. It is now apparent that there is a need for simplification of interventions especially for occasional rescuers together with preparedness to modify procedures at intervals between publication of international guidelines as more objective data become available. We anticipate that expansion of voice prompts such as those presently incorporated in AEDs will represent a major asset. More precise prompts will require that noninvasive cardiopulmonary measurements are substantially expanded including electrocardiographic predictors of successful defibrillation (56). Such improvements are also likely to be responsive to the search for consistency in performance and the prompts that represent quality controls that are likely to further improve performance.

AUTOMATED DEFIBRILLATION

Until early AED defibrillation programs in moderate-sized hospitals are shown to improve hospital survival, such

cannot be widely recommended (57). Nevertheless, we favor newer and more efficient biphasic waveform defibrillators, although such impose new health care costs. Biphasic waveforms that deliver energy levels of 150 J (58) reduces the incidence and severity of postresuscitation myocardial dysfunction.

Prompt intervention is highly cost-effective if it more rapidly restores spontaneous circulation (59). Yet when response times are prolonged by the large distances that rescue teams must often travel, the decentralization of resuscitation teams should be considered, including supplying first responder teams with AEDs (60).

VENTILATION DURING IN-HOSPITAL CARDIAC ARREST

The importance of continuous, well-performed chest compressions not only for effective electrical defibrillation after ≥ 3 mins of cardiac arrest but also for overall survival has been re-emphasized in several laboratory investigations during the last 5 yrs (61, 62). In contrast, for out-of-hospital cardiac arrest, ventilation as part of initial life support is of lesser importance (63–65). Management of cardiac arrest is time-sensitive (66) and it is likely that in the first 5 mins after the onset of cardiac arrest of primary cardiac cause and presenting as ventricular fibrillation, ventilation is likely to be of no benefit. Accordingly, Spearpoint and colleagues (67) documented favorable outcomes for IHCA patients in whom electrical defibrillation was prompt and no mechanical ventilation was provided before defibrillation. Experimental evidence supports the notion that even during prolonged states of hypoxemia, the need to maintain adequate perfusion takes priority over ventilation (68, 69). Nevertheless, there is as yet appropriate concern that after prolonged cardiac arrest, artificial ventilation cannot be discarded as an integral component during resuscitation from IHCA.

PREVENTION OF CARDIAC ARREST

Although the NRCPR provides data that justify some optimism of better outcomes after in-hospital cardiac arrest, there are disproportionate resources used with equivocal benefit, typically at the end of life. The likelihood is that the effectiveness of CPR may be improved

without major increases in cost by securing early response by appropriately trained rescuers (59). At present, the total cost of each life saved by CPR is estimated to exceed 400,000 U.S. dollars (70). When this huge cost is put into perspective, there is a large cost of failed CPR and, more precisely, disappointingly low yield of meaningful survival.

As the late Professor Peter Safar (71) pointed out as early as 1974, “The most sophisticated Intensive Care Unit may become an unnecessarily expensive terminal care facility when we fail to recognize the terminal course of patients who are critically ill or injured.” The focus is therefore on prevention of cardiac arrest. Early warnings of imminent arrest including altered breathing, pulse rate, and consciousness in the absence of a fatal disease deserve early monitoring and intervention in a critical care setting (72–74). Failure to intervene promptly is to invite preventable cardiac arrests (75–78). However, it is a reality that some patients are transferred too late from general wards to intensive care units to reverse the risk (79–81).

LOOKING TO THE FUTURE

We stress the key role of professional nurses in preventing cardiac arrest. The decreased availability of highly skilled professional nurses, especially in the United States, translates into more dilute patient-to-nurse ratios and higher incidences of death (82–84). The critical shortage of well-trained critical nurse specialists and the resulting lack of available critical care beds often delay timely transfer and early recognition of warning signs and therefore the prevention of imminent cardiac arrest.

