REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

Fuchs: There were no randomized controlled, quasi-randomized controlled trials or any study in children which looked at the specific question: In infants and children with bradycardia that is unresponsive to oxygenation and/or ventilation, dose the use of atropine as compared to epinephrine improve patient outcome.

The studies that were supportive of atropine in some aspect include the case series by Brown (LOE 5) which involved 8 adults in cardiac arrest, all whom were in asystole as the initial rhythm or as a result of defibrillation. Six failed to respond to epinephrine, but responded to atropine. And 50% of these patients were discharged from the hospital. In the prehospital study by Stueven (LOE 5), which was a retrospective review, there were 84 adult patients in asystole who remained in asystole after epinephrine (and sodium bicarbonate). Of these patients, 43 also received atropine, and 6 had successful resuscitation, which was defined as conveyance of a patient with a rhythm and pulse to an emergency department vs 0/41 of the epinephrine, sodium bicarbonate group, (P<.04). However, none of the patients who received atropine survived to hospital discharge. Therefore, this study is neutral with respect to survival to hospital discharge.

The only pediatric study to support the use of atropine involved 4 infants who had undergone cardiac surgery (Fullerton LOE 4). Three experienced hypotension, followed by bradycardia and asystole. Two did not respond to epinephrine, but all responded to atropine. One other infant had episodes of hypotension without bradycardia, and responded to atropine. It was thought that these episodes were secondary to the Bezold-Jarisch reflex. This reflex is initiated by activation of mechanical stretch receptors located mainly in the wall of the left ventricle, with afferents carried by the right vagus nerve. Activation of this reflex results in hypotension and bradycardia mediated by cholinergic vasodilatation and withdrawal of sympathetic tone. The continuous administration of atropine in all cases prevented the recurrence of this reflex in these patients. This concept may support the use of atropine in vagally mediated bradycardia, as the current PALS bradycardia algorithm suggests.

Most of the studies were neutral with respect to the question. Angelos (LOE 5) evaluated ROSC in a rat model utilizing epinephrine vs placebo, and found that as the duration of cardiac arrest increased, epinephrine is more important to attain ROSC, but there was greater post-ROSC myocardial,depression. Brady (LOE 5) was a study involving adult patients with hemodynamically compromising bradycardia or AVB with evidence of spontaneous circulation who received atropine delivered by EMS personnel, and in the hospital. 86 patients had bradycardia and approximately one-third of patients who received atropine in the prehospital setting for bradycardia had either a partial or complete response to therapy. The Chow study (LOE 5) was a histiochemical and immunochemical analysis of the autonomic innervation of the human cardiac conduction system that demonstrated initial sympathetic dominance in infancy with gradual transition to sympathetic and parasympathetic innervation in adulthood. Kaplan (LOE 5) compared BG-9719, a selective A1AdoR antagonist to atropine or saline in a vagotomized, hypoxic rat model. Atropine and saline did not prolong survival or attenuate posthypoxic decreases in heart rate compared to BG-9719. McCaul (LOE 5) evaluated a brief asphyxial arrest rat model utilizing 10 or 30 mcg/kg of epinephrine vs saline, and demonstrated that epinephrine increased mortality, especially with the higher dose. The retrospective study by Iseri (LOE 5) evaluated adult patients in the prehospital setting in ventricular fibrillation or extreme bradycardia or asystole. Epinephrine or isoproterenol was given to 14 bradycardic patients, and atropine in 12 patients (either as treatment 1, 2 or 3), but results were inconsistent and only 1 patient survived to hospital day 12. Leinhart (LOE 4) was a case report on a 20 month old infant who suffered a near drowning. The first dose of epinephrine and atropine has no effect, but another dose of epinephrine and vasopressin resulted in ROSC.

There were only 2 studies that opposed the use of atropine. The Coon study (LOE 5) evaluated atropine after epinephrine (and other drugs).Twenty one prehospital adults who suffered cardiac arrest and were then in asystole or pulseless idioventricular rhythm (PIVR) were studied. There was no difference between the 2 groups (control n=11) and atropine (N=10) with respect to rhythm changes, pulse, admission or hospital discharge, so atropine did not improve outcome. The other study to oppose the use of atropine was a randomized study by Horigome (LOE1), which involved 34 children undergoing halothane anesthesia for minor surgery. Echocardiographic recordings and indices were before, after induction of general anesthesia, and after IV atropine administration (either 0.01 mg/kg or 0.02 mg/kg). Following halothane anesthesia, heart rate and mean blood pressure fell from preinduction levels in both groups. The left systolic time interval ration (LSTI), and the left ventricular end-diastolic dimension (LVEDD/preload) were reduced, and the left ventricular shortening fraction (LVSF) was increased in both groups. After injection of atropine, the heart rate increased above baseline (more for the 0.02 mg/kg group), the mean blood pressure returned to baseline in both groups. The other parameters LSTI, LVEDD and LVSF remained unchanged in both groups, but the LSTI and LVEDD were larger and the LVSF smaller than pre-induction. What this research demonstrated was that atropine can counteract the bradycardia caused by halothane anesthesia, but myocardial contractility remains depressed. There was no advantage

of a dose of 0.02 mg/kg over 0.01 mg/kg. While this does not answer the question about if epinephrine is better than atropine in bradycardia, it is known that epinephrine increases the heart rate and myocardial contractility, so it could be of more benefit in bradycardia unresponsive to oxygenation and ventilation.

Kurosawa: Some adult studies (Smith, Yilmaz ,Brady, Chadda, all LOE 5) and a pediatrics study (Zimmerman LOE 4) indicated that iv atropine improved heart rate in symptomatic bradycardia. Atropine is effective for vagal stimulation, AV block, intoxication, etc.
Zimmerman (LOE 4). As common causes of intraoperative bradycardia are hypoxia or vagal activity, such therapy should consist of ventilation with oxygen and iv atropine. Yilmaz (LOE 5) 66 patients were hospitalized with a variety of symptoms (nausea, vomiting, salivation, dizziness, weakness, hypotension, bradycardia and syncope) several hours after the ingestion of small amount of honey. All patients had hypotension, and majority had bradycardia. These features resolved completely in 24h with iv fluids and atropine. Brady (See above). Smith (LOE 5) 64 adult patients who received general anesthesia (sufentanyl + N2O + vecuronium) were allocated randomly to received either atropine, 5μg/kg(Group 1), glycopyrrolate, 2.5μg/kg(Group 2), or transesophageal atrial pacing (Group 3) after the onset of bradycardia, defined as a heart rate of ≤ 50bpm (or ≤ 60bpm with concurrent of hypotension). Bradycardia occurred in 15 patients of each group. The therapeutic response was significantly more rapid in Group 3. But the therapy was effective in all groups and there is no great difference in incidence of side effects between the three groups. Chadda (LOE 5) The effect of 0.4 to 1.5 mg intravenously administered atropine were evaluated in 100 adult patients with a heart rate < 60/min following acute myocardial infarction. There was a statistically significant correlation between the dose of atropine and the increment in heart rate.

There are some Utstein reports in pediatrics. In these reports (Tibballs, Guay, Reis, all LOE 4), the percentage of hypotensive bradycardia in all patients who received cardiopulmonary resuscitation was relatively high. And most of these patients received epinephrine rather than atropine during resuscitation. Tibballs (LOE 4) Resuscitation was attempted in total of 111 cases. Of these patients who had cardiac arrests, hypotensive-bradycardia was identified in 73 cases, which is two third of all cases, and epinephrine was used in around 90% (97/111) of all cases as the first line drug. Guay (LOE 4) Of all 203 cases, initial rhythm was bradycardia in 102 cases (50%), and 101 cases(50%) were received epinephrine. There was no mention of administration of atropine. Reis (LOE 4) Chest compressions and assisted ventilation were provided for total of 129 patients. Of all cases, bradycardia with hypoperfusion, unresponsive to oxygenation and ventilation, was noted in 43 cases which is one third of all cases. Most of the patients received epinephrine rather than atropine during resuscitation which is almost over 80% of all cases. Even in adults, one study (see Coon LOE 5 above) shows that atropine may not superior to epinephrine in pre-arrest state.

Nitta: Symptomatic bradycardia is the most common initial rhythm in pediatric cardiac arrest (asphyxial arrest). Epinephrine is the first line drug in this setting. In CoSTR 2005, there was no evidence to eliminate atropine for asystole in pediatrics. Atropine for asystole in adults was reviewed in two work sheets (W97A, W97B).

There are few articles related to this topic in pediatrics which are supportive of atropine. The Stueven and Brown studies are mentioned above. Using a prospective, controlled, blinded, adult canine model of PEA induced by ventricular fibrillation followed by external defibrillation, Blecic (LOE 5) demonstrated that atropine increased survival and shortened CPR time compared to the control group treated with D5W. In treatment group, 91% (10/11) achieved of ROSC with atropine, but only 67% (8/12) with 5% dextrose, control. Additionally, the atropine treated group had higher arterial pressure, heart rate, cardiac output, stroke volume and decreased time to recovery. The administration of atropine with epinephrine enhanced the recovery in this experimental canine model.

Stiell (LOE 5) reported a large observational cohort study of cardiac arrest in adult cases. 529 adult patients who suffered in-hospital and out-of-hospital cardiac arrest were studied. The odds ratio (95% CIs) for successful resuscitation with atropine, after multivariate adjustment for potential confounders, was 1.2 (1.0-1.3).

From the National Registry of Cardiopulmonary Resuscitation (NRCPR), Meany. (LOE 3) reported 464 pediatric ICU arrests The odds ratio (95% CIs) for survival to discharge with atropine was 2.38 (1.20-4.74) using multivariate logistic regression analysis. In a second NRCPR study, (Reis 2002) 129 pediatric patients who received cardiopulmonary resuscitation for cardiac arrest or symptomatic bradycardia were studied. The relative risk of death at 24 hours with atropine was 0.98 (0.58-1.90) using multivariate logistic regression analysis. These results suggest that atropine may be effective in cardiac arrest or resuscitated symptomatic bradycardia. But it was not clear whether atropine was given while CPR in progress.

There are one adult (Sorensen, LOE 5) and two pediatric case series (Fullerton, Thrush, both LOE 4), evaluating treatment of bradycardia presumed to be caused by vagal stimulation. Four cardiac surgical patients exhibited

cardiovascular collapse in early postoperative course and were resuscitated. The vaso-vagal reflex was suspected and treated with atropine (Fullerton). Severe hypertension with reflex bradycardia progressed to cardiac arrest caused by drug and treated with atropine and cardiopulmonary resuscitation (Thrush). These studies support atropine use for pediatric in-hospital asystolic cardiac arrest or symptomatic bradycardia caused by increased vagal activity.

There are some studies which do not support the use of atropine The Coon study is mentioned above. A prospective, controlled, blinded canine asphyxial PEA model; pediatric asphyxial cardiac arrest model was used by DeBehnke(1995). After 10 minutes untreated PEA, the animals were block randomized to one of five groups and each group was treated with different dose of atropine. The standard dose of atropine did not improve ROSC rate compared with control group. Increasing dose of atropine tended to decrease ROSC rates compared with control group and standard dose group.

Two cohort studies of out-of-cardiac arrest showed no evidence that treatment with atropine increase the chance of survival among asystolic patients (Engdahl, 2000) and cardiac arrest patients (Herlitz, 2003). Although these studies included pediatric patients in cardiac arrest, they were not separated in the analysis.

In pediatric patients, hypoxemia, hypothermia, acidosis, hypotension, hypoglycemia, central nervous system insults and excessive vagal stimulation may produce symptomatic bradycardia and asystole. Asystole can be exacerbated by excessive vagal tone and the administration of atropine is reasonable for its physiological effects.

Conclusion

CONSENSUS ON SCIENCE:
052: Evidence from 2 adults studies (LOE 5, Brown 1979,448-adult case series, Stueven 1984,815-adult retrospective control), demonstrated a change of cardiac rhythm from asystole after atropine, when there had been no change after epinephrine, however survival to hospital discharge was no different.

Several adult studies and one pediatric study showed the efficacy of atropine for bradycardia caused by vagal stimulation, AV block, intoxication (LOE 5) Yalmaz, 2006, 405; Brady, 1999, 47; Smith, 1994, 245; Zimmerman, 1986, 320; Chadda, 1977, 503). One pediatric case series (LOE 4: Fullerton 1991,534) demonstrated a beneficial effect of atropine after epinephrine for children who developed hypotension after cardiac surgery (Bezold-Jarisch refllex mediated).

Evidence from several adult studies (LOE 5: Brady 1999,47, Chow 2001,169, Coon 1981,462, Iseri 1978,741, Steuven 1984,815), animal studies (LOE 5: Angelos 2008,101, Kaplan 2003,923, McCaul 2006,102), and 1case series on a child (LOE 4: Lienhart 2005,486) demonstrate no benefit from the use of atropine after epinephrine. One randomized pediatric study (LOE 2: Horigome 1993,513) demonstrated that atropine only increased heart rate and mean blood pressure, but did not improve myocardial depression induced by halothane anesthesia. One LOE 5 adult study (Coon 1981,462) also demonstrated no benefit of atropine over epinephrine with respect to ROSC, survival or event or hospital discharge.

Large pediatric Utstein studies demonstrated the significant volumes of hypotensive-bradycardia, which is indicating this specific feature in pediatrics (LOE 4) [Tibballs, 2006, 310; Guay, 2004, 378; Reis, 2002, 200]. In this context, epinephrine is the first line drug rather than atropine. Even in adults, one study shows that atropine may not superior than epinephrine in pre-arrest state (LOE 5)(Coons, 1981, 462).

042: There is extremely limited data on the use of atropine in pediatric cardiac arrest, and poor quality data supporting its use in adult cardiac arrest. Evidence from two LOE 3 studies of in-hospital pediatric cardiac arrest [Meany 2006, 2424, Reis 2002, 200] showed some improvement in survival to discharge, but another demonstrated no decrease in risk of death. Evidence from one LOE 4 study [Fullerton, 1991, 534] and one LOE 5 study in adults [Brown, 1979, 448] demonstrated the some efficacy of atropine in symptomatic bradycardia requiring resuscitation. Evidence from adults studies, one level 5 study [Stueven, 1984, 815], one level 5 study [Brown, 1979, 448] and one level 5 animal study [Blecic, 1992, 515] demonstrated the efficacy of atropine in cardiac arrest (ROSC). Evidence from one level 5 animal study [DeBehnke, 1995, 1034] demonstrated no improvement with atropine in canine asphyxial cardiac arrest.

TREATMENT RECOMMENDATION:
(052A: Combined Fuchs and Kurosawa): There is no supportive evidence to demonstrate that atropine is superior to epinephrine in the case of bradycardia unresponsive to oxygenation and/or ventilation (excluding those with vagal mediation).