We therefore return to the issue that prompted this contribution: Is there appropriate and adequately trained professional staffing and equipment to improve survival from in-hospital cardiac arrest? We conclude, “Not yet!” The problem is multifactorial and includes not only medical decision making but also educational, technical, financial, and legal constraints. The professional consensus provided by the current guidelines themselves have limitations, both for medical decision making by the individual clinician and communicating some insecurity with the mandates based largely on consensus. Yet there is increasing opportunity for improvement both by the hospital and by the provider. Aggressive

Early recognition of the risk of cardiac arrest and early transfer to monitored beds that provide skilled life support by professional medical and nursing staffs with the capability to respond immediately mitigate the risk and the need for cardiopulmonary resuscitation.

treatment strategies in appropriately defined patients may include extracorporeal membrane oxygenation, cardiopulmonary bypass, extracorporeal assist devices, or internal cardiac massage (85–89). Although these highly invasive procedures are promising contenders in the arsenal of potential treatment strategies, they require proof of improved outcomes. Yet the promise of more favorable outcomes prompts us to emphasize the need for both research support and a regulatory climate for pursuit of such clinical research.

A larger investment in research on CPR followed the American PULSE initiative (90). We also anticipate advances guided by data from the NRCPR (18). We acknowledge the promise of improved outcomes. We witness an increasing resource of objective knowledge that triggers better management and advanced technology for better CPR in both in-hospital and out-of hospital settings.

CONCLUSIONS

What is therefore apparent, in our view, is that both prevention and management of cardiac arrest within the hospital may be improved. Early recognition of the risk of cardiac arrest and early transfer to monitored beds that provide skilled life support by professional medical and nursing staffs with the capability to respond immediately mitigate the risk and the need for CPR. In hospitals in which established and competent cardiac arrest teams have prolonged response

times and especially when units are remote, decentralization of CPR with emphasis on the capability of local first responders who may be equipped with AEDs deserves consideration. Although the guidelines are subject to change, the basic elements of CPR incorporated in the chain of survival have stood the test of time. With as yet disappointing outcomes, the challenge is large but, in our opinion, improvements in outcome are achievable.