Epinephrine is the first line drug for poorly perfused infants and children with bradycardia (heart rate <60 beats/min) that is unresponsive to oxygenation and/or ventilation.

If bradycardia is caused by increased vagal tone, cholinergic drug toxicity, or primary AV block, administer atropine rather than epinephrine.

042: Nitta (Atropine vs no atropine): There is insufficient evidence to support or refute the use of atropine for symptomatic bradycardia or pediatric cardiac arrest.

Acknowledgements:

Citation List

Angelos MG, Butke RL, Panchal AR et al. Cardiovascular response to epinephrine varies with increasing duration of cardiac arrest. Resuscitation 2008; 77:101-110.
LOE 5, neutral. Animal (rat) study Quality of evidence good.
Sponsored by Roessler Scholarship Fund, Ohio State Univ, SAEM Institutional Training Award, Ohio State Initiatives Grant and The American Heart Association, Ohio Affiliate.

Objective: Epinephrine (adrenaline) is widely used as a primary adjuvant for improving perfusion pressure and resuscitation rates during cardiopulmonary resuscitation (CPR). Epinephrine is also associated with significant myocardial dysfunction in the post-resuscitation period. We tested the hypothesis that the cardiac effects of epinephrine vary according to the duration of cardiac arrest. Methods and materials: Cardiac arrest (CA) was induced in Sprague-Dawley rats with an IV bolus of KCl (40 mug/g). Three series of experiments were performed with CPR begun after 2, 4, or 6 min of cardiac arrest. Epinephrine (0.01 mg/kg) IV or placebo was given immediately in the 2 and 4 min CA groups. In the 6 min group, CPR was started after 6 min CA and epinephrine was given at 15 min if no return of spontaneous circulation (ROSC) occurred. Time to ROSC was recorded in all groups. Cardiac function was determined with trans-thoracic echocardiography at baseline, 5, 30 and 60 min after ROSC. Results: After 2 min CA, 8/8 (100%) placebo animals and 8/8 (100%) epinephrine animals attained ROSC. Cardiac index was significantly increased during the first 60 min in the epinephrine group compared with the placebo group ($p < 0.01$). After 4 min of cardiac arrest, 14/29 (48%) placebo animals and 14/16 (88%) epinephrine animals attained ROSC ($p < 0.01$). Cardiac index after ROSC returned to baseline in both groups, although tended to be lower in the epinephrine group. After 6 min CA, 10/31 (32%) animals attained ROSC without epinephrine and 17/21 (81%) animals with epinephrine ($p < 0.01$). Post-ROSC depression of cardiac index was greatest in the epinephrine group ($p < 0.05$). Conclusions: As the duration of cardiac arrest increases, a paradoxical myocardial epinephrine response develops, in which epinephrine becomes increasingly more important to attain ROSC, but is increasingly associated with post-ROSC myocardial depression.
Summary: Rat model study; epi vs placebo-as duration of cardiac arrest increases, a paradoxical myocardial epinephrine response develops, in which epi becomes more important to attain ROSC, but is associated with increasing post-ROSC myocardial depression.

Blecic, S., C. Chaskis, et al. (1992). "Atropine administration in experimental electromechanical dissociation." Am J Emerg Med **10**(6): 515-518.
Comments: Level 5; good. Supportive

Atropine can have a place during cardiopulmonary resuscitation (CPR) in the management of asystole, where parasympathetic influence might be excessive. However, the beneficial effects of atropine in electromechanical dissociation (EMD) have not been clearly demonstrated. The authors studied the effects of atropine in combination with epinephrine on an experimental model of EMD in the closed-chested dog. In 15 pentobarbital-anesthetized, mechanically ventilated dogs (mean weight 20 kg), EMD was induced by ventricular fibrillation followed by an external countershock, and was observed for 2 minutes before CPR was started. After 5 minutes of chest compression using a CPR thumper, either atropine 0.5 mg or D5W was administered, and the same injection was repeated every 5 minutes until recovery. Epinephrine 1 mg was submitted to two successive episodes of CPR, using either atropine or D5W, in a randomized order. Of a total of 28 CPRs, five were successful with chest compression alone. In the treatment groups, 10 of 11 were successful with atropine, but only eight of 12 with D5W ($P < .01$). The duration of

CPR was also significantly shorter when atropine was used (9 minutes 56 seconds (plus or minus) 14 seconds versus 12 minutes 08 seconds (plus or minus) 43 seconds, P < .001). During the recovery period, atropine-treated animals had higher arterial pressure, heart rate, cardiac output and stroke volume. On this experimental model, the administration of high doses of atropine together with epinephrine enhances the recovery from EMD and results in a better cardiac function during recovery.
Summary: This study is small prospective, controlled, blinded canine coutershock PEA model with higher dose of atropine (0.05 mg/kg) and adrenaline.

Brady WJ, Swart G, DeBehnke DJ et al:. The efficacy of atropine in the treatment of hemodynamically unstable bradycardia and atrioventricular block: prehospital and emergency department considerations. Resuscitation 1999;41:47-55.
LOE 5, neutral. Adult population. Quality of evidence fair.
No industry funding.

OBJECTIVE: To determine the efficacy of atropine therapy in patients with hemodynamically compromising bradycardia or atrioventricular block (AVB) in the prehospital and emergency department settings. **METHODS: DESIGN:** Retrospective review of prehospital, emergency department, and hospital records. **PARTICIPANTS:** Prehospital patients with hemodynamically compromising bradycardia or AVB with evidence of spontaneous circulation who received atropine as delivered by emergency medical services personnel (advanced life support level). **SETTING:** Urban/suburban fire department-based emergency medical service system with on-line medical control serving a population of approximately 1.6 million persons. **DEFINITIONS:** Hemodynamic instability was defined as the presence of any of the following: ischemic chest pain, dyspnea, syncope, altered mental status, and systolic blood pressure less than 90 mmHg. Bradycardia was defined as sinus bradycardia, junctional bradycardia, or idioventricular bradycardia (grouped as bradycardia) while AVB included first-, second- (types I and II), or third-degree (grouped as AVB). The response that occurred within one minute following each dose of atropine was defined as none, partial, complete, or adverse. **MAIN RESULTS:** Of 172 patients meeting entry criterion complete data was available for 131 (76.1%) and constitutes the study population. The mean age was 71 years. Fifty-one percent were female. Forty-five patients had AVB and 86 bradycardia. Patients with AVB were more likely to have a presenting systolic blood pressure less than 90 mmHg than those with bradycardia. In the 131 patients, responses to atropine were as follows: 26 (19.8%) = partial, 36 (27.5%) = complete, 65 (49.6%) = none, and 4 (2.3%) = adverse. Patients presenting with bradycardia (compared to AVB) more commonly: (1) received a single dose of atropine; (2) a lower total dose of atropine in the prehospital interval; (3) were more likely to arrive in the ED with a normal sinus rhythm; and (4) were less likely to receive additional atropine or isoproterenol in the ED. Those patients who achieved normal sinus rhythm over the total course of care were likely to have achieved that rhythm during the prehospital interval. There was no difference between groups in the likelihood of leaving the ED with a normal sinus rhythm achieved during the ED interval. Acute myocardial infarction was more common in patients presenting with AVB (55.5%) than with bradycardia (23.2%, P = 0.001). **CONCLUSIONS:** Approximately one-half of patients who received atropine in the prehospital setting for compromising rhythms had either a partial or complete response to therapy. Adverse responses were uncommon. Those patients who presented with hemodynamically unstable bradycardia to EMS personnel responded more commonly to a single dose and a lower total dose of atropine compared to similar patients with AVB. Those patients who achieve normal sinus rhythm by ED discharge were likely to have achieved it during the prehospital interval.
Summary: Retrospective review of adult patients with hemodynamically compromising bradycardia or AVB with evidence of spontaneous circulation; approx 50% had complete or partial response to atropine

Brown DC, Lewis AJ, Criley JM. Asystole and its treatment: The possible role of the parasympathetic nervous system in cardiac arrest. JACEP1979; 8: 448-452.
LOE 5, atropine better than epinephrine. Adult study. Quality of evidence poor.
No industry funding.

Parasympathetic tone may be high during ventricular asystole because of reflex vagal stimulation from a number of sources. Eight patients in cardiac arrest were treated with cardiopulmonary resuscitation. All eight patients had ventricular asystole as the initial rhythm or as the result of defibrillation. Six patients failed to respond to 5 cc to 20 cc of 1:10,000 epinephrine intravenously (IV). In all eight cases a regular rhythm (sinus in seven, idioventricular in one) appeared within 30 seconds of administration of the last dose of atropine (1 mg to 2 mg IV). Five patients (62.5%) lived 12 hours, three (37.5%) were discharged from the hospital. These results suggest that atropine may be of value in the treatment of ventricular asystole.
Summary: Case series in adults atropine better than epinephrine

Chadda KD, Lichstein E, et al. Effects of atropine in patients with bradyarrhythmia complicating myocardial infarction. Usefulness of an optimum dose for overdrive. Am J Med 1977; **63**(4): 503-10.

The effects of 0.4 to 1.5 mg intravenously administered atropine were evaluated in 100 patients with a heart rate <60/min following acute myocardial infarction. Prior to the administration of atropine the mean heart rate was 45 ± 7/min, the incidence of ventricular premature beats was 12 ± 4/min, and two patients had angina Based on the maximum heart rate response to atropine, the patients were divided into two groups. Heart rate increased to <100/min in 70 patients (group 1) and ≥100/min in 21 patients (group II) Ventricular premature beats decreased significantly (p<0.01) in both groups (2 ± 4/min in group I and 2.4 ± 0.8 in group II). In only one patient in group II did ventricular premature beats first appear following the administration of atropine. Blood pressure did not change significantly after the administration of atropine in either group. In two patients (group I), angina disappeared and in two others (group II) angina appeared following the administration of atropine. Dose-heart rate analysis revealed that 70per cent of the patients in group II and only 17 percent of those in group I received ≥0.8 mg atropine (p<0.01). There was a statistically significant correlation between the dose of atropine and the increment in heart rate (r=0.41 p<0.01). Thus, a relatively lower dose of atropine (<0.8 mg) had a beneficial antiarrhythmic effect. Higher doses caused an inappropriate tachycardia, angina and ventricular premature beats and should be avoided.

Cheung Chow TS, Ming Chow SS, Anderson RH at al. Autonomic innervation of the human cardiac conduction system: changes from infancy to senility-An immunohistochemical and histochemical analysis. Anat Rec 2001;264:169-182.
LOE 5: Neutral. Mechanical model/histochemical analysis. Quality of evidence fair.
No industry funding.

In order to study the changes in the pattern of autonomic innervation of the human cardiac conduction system m relation to age, the innervation of the conduction system of 24 human hearts (the age of the individuals ranged from newborn to 80 years), freshly obtained at autopsy, was evaluated by a combination of immunofluorescence and histochemical techniques. The pattern of distribution and density of nerves exhibiting immunoreactivity against protein gene product 9.5 (PGP), a general neural marker, dopamine beta-hydroxylase (DBH) and tyrosine hydroxylase (TH), indicators for presumptive sympathetic neural tissue, and those demonstrating positive acetylcholinesterase (AChE) activity, were studied. All these nerves showed a similar pattern of distribution and developmental changes. The density of innervation, assessed semiquantitatively, was highest in the sinus node, and exhibited a decreasing gradient through the atrioventricular node, penetrating and branching bundle, to the bundle branches. Other than a paucity of those showing AChE activity, nerves were present in substantial quantities in infancy. They then increased in density to a maximum in childhood, at which time the adult pattern was achieved and then gradually decreased in density in the elders to a level similar to or slightly less than that in infancy. In contrast, only scattered AChE-positive nerves were found in the sinus and atrioventricular nodes, but were absent from the bundle branches of the infant heart, whereas these conduction tissues themselves possessing a substantial amount of pseudocholinesterase. During maturation into adulthood, however, the conduction tissues gradually lost their content of pseudocholinesterase but acquired a rich supply of AChE-positive nerves, comparable in density to those of DBH and TH nerves. The decline in density of AChE-positive nerves in the conduction tissues in the elders was also similar to those of DBH and TH nerves. Our findings of initial sympathetic dominance in the neural supply to the human cardiac conduction system in infancy, and its gradual transition into a sympathetic and parasympathetic codominance in adulthood, correlate well with the physiologic alterations known to occur in cardiac rate during postnatal development. The finding of reduction in density of innervation of the conduction tissue with ageing is also in agreement with clinical and electrophysiological findings such as age-associated reduction in cardiac response to parasympathetic stimulation. Finally, our findings also support the hypothesis that, in addition to the para-arterial route, the parafascicular route of extension along the conduction tissue constitutes another pathway for the innervation of the conduction system of the human heart during development
Summary: An interesting study which demonstrated increased sympathetic tone in infant hearts, as compared to child/adolescent and adult hearts which have increased parasympathetic tone.

Coon GA, Clinton JE, Ruiz E. Use of atropine for brady-asystolic prehospital cardiac arrest. Ann Emerg Med 1981;10:462-467.
LOE 5: Controlled, prospective study in adults, neutral with respect to change in rhythm or survival.
No industry funding. Quality of evidence good

The efficacy of atropine in treating prehospital cardiac arrest patients developing asystole slow pulseless idioventricular rhythms (PIVR) was evaluated in a controlled, prospective study. Twenty-one prehospital cardiac-arrested patients developing asystole or PIVR (less than 40) were divided into atropine-treated or non-atropine (control) groups. Control group patients received treatment including bicarbonate, epinephrine, calcium, isoproterenol, dexamethasone, and transthoracic pacing. Atropine-treated patients received 1 mg atropine intravenously with a repeat dose at one minute if no rhythm change occurred. These patients then received the same therapy as the control group. In both groups, rhythm changes were treated as appropriate for the specific circumstances. No differences in mortality or effected rhythm changes were observed. Ten of the 11 controls and eight of 10 atropine patients developed rhythms other than asystole

or PIVR less than 40. However, only two patients in each group were successfully resuscitated in the emergency department and only one control group patient was discharged alive. Our findings are not in agreement with those of previous authors who have advocated the use of atropine in cardiac arrest patients with these arrhythmias. We question the usefulness of atropine in this setting. More study is necessary in order to clearly define its role in the resuscitation of patients who have sustained brady-asystolic arrests.
Summary: Prospective, controlled study in adults: epinephrine=atropine

DeBehnke, D. J., G. L. Swart, et al. (1995). "Standard and higher doses of atropine in a canine model of pulseless electrical activity." Acad Emerg Med **2**(12): 1034-41.
Comments: Level 5; Good. Opposing