REFERENCES

1. Safar P, Escarraga LA, Elam JO: A comparison of the mouth-to-mouth and mouth-to-airway methods of artificial respiration with the chest-pressure arm-lift methods. *N Engl J Med* 1958; 258:671–677
2. Kouwenhoven WB, Jude JR, Knickerbocker GG: Closed-chest cardiac massage. *JAMA* 1960; 173:1064–1067
3. Stiell IG, Wells GA, Field BJ, et al: Improved out-of-hospital cardiac arrest survival through the inexpensive optimization of an existing defibrillation program: OPALS study phase II. Ontario Prehospital Advanced Life Support. *JAMA* 1999; 281:1175–1181
4. Valenzuela TD, Roe DJ, Nichol G, et al: Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. *N Engl J Med* 2000; 343:1206–1209
5. Hallstrom AP, Ornato JP, Weisfeldt M, et al: Public-access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med* 2004; 351:637–646
6. Herlitz J, Bahr J, Fischer M, et al: Resuscitation in Europe: A tale of five European regions. *Resuscitation* 1999; 41:121–131
7. Berger R, Kelley M: Survival after in-hospital cardiopulmonary arrest of noncritically ill patients. A prospective study. *Chest* 1994; 106:3872–3879
8. Eisenberg MS, Horwood BT, Cummins RO, et al: Cardiac arrest and resuscitation: A tale of 29 cities. *Ann Emerg Med* 1990; 19: 179–186
9. Nichol G, Stiell IG, Laupacis A, et al: A cumulative meta-analysis of the effectiveness of defibrillator-capable emergency medical services for victims of out-of-hospital cardiac arrest. *Ann Emerg Med* 1999; 34:517–525
10. Diem SJ, Lantos JD, Tulsy JA: Cardiopulmonary resuscitation on television. Miracles and misinformation. *N Engl J Med* 1996; 334: 1578–1582
11. Gordon PN, Williamson S, Lawler PG: As seen on TV: Observational study of cardiopulmonary resuscitation in British television medical dramas. *BMJ* 1998; 317:780–783
12. McGrath RB: In-house cardiopulmonary resuscitation—After a quarter of a century. *Ann Emerg Med* 1987; 16:1365–1368
13. Robinson GR II, Hess D: Postdischarge survival and functional status following in-hospital cardiopulmonary resuscitation. *Chest* 1994; 105:991–996
14. Rosenberg M, Wang C, Hoffman-Wilde S, et al: Results of cardiopulmonary resuscitation. Failure to predict survival in two community hospitals. *Arch Intern Med* 1993; 153: 1370–1375
15. Tresch D, Heudebert G, Kutty K, et al: Cardiopulmonary resuscitation in elderly patients hospitalized in the 1990s: A favorable outcome. *J Am Geriatr Soc* 1994; 42:137–141
16. 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; 84:960–975
17. Cummins RO, Chamberlain D, Hazinski MF, et al: Recommended guidelines for reviewing, reporting, and conducting research on in-hospital resuscitation: The in-hospital “Utstein style.” American Heart Association. *Circulation* 1997; 95:2213–2239
18. Peberdy MA, Kaye W, Ornato JP, et al: Cardiopulmonary resuscitation of adults in the hospital: A report of 14720 cardiac arrests from the National Registry of Cardiopulmonary Resuscitation. *Resuscitation* 2003; 58: 297–308
19. Brindley PG, Markland DM, Mayers I, et al: Predictors of survival following in-hospital adult cardiopulmonary resuscitation. *CMAJ* 2002; 167:343–348
20. Cohn AC, Wilson WM, Yan B, et al: Analysis of clinical outcomes following in-hospital adult cardiac arrest. *Intern Med J* 2004; 34: 398–402
21. Sandroni C, Ferro G, Santangelo S, et al: In-hospital cardiac arrest: survival depends mainly on the effectiveness of the emergency response. *Resuscitation* 2004; 62:291–297
22. Herlitz J, Bang A, Gunnarsson J, et al: Factors associated with survival to hospital discharge among patients hospitalised alive after out of hospital cardiac arrest: Change in outcome over 20 years in the community of Goteborg, Sweden. *Heart* 2003; 89:25–30
23. Rabinstein AA, McClelland RL, Wijdicks EF, et al: Cardiopulmonary resuscitation in critically ill neurologic-neurosurgical patients. *Mayo Clin Proc* 2004; 79:1391–1395
24. Taffet GE, Teasdale TA, Luchi RJ: In-hospital cardiopulmonary resuscitation. *JAMA* 1988; 260:2069–2072
25. Urberg M, Ways C: Survival after cardiopulmonary resuscitation for an in-hospital cardiac arrest. *J Fam Pract* 1987; 25:41–44
26. Bedell SE, Delbanco TL, Cook EF, et al: Survival after cardiopulmonary resuscitation in the hospital. *N Engl J Med* 1983; 309: 569–576
27. Peatfield RC, Sillett RW, Taylor D, et al: Survival after cardiac arrest in hospital. *Lancet* 1977; 1:1223–1225