OBJECTIVE: To determine whether standard or increased doses of atropine improve the return of spontaneous circulation (ROSC) rate in a canine model of pulseless electrical activity (PEA). METHODS: A prospective, controlled, blinded laboratory investigation was performed using an asphyxial canine cardiac arrest model. After the production of asphyxial PEA, 75 dogs remained in untreated PEA for 10 minutes and then were randomized to receive placebo (group 1) or one of four doses of atropine (group 2, 0.04 mg/kg; group 3, 0.1 mg/kg; group 4, 0.2 mg/kg; group 5, 0.4 mg/kg). All the animals received mechanical external CPR and epinephrine (0.02 mg/kg every 3 minutes) throughout resuscitation. RESULTS: The ROSC rates were not significantly different between the groups (group 1, 73%; group 2, 67%; group 3, 40%; group 4, 47%; group 5, 27%; p = 0.06). The heart rates and hemodynamics during resuscitation were not significantly different between the groups. CONCLUSION: In this canine model of asphyxial PEA cardiac arrest, standard-dose atropine did not improve ROSC rates, compared with placebo. Increasing doses of atropine tended to decrease ROSC rates, compared with placebo and standard-dose atropine.
Summary: This animal model may be more representative of pediatric asphyxial cardiac arrest than adult PEA. In their previous study of canine asphyxial PEA model, they had found that vagotomized animals had better ROSC rate. But this study shows conflicting results. They suggest the pharmacologic actions of atropine on vagal afferent activity.

Engdahl, J., A. Bang, et al. (2000). "Can we define patients with no and those with some chance of survival when found in asystole out of hospital?" Am J Cardiol **86**(6): 610-4.
Comments: Level 3; Poor. Opposing

We describe the epidemiology, prognosis, and circumstances at resuscitation among a consecutive population of patients with out-of-hospital cardiac arrest (OHCA) with asystole as the arrhythmia first recorded by the Emergency Medical Service (EMS), and identify factors associated with survival. We included all patients in the municipality of Goteborg, regardless of age and etiology, who experienced an OHCA between 1981 and 1997. There were a total of 4,662 cardiac arrests attended by the EMS during the study period. Of these, 1,635 (35%) were judged as having asystole as the first-recorded arrhythmia: 156 of these patients (10%) were admitted alive to hospital, and 32 (2%) were discharged alive. Survivors were younger (median age 58 vs 68 years) and had a witnessed cardiac arrest more often than nonsurvivors (78% vs 50%). Survivors also had shorter intervals from collapse to arrival of ambulance (3.5 vs 6 minutes) and the mobile coronary care unit (MCCU) (5 vs 10 min), and they received atropine less often on scene. There were also a greater proportion of survivors with noncardiac etiologies of cardiac arrest (48% vs 27%). Survivors to discharge also displayed higher degrees of consciousness on arrival to the emergency department in comparison to nonsurvivors. Multivariate analysis among all patients with asystole indicated age ($p = 0.01$) and witnessed arrest ($p = 0.03$) as independent predictors of an increased chance of survival. Multivariate analysis among witnessed arrests indicated short time to arrival of the MCCU ($p < 0.001$) and no treatment with atropine ($p = 0.05$) as independent predictors of survival. Fifty-five percent of patients discharged alive had none or small neurologic deficits (cerebral performance categories 1 or 2). No patients > 70 years old with unwitnessed arrests (n = 211) survived to discharge.
Summary: 1635 patients were judged as having asystole as the first-recorded arrhythmia. Only 32 patients were survived. 16% of survivors and 34% of nonsurvivors received atropine. Multivariate analysis among witnessed arrests indicated no treatment with atropine (p=0.05) as independent predictors of survival. In this treatment algorithm, adrenaline is given before atropine. And 50% of survivors to discharge did not receive any prehospital intravenous medication at all. The author concluded that the survivors more often responded with rhythm changes after the initial adrenalin injection, and therefore, no longer needed atropine. This study did not show how many pediatric patients were included.

Fullerton DA, St Cyr JA, Clarke DR, et al; Bezold-Jarisch reflex in postoperative pediatric cardiac surgical patients Ann Thorac Surg 1991;52:534-536.
LOE 4, Case series. Atropine better than epinephrine. Quality of evidence poor.
No industry funding

The Bezold-Jarisch reflex is an inhibitory reflex that originates from the heart, is mediated by the vagus nerve, and is manifested by hypotension and bradycardia. We present 4 pediatric cardiac surgical patients, aged 1 day to 9 months, who exhibited cardiovascular collapse in their early postoperative course. In each patient, cardiovascular deterioration was marked by an insidious decrease in arterial blood pressure without an associated change in heart rate, central venous pressure, or airway pressure. Bradycardia followed the decrease in blood pressure. The Bezold-Jarisch reflex was suspected and atropine was administered, first as a bolus injection at 0.01 mg/kg, and later, as a continuous infusion at 0.01 mg.kg-1.h-1. Atropine prevented recurrent episodes of hypotension and bradycardia. We believe the Bezold-Jarisch reflex is more prevalent than previously suspected in postoperative pediatric cardiac surgical patients.
Summary: Case series in children; developed hypotension followed by bradycardia-all responded to atropine (2 had epi first); all were being ventilated (so not hypoxic)

Guay J, Lortie L. An evaluation of pediatric in-hospital advanced life support interventions using the pediatric Utstein guidelines: a review of 203 cardiorespiratory arrests. Can J Anaesth 2004; **51**(4): 373-8.

PURPOSE: Evaluate the efficacy of advanced life support interventions using the pediatric Utstein guidelines. METHODS: Charts from all patients for whom a cardiorespiratory arrest code was called during a six-year period in a university affiliated centre were reviewed. Data were recorded according to the pediatric Utstein guidelines and a $P < 0.05$ was considered significant. RESULTS: Of the 234 calls, 203 were retained for analysis. The overall survival rate at one year was 26.0% of which 10% had deterioration of their neurologic status compared to the pre-cardiorespiratory arrest evaluation. Time to achieve sustained return of spontaneous circulation (ROSC; $P < 0.0001$) and sustained measurable blood pressure ($P = 0.002$), to perform endotracheal intubation ($P = 0.04$) and the dose of sodium bicarbonate ($P < 0.0001$) were indicators of long-term survival. Two patients were alive at one year with unchanged neurologic status despite a time to achieve sustained ROSC longer than 30 min (38 and 44 min). The mean first epinephrine dose of patients for whom ROSC was achieved but unsustained was higher than those for whom ROSC was achieved and sustained (0.038 +/- 0.069 mg*kg(-1) vs 0.011 +/- 0.006 mg*kg(-1); $P = 0.004$). Survival rate and mean first epinephrine dose of patients who received their first epinephrine dose endotracheally (13.3%; 0.011 +/- 0.004 mg*kg(-1)) were comparable to those of patients who received their first epinephrine dose intravenously (7%; 0.015 +/- 0.027 mg*kg(-1)). CONCLUSIONS: For intravenously administered epinephrine, a dose of 0.01 mg*kg(-1) seems appropriate as the first dose. The endotracheal route is a valuable alternative for epinephrine administration and, for infants, the dose does not need to be increased. A minimal resuscitation duration time of 30 min can be misleading if ROSC is used as the indicator.

Herlitz, J., L. Ekstrom, et al. (1994). "Predictors of early and late survival after out-of-hospital cardiac arrest in which asystole was the first recorded arrhythmia on scene." Resuscitation **28**(1): 27-36.
Comments: Level 3; Poor. Opposing

BACKGROUND: A large proportion of patients who suffer out-of-hospital cardiac arrest have asystole as the initial recorded arrhythmia. Since they have a poor prognosis, less attention has been paid to this group of patients. AIM: To describe a consecutive population of patients with out-of-hospital cardiac arrest with asystole as the first recorded arrhythmia and to try to define indicators for an increased chance of survival in this population. SETTING: The community of Gothenburg. PATIENTS: All patients who suffered out-of-hospital cardiac arrest during 1981 to 1992 and were reached by our emergency medical service (EMS) system and where cardiopulmonary resuscitation (CPR) was attempted. RESULTS: In all there were 3434 cardiac arrests of which 1222 (35%) showed asystole as the first recorded arrhythmia. They differed from patients with ventricular fibrillation by being younger, including more women and having a longer interval between collapse and arrival of the first ambulance. In all 90 patients (7%) were hospitalized alive and 20 (2%) could be discharged from hospital. Independent predictors for an increased chance of survival were: (a) a short interval between the collapse and arrival of the first ambulance ($P < 0.001$) and the time the collapse occurred ($P < 0.05$). Initial treatment given in some cases with adrenaline, atropine and tribonate were not associated with an increased survival. CONCLUSIONS: Of all the patients with out-of-hospital cardiac arrest, 35% were found in asystole. Of these, 7% were hospitalized alive and 2% could be discharged from hospital. Efforts should be made to improve still further the interval between collapse and arrival of the first ambulance.
Summary: 3434 patients who suffered OHCA was attempted CPR during 1981 to 1992. Initial treatment given in some cases with adrenaline, atropine and tribonate were not associated with increased chance of survival. Only 24% of asystolic patients received atropine. In multivariate analysis the administration of atropine were worse of discharged alive. This study did not show how many pediatric patients were included.

Herlitz, J., A. Bang, et al. (2003). "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 **89**(1): 25-30.
Comments: Level 3; Poor. Opposing

OBJECTIVE: To describe the change in survival and factors associated with survival during a 20 year period among patients suffering from out of hospital cardiac arrest and being hospitalised alive. PATIENTS: All patients hospitalised alive in the community of Goteborg after out of hospital cardiac arrest between 1 October 1980 and 1 October 2000 were included. METHODS: Patient data were prospectively computerised with regard to factors at resuscitation. Data on medical history and hospitalisation were retrospectively recorded. Patients were divided into two groups (the first and second 10 year periods). SETTING: Community of Goteborg, Sweden. RESULTS: 5505 patients suffered from cardiac arrest during the time of the survey. Among them 1310 patients (24%) were hospitalised alive. Survival (discharged alive) was 37.5% during the first part and 35.1% during the second part (NS). The following were independent predictors of an increased chance of survival: ventricular fibrillation/tachycardia as the first recorded rhythm (odds ratio (OR) 3.46, 95% confidence interval (CI) 2.36 to 5.07); witnessed arrest (OR 2.50, 95% CI 1.52 to 4.10); bystander initiated cardiopulmonary resuscitation (OR 2.00, 95% CI 1.42 to 2.80); the patient being conscious on admission to hospital (OR 6.43, 95% CI 3.61 to 11.45); sinus rhythm on admission to hospital (OR 1.53, 95% CI 1.12 to 2.10); and treatment with lidocaine in the emergency department (OR 1.64, 95% CI 1.16 to 2.31). The following were independent predictors of a low chance of survival: age > 70 years (median) (OR 0.65, 95% CI 0.47 to 0.88); atropine required in the emergency department (OR 0.35, 95% CI 0.16 to 0.75); and chronic treatment with diuretics before hospital admission (OR 0.59, 95% CI 0.43 to 0.81). CONCLUSION: There was no improvement in survival over time among initial survivors of out of hospital cardiac arrest during a 20 year period. Major indicators for an increased chance of survival were initial ventricular fibrillation/tachycardia, bystander cardiopulmonary resuscitation, arrest being witnessed, and the patient being conscious on admission. Major indicators for a lower chance were high age, requirement for atropine in the emergency department, and chronic treatment with diuretics before cardiac arrest.
Summary: They suggested that the patients who require atropine are those in whom the resuscitation attempt was not immediately successful. This study did not show how many pediatric patients were included.

Horigome H, Tsuji M, Yamashita M, et al. Echocardiographic evaluation of vagolytic effects of atropine sulfate during pediatric halothane anesthesia. Acta Paediatrica Japonica 1993;35:513-517.
LOE 1, randomized, controlled study in children. Against the use of atropine to improve myocardial depression caused by halothane anesthesia. Quality of evidence good.
No industry funding

The aims of this study were to define the antagonistic effects of atropine sulfate to halothane-induced cardiovascular depression in children, and to clarify whether or not a larger dose of atropine is more effective in attenuating the cardiovascular depression. Thirty-four children aged 1-12 years who had undergone minor surgery, free from cardiac or pulmonary disease, were assigned at random to two groups. M-mode echocardiographic evaluation of left ventricular function in each patient was performed at three points (before induction, point A; after induction, point B; and following administration of atropine, point C). Results were compared between points A and B, B and C and C and A, and between the two study groups with different doses of atropine (0.01 mg/kg vs 0.02 mg/kg). Heart rate (HR), mean blood pressure (MBP) and left ventricular shortening fraction (LVSF) decreased, and left ventricular end-diastolic dimension (LVEDD) were increased significantly by halothane induction. Although HR and MBP recovered following atropine, LVSF and LVEDD remained unchanged. There were no differences found between the values after vagolysis in both study groups, except for HR and mean velocity of circumferential fiber shortening (mVcf). Heart rate increased above that of pre-induction, even following the smaller dose of atropine. The myocardial depression cannot be necessarily attenuated by vagolysis regardless of the dosage of atropine. The smaller dose (i.e. 0.01 mg/kg) seems to be sufficient only to antagonize the bradycardia and hypotension during halothane anesthesia in children.
Summary: Randomized study of children undergoing halothane anesthesia. Monitored HR, Mean BP left ventricular end diastolic dimension (LVEDD), LV shortening fraction(LVSF) with 2 doses of atropine (0.01 mg/kg and 0.02 mg/kg). Atropine only increased HR and MBP, but had no effect on LVSF (which was decreased by halothane), or LVEDD (which was increased by halothane). Conclusion-atropine does not improve the myocardial depression caused by halothane, and a dose o 0.02 mg/kg is no better than 0.01 mg/kg.