28. Rozenbaum EA, Shenkman L: Predicting outcome of in-hospital cardiopulmonary resuscitation. *Crit Care Med* 1988; 16:583–586
29. Tortolani AJ, Risucci DA, Rosati RJ, et al: In-hospital cardiopulmonary resuscitation: Patient, arrest and resuscitation factors associated with survival. *Resuscitation* 1990; 20: 115–128
30. Hendrick JM, Pijls NH, van der Werf T, et al: Cardiopulmonary resuscitation on the general ward: No category of patients should be excluded in advance. *Resuscitation* 1990; 20: 163–171
31. Smith GB, Poplett N, Williams D: Staff awareness of “Do not attempt resuscitation” policy in a district general hospital. *Resuscitation*, In Press
32. Skrifvars MB, Hilden HM, Finne P, et al: Prevalence of “do not attempt resuscitation” orders and living wills among patients suffering cardiac arrest in four secondary hospitals. *Resuscitation* 2003; 58:65–71
33. Weil MH, Weil CJ, Rackow EC: Guide to ethical decision-making for the critically ill: The three R's and Q.C. *Crit Care Med* 1988; 16:636–641
34. Ostermann ME, Nelson SR: Haemodialysis patients' views on their resuscitation status. *Nephrol Dial Transplant* 2003; 18: 1644–1647
35. Weil MH, Weil CJ: How to respond to family demands for futile life support and cardiopulmonary resuscitation. *Crit Care Med* 2000; 28:3339–3340
36. Ladwig KH, Schoefinius A, Danner R, et al: Effects of early defibrillation by ambulance personnel on short- and long-term outcome of cardiac arrest survival: The Munich experiment. *Chest* 1997; 112:1584–1591
37. Capucci A, Aschieri D, Piepoli MF, et al: Tripling survival from sudden cardiac arrest via early defibrillation without traditional education in cardiopulmonary resuscitation. *Circulation* 2002; 106:1065–1070
38. Destro A, Marzaloni M, Sermasi S, et al: Automatic external defibrillators in the hospital as well? *Resuscitation* 1996; 31:39–43
39. Smith GB, Poplett N: Impact of attending a 1-day multi-professional course (ALERT) on the knowledge of acute care in trainee doctors. *Resuscitation* 2004; 61:117–122
40. Smith GB, Poplett N: Knowledge of aspects of acute care in trainee doctors. *Postgrad Med J* 2002; 78:335–358
41. Tok D, Keles GT, Tasyuz T, et al: Basic life support skills of doctors in a hospital resuscitation team. *Tohoku J Exp Med* 2004; 203: 123–128
42. Ruppert M, Reith MW, Widmann JH, et al: Checking for breathing: Evaluation of the diagnostic capability of emergency medical services personnel, physicians, medical students, and medical laypersons. *Ann Emerg Med* 1999; 34:720–729
43. Harrison GA, Hillman KM, Fulde GW, et al: The need for undergraduate education in critical care. (Results of a questionnaire to year 6 medical undergraduates, University of New South Wales and recommendations on a curriculum in critical care). *Anaesth Intensive Care* 1999; 27:53–58
44. Buchman TG, Dellinger RP, Raphaely RC, et al: Undergraduate education in critical care medicine. *Crit Care Med* 1992; 20:1595–1603
45. Bossaert LL, Putzeys T, Monsieurs KG, et al: Knowledge, skills and counseling behaviour of Belgian general practitioners on CPR-related issues. *Resuscitation* 1992; 24:49–54
46. Kaye W, Mancini ME: Retention of cardiopulmonary resuscitation skills by physicians, registered nurses, and the general public. *Crit Care Med* 1986; 14:620–622
47. Berden HJ, Hendrick JM, van Doornen JP, et al: A comparison of resuscitation skills of qualified general nurses and ambulance nurses in The Netherlands. *Heart Lung* 1993; 22:509–515
48. Brenner BE, Kauffman J: Response to cardiac arrests in a hospital setting: Delays in ventilation. *Abstr. Circulation* 1995; 92:1-762
49. Buck-Barrett I, Squire I: The use of basic life support skills by hospital staff: What skills should be taught? *Resuscitation* 2004; 60: 39–44
50. Mancini ME, Kaye W: The effect of time since training on house officers' retention of cardiopulmonary resuscitation skills. *Am J Emerg Med* 1985; 3:31–32
51. Beckers S, Fries M, Bickenbach J, et al: Minimal instructions improve the performance of laypersons in the use of semiautomatic and automatic external defibrillators. *Crit Care* 2005; 9:R110–R116