Iseri LT, Humphrey SB, Siner EJ. Prehospital brady-asystolic cardiac arrest. Ann Int Med 1978;88:741-745.
LOE 5. Neutral. Adult study. Quality of evidence poor.
NHLBI funded

Of 133 persons with spontaneous cardiac arrest attended by paramedics within 10 minutes, 100 (75%) had ventricular fibrillation as the initial rhythm and 33 (25%) had extreme bradycardia or asystole. The latter group of arrhythmias was characterized by sinus arrest or severe sinus bradycardia (90%) and complete A-V block (10%). Junctional escape rhythm was also absent or markedly retarded. Despite cardiopulmonary resuscitation and the administration of epinephrine, atropine, isoproterenol, and sodium bicarbonate, recovery of the sinus and junctional tissues was infrequent. Ventricular fibrillation developed in 11 cases (33%). One patient lived 12 days, but all others were dead on arrival or died

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循環器疾患・糖尿病等生活習慣疾病対策総合研究事業
循環器疾患等の救命率向上に資する効果的な救急蘇生法の普及啓発に関する研究
(H21-心筋-一般-001)
(研究代表者　丸川征四郎)

平成22年度研究報告

分担研究報告

ドクターヘリによる循環器疾患の救命率向上についての研究

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ドクターヘリによる循環器疾患の救命率向上についての研究

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研究要旨：急性冠症候群では症状発現から専門的治療開始までの時間短縮が救命率を向上させることから、ドクターヘリでの搬送は適していると考える。昨年の研究の結果、確実で安全な心肺蘇生術と除細動を施行する際の指針の作成が必要との結論に至った。そこで、今回、25施設に急性冠症候群における心肺蘇生の件数、除細動施行件数などの心肺蘇生法についての実態調査を行った。その結果、急性冠症候群への診療件数の率が昨年の調査結果に比して倍増し、それに伴い電気的除細動施行件数も増加していた。電気除細動器については6器種が使用されており、その中で1件の誤作動の報告があったが、その原因は不明であった。心肺蘇生法についての調査では、効果的な胸骨圧迫による心臓マッサージ法が行われているのか不明であり、また、医療従事者の安全面の配慮が行われていなかった。今後、安全かつ確実な心肺蘇生・電気的除細動の施行における指針を作成するに至っては、実際の飛行下での電気除細動器、自動心臓マッサージ器の実験研究を行う必要があると考えられた。

A．研究目的

急性冠症候群では症状発現から専門的治療開始までの時間短縮が救命率を向上させる。近年ではドクターヘリによる病院前救急医療も全国 25 ヶ所の基地病院で行われるようになり、年間出動件数も件を上回るようになってきた。

昨年の調査においては、ドクターヘリによる急性冠症候群における、出動要請についての実態調査と搬送中の致死的不整脈に対する機内での電気除細動器（ＤＣ）の使用状況について研究を行った。その結果、ドクターヘリ機内での心肺蘇生術については偏りがあり、今後、確実で安全な心肺蘇生術と除細動を施行する際の指針の作成が必要との結論に至った。そこで、今回、22年度ドクターヘリ運航を行っている施設に、急性冠症候群症例の心肺蘇生の件数、除細動施行件数等の実態調査とドクターヘリ機内での心肺蘇生法の調査を行って、その問題点を抽出することを目的とする。

B．研究方法

全国 21 施設のドクターヘリ基地病院へ、平成 21 年度のドクターヘリ出動状況を質問紙法にてアンケート調査を行った。アンケートでは、acute coronary syndrome（以下ＡＣＳ）の疾患でヘリ要請され、病院収容までの out-of-hospital cardiopulmonary arrest(以下ＣＰＡ）件数、致死性不整脈における除細動器使用件数、除細動施行経験がある施設においては、施行における実態調査を行った。また、平成22年度運航の25施設に対して、ヘリ搬送中に心肺機能停止症例に対する心肺蘇生施行の現状について、除細動器種、除細動時の不具合、心マッサージ法などにつきアンケート調査（別添；資料 1）を行い、ドクターヘリ出動時の急性冠症候群に対する致死的不整脈や心停止時の対応についての調査を行った。

C．研究結果

25 施設へのアンケート依頼に対して 25 施設からの回答を得た（回答率 100%）が、そ

のうちの21年度運航した21施設のうち、不備が認められた1施設は除外して20施設で急性冠症候群に対しての検討をおこなった。

1．急性冠症候群に対するドクターヘリ出動時のＣＰＡ症例と除細動回数

ドクターヘリの急性冠症候群に対する出動時のＣＰＡ件数については、有効な20施設のデータにて検討した。20施設の1年間の総出動数が6,808件で、その中で急性冠症候群症例は435例（6.4%）であった。この急性冠症候群症例への出動でＣＰＡとなった症例は59例で、ドクターヘリ急性冠症候群の出動のなかの12.9%であった。この59例の中で致死的な不整脈に対して除細動を行った症例は、30例（31回）で急性冠症候群総出動の6.2%であった。図1にドクターヘリ運航施設ごとのＡＣＳでのＣＡＰ症例数と除細動施行回数を示した。14施設においてＡＣＳ症例診療中にＣＰＡとなり、そのうちの10施設でＤＣを行っていた。

また、除細動を行った場所としては、現場および救急車内が28回、ヘリ機内（駐機中）が1回、ヘリ機内（飛行中）が2回であった（1例に2回行ったものあり、図2）。

2、ドクターヘリに搭載している除細動器種

ドクターヘリ所有の施設に搭載している除細動器種の内訳は、ＰＨＬＩＰＳ社製；自動体外式除細動器ハートスタートが4施設、ＰＨＬＩＰＳ社製；自動体外式除細動器ＭＲＸが7施設、日本光電社製；ディフイブリレータＴＥＣが4施設、日本光電社製;Cardio Lifeが2施設、フクダ電子社製；ＦＣが4施設、メドトロニック社製；Life Packが2施設であり、わずかな規格の違いを除けば概ね6器種（12種類）の除細動器を搭載していることが分かった。

3、除細動の誤作動件数

回答があった25施設において、除細動時の誤作動の経験がある施設は1施設、1件であった。その器種は、フクダ電子社製;ＦＣ-2040で、誤作動の内容としては、充電をした後に放電が出来ず、その原因については不明とのことであった。また、飛行中に除細動器でのモニターリングを行うことやモニターリング中の無線交信などを行うことによるアーチファクトの経験はないとのことであった。

4、ヘリコプター機内でのＣＰＲの実態調査

ＣＰＲが必要な症例の場合、ＣＰＲを継続しながら、ヘリ搬送を行うかの問いに対して、複数回答で、継続しながら搬送を行うが12施設で、ヘリ搬送はせずに近隣の救急医療施設に搬送するが15施設であった。次に、ＣＰＲを行いながら搬送する施設において、ヘリ内の胸骨圧迫の方法を尋ねたところ、用手的胸骨圧迫法が13施設、自動心臓マッサージ器使用が3施設であった。ヘリ機内で胸骨圧迫法を施行する際に、どの方向から行うかの問いに対して、頭側4施設、横側2施設。頭側・横側交互が6施設であった。また、胸骨圧迫を行う際には、シートベルトの着用を行っているかの問いに対して、着用して胸骨圧迫を行うが4施設、着用しないが9施設であった。次に、ヘリ内で胸骨圧迫は効果的と考えるかの問いに対して、効果的であるが1施設、多少の効果があるが17施設、効果がないが4施設であった。

D．考察

厚生労働省ドクターヘリ導入促進事業による本邦でのドクターヘリ運航が開始されてから9年が経過し、平成22年3月までには25ヶ所の基地病院にて、そのドクターヘリ事業が行われている。また、平成19年には救急医療用ヘリコプターを用いた救急医療の確保に関する特別措置法（ドクターヘリ特措法）が制定されたことによりその機運も一気に高まり、全国各地で病院前救急医療の重要さが理

解されてドクターヘリ事業が全国展開へと進行しつつある。

昨年は、ドクターヘリによる救急現場からの急性冠症候群の診療体制について検討した結果、過去3年間の総出動件数に対するＡＣＳへの出動率は 3.6%であったが、この平成21年度の1年間での出動率は6.4%と倍増していた。また、これに伴い心肺停止症例も多くなり、致死的な不整脈による電気的除細動施行施設も増加していた。また、ヘリコプター内での電気除細動器の使用については未だに明確な指針は出されていないために、今回は除細動器種や除細動時の問題点など、心肺蘇生における現状を把握するための調査を行った。