52. Abella BS, Sandbo N, Vassilatos P, et al: Chest compression rates during cardiopulmonary resuscitation are suboptimal: A prospective study during in-hospital cardiac arrest. *Circulation* 2005; 111:428–434
53. Abella BS, Alvarado JP, Myklebust H, et al: Quality of cardiopulmonary resuscitation during in-hospital cardiac arrest. *JAMA* 2005; 293:305–310
54. Aufderheide TP, Sigurdsson G, Pirralo RG, et al: Hyperventilation-induced hypotension during cardiopulmonary resuscitation. *Circulation* 2004; 109:1960–1965
55. Aufderheide TP, Lurie KG: Death by hyperventilation: A common and life-threatening problem during cardiopulmonary resuscitation. *Crit Care Med* 2004; 32:S345–S351
56. Young C, Bisera J, Gehman S, et al: Amplitude spectrum area: measuring the probability of successful defibrillation as applied to human data. *Crit Care Med* 2004; 32(Suppl): S356–S358
57. Zafari AM, Zarter SK, Heggen V, et al: A program encouraging early defibrillation results in improved in-hospital resuscitation efficacy. *J Am Coll Cardiol* 2004; 44:846–852
58. Tang W, Weil MH, Sun S, et al: The effects of biphasic waveform design on post-resuscitation myocardial function. *J Am Coll Cardiol* 2004; 43:1228–1235
59. van Alem AP, Dijkgraaf MG, et al: Health system costs of out-of-hospital cardiac arrest in relation to time to shock. *Circulation* 2004; 110:1967–1973
60. Bickenbach J, Fries M, Beckers S, et al: Requirements for the use of automated external defibrillators in German hospitals. *Anaesthetist* 2004; 53:555–560
61. Yu T, Weil MH, Tang W, et al: Adverse outcomes of interrupted precordial compression during automated defibrillation. *Circulation* 2002; 106:368–372
62. Berg RA, Sanders AB, Kern KB, et al: Adverse hemodynamic effects of interrupting chest compressions for rescue breathing during cardiopulmonary resuscitation for ventricular fibrillation cardiac arrest. *Circulation* 2001; 104:2465–2470
63. Hallstrom A, Cobb L, Johnson E, et al: Cardiopulmonary resuscitation by chest compression alone or with mouth-to-mouth ventilation. *N Engl J Med* 2000; 342:1546–1553
64. Van Hoeyweghen RJ, Bossaert LL, Mullie A, et al: Quality and efficiency of bystander CPR. Belgian Cerebral Resuscitation Study Group. *Resuscitation* 1993; 26:47–52
65. Waalewijn RA, Tijssen JG, Koster RW: Bystander initiated actions in out-of-hospital cardiopulmonary resuscitation: Results from the Amsterdam Resuscitation Study (ARRESTUS). *Resuscitation* 2001; 50:273–279
66. Weisfeldt ML, Becker LB: Resuscitation after cardiac arrest: A 3-phase time-sensitive model. *JAMA* 2002; 288:3035–3038
67. Spearpoint KG, McLean CP, Zideman DA: Early defibrillation and the chain of survival in “in-hospital” adult cardiac arrest: Minutes count. *Resuscitation* 2000; 44:165–169
68. de Courten-Myers GM, Yamaguchi S, Wagner KR, et al: Brain injury from marked hypoxia in cats: Role of hypotension and hyperglycemia. *Stroke* 1985; 16:1016–1021
69. Miyamoto O, Auer RN: Hypoxia, hyperoxia, ischemia, and brain necrosis. *Neurology* 2000; 54:362–371
70. Lee KH, Angus DC, Abramson NS: Cardiopulmonary resuscitation: What cost to cheat death? *Crit Care Med* 1996; 24:2046–2052
71. Safar P: Critical care medicine—Quo vadis? *Crit Care Med* 1974; 2:1–5
72. Schein RM, Hazday N, Pena M, et al: Clinical antecedents to in-hospital cardiopulmonary arrest. *Chest* 1990; 98:1388–1392
73. Bedell SE, Deitz DC, Leeman D, et al: Incidence and characteristics of preventable iatrogenic cardiac arrests. *JAMA* 1991; 265: 2815–2820
74. Franklin C, Mathew J: Developing strategies to prevent in hospital cardiac arrest: analyzing responses of physicians and nurses in the hours before the event. *Crit Care Med* 1994; 22:244–247
75. Brennan TA, Leape LL, Laird NM, et al: Incidence of adverse events and negligence in hospitalized patients. Results of the Harvard Medical Practice Study I. *N Engl J Med* 1991; 324:370–376
76. Leape LL, Brennan TA, Laird N, et al: The nature of adverse events in hospitalized pa-

- tients. Results of the Harvard Medical Practice Study II. *N Engl J Med* 1991; 324: 377-384
77. Brennan TA, Hebert LE, Laird NM, et al: Hospital characteristics associated with adverse events and substandard care. *JAMA* 1991; 265:3265-3269
 78. Wilson RM, Runciman WB, Gibberd RW, et al: The Quality in Australian Health Care Study. *Med J Aust* 1995; 163:458-471
 79. McQuillan P, Pilkington S, Allan A, et al: Confidential inquiry into quality of care before admission to intensive care. *BMJ* 1998; 316:1853-1858
 80. Gutierrez G, Palizas F, Doglio G, et al: Gastric intramucosal pH as a therapeutic index of tissue oxygenation in critically ill patients. *Lancet* 1992; 339:195-199
 81. Bishop MH, Shoemaker WC, Appel PL, et al: Prospective, randomized trial of survivor values of cardiac index, oxygen delivery, and oxygen consumption as resuscitation endpoints in severe trauma. *J Trauma* 1995; 38:780-787
 82. Institute of Medicine Report. To Err Is Human: Building a Safer Health System. Washington, DC, Institute of Medicine, 1999
 83. Aiken LH, Clarke SP, Sloane DM, et al: Hospital nurse staffing and patient mortality, nurse burnout, and job dissatisfaction. *JAMA* 2002; 288:1987-1993
 84. Needleman J, Buerhaus P, Mattke S, et al: Nurse-staffing levels and the quality of care in hospitals. *N Engl J Med* 2002; 346: 1715-1722
 85. Chen YS, Chao A, Yu HY, et al: Analysis and results of prolonged resuscitation in cardiac arrest patients rescued by extracorporeal membrane oxygenation. *J Am Coll Cardiol* 2003; 41:197-203
 86. Grinda JM, Chevalier P, D'Attellis N et al: Fulminant myocarditis in adults and children: Bi-ventricular assist device for recovery. *Eur J Cardiothorac Surg* 2004; 26: 1169-1173
 87. Morris MC, Wernovsky G, Nadkarni VM: Survival outcomes after extracorporeal cardiopulmonary resuscitation instituted during active chest compressions following refractory in-hospital pediatric cardiac arrest. *Pediatr Crit Care Med* 2004; 5:440-446
 88. Mackay JH, Powell SJ, Osgathorp J, et al: Six-year prospective audit of chest reopening after cardiac arrest. *Eur J Cardiothorac Surg* 2002; 22:421-425
 89. Birdi I, Chaudhuri N, Lenthall K, et al: Emergency reinstatement of cardiopulmonary bypass following cardiac surgery: Outcome justifies the cost. *Eur J Cardiothorac Surg* 2000; 17:743-746
 90. Weil MH, Becker L, Budinger T, et al: Workshop Executive Summary Report: Post-resuscitative and initial Utility in Life Saving Efforts (PULSE): June 29-30, 2000; Lansdowne Resort and Conference Center; Leesburg, VA. *Circulation* 2001;103: 1182-1184