電気的除細動においては、6 器種の除細動器が使用されており、それぞれの施設によりばらつきがみられた。このことは、施設においても、どの器種が航空機搬送に適している除細動器なのかで選択したのではなく、使い慣れた除細動器を選択しているものと思われた。また、除細動時の問題点につては、誤作動の報告が1件あったが、それが人為的なものか、機械的な不具合によるものなのか、原因は解明できていない。したがって、今後はますますＡＣＳに対するドクターヘリ出動が増加してくるものと思われるために、現在ヘリコプター機内で使用されている除細動器において、ヘリコプターのメインローターの回転中に自動体外式電気除細動器（AED）が除細動の必要性を判断できるのか、ヘリ離陸時、飛行中、無線交信中、着陸時のアーチファクトの有無などの安全性の調査と器種による特性を検討する必要があると考える。

また、心肺蘇生については、2 施設では年間で5例以上のCPR症例を経験しているが、その他の施設においては年間に0～4症例と、昨年同様に施設により偏りがあり、施設による心肺停止（CPA）症例への、ヘリ搬送の対応（出動条件など）が異なっていることがうかがわれた。さらに今回、心肺蘇生における実態調査を行ったが、ヘリ内における胸骨圧迫は効果的と答えた施設は1施設のみで、他の施設では多少は効果的が17施設、効果的ではないとの回答は4施設であり、施設によって心肺蘇生効果への認識の違いがあることが分かった。これは、「これまでに行った胸骨圧迫での心拍再開があった」などの経験から、そのような回答に至ったものと考えられた。また、狭いヘリ機内での胸骨圧迫の方向においても、頭側、横側と一方向のみと答えられた施設が半数あった。これは1人の医療従事者のみで胸骨圧迫を行うことは、医療従事者の疲労の面からも時間経過とともに、有効な胸骨圧迫の深さが保てないと考えられた。これらのことより、狭いヘリコプター内では有効なCPRが十分に行える状況にはなく、そこにも問題が有ることが示唆され、有効な胸骨圧迫を継続して航空機搬送することは、難しいことが示唆された。また、ヘリコプター内での揺れる機内においてのCPRは、医療従事者に対して、十分な安全運航危機管理が行われているとは思われなかった。そこで、そのＣＰＲ施行時の安全危機管理（シートベルト装着）についても調査を行ったが、9 施設がＣＰＲ中はシートベルトを着用しないとのことであり、医療従事者の安全面への対応は不十分であることがうかがわれた。しかし、1施設のみ安全面を配慮した固定用具を用いてＣＰＲを行っていることが分かった。そこで、この安全面を考慮したヘリコプター内における自動心臓マッサージ器の使用について尋ねたところ、3施設のみが現在使用していたが、その効果についての検証も必要である。今後は、心臓マッサージ中の固定用具の開発、もしくは自動心臓マッサージの搭載が推奨されると考えるが、その機材においても、飛行中のゆれにより、的確な胸骨圧迫が出来るのか疑問が残ることから、ヘリに搭載している自動心臓マッサージの器種調査ならびに、実際に飛行下での胸骨圧迫を行い、胸骨圧迫の位置のずれ、深さなどの実験的研究も必要と考

える。これに対しても今後、飛行下においての自動心臓マッサージ器の実験的研究を行う必要であると考える。したがって、ヘリコプター内での心肺蘇生時においても安全で確実な施行指針が必要であるとの結論に至った。

E．結論

全国 25 ヶ所のドクターヘリ運航基地施設へ急性冠症候群症例での電気的除細動・心肺蘇生施行における実態調査を行った。急性冠症候群症例への出動率は昨年度調査に比して増加しており、除細動症例も増加していた。電気除細動器については 6 器種が使用されており、そのうちの 1 件に誤作動の報告があったが、その原因は不明であった。またドクターヘリ機内での心肺蘇生法については施設間で偏りがあり、医療者への安全面の対応は不十分であった。今後は、心臓マッサージ施行時の固定器具の開発、自動心臓マッサージの導入の検討も必要と考えられる。したがって、今後は実機による電気除細動器、自動心臓マッサージ器の実験的検証を行い、安全で確実なドクターヘリ運航における心肺蘇生法の明確な指針が必要である。

F．健康危険情報

なし

G．研究発表

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H．知的財産権の出願・登録状況

なし

図１．施設ごとの急性冠症候群でのＣＰＡ症例数と除細動施行回数

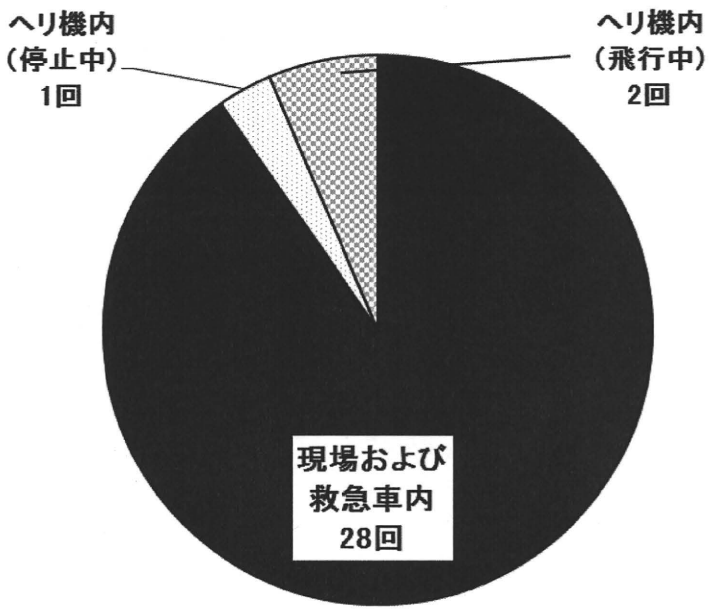

図２．ＡＣＳ出動中の除細動施行場所

別添資料　1

『ドクターヘリによる循環器疾患の救命率向上についての研究』
アンケート用紙

ドクターヘリ施設名（　　）

下記の項目についてお答え下さい

【全施設共通質問項目】

1. 貴施設においてACS(acute coronary syndrome：急性冠症候群)の疾患で、ヘリ要請された際に病院収容までにCPA（out-of-hospital cardiopulmonary arrest：院外心肺停止）になった症例は何例ありますか？またその症例において、ＶＦ・無脈性ＶＴなどで、除細動器を使用した症例は何例ありますか？

ＣＰＡ症例	例・・・経験のない施設は3へお進み下さい
除細動を施行した症例	例・・・経験のない施設は3へお進み下さい

2. 上記の問いで除細動を施行した経験のある施設に質問です。除細動を何処で行いましたか？

救急車・現場（傷病者自宅等）	例
ヘリ機内（停止中）	例
ヘリ機内（飛行中）	例

【全施設共通質問項目】

3. 貴施設のドクターヘリ（消防・防災ヘリ）に搭載している除細動機は何ですか？
（例：PHLIPS社製　自動体外式除細動器ハートスタートＦＲ２）

4. これまでに、除細動を使用した際に、アーチファクトが出た経験はありますか？
下記に☑をお願いします

□ある・・・5へお進み下さい

□ない・・・6へお進み下さい

5.であるとお答えした施設に質問です。アーチファクトはどの状態で出現したでしょうか？
下記に☑をお願いします

□離陸時

□飛行中

□着陸（体制に入った）時

【全施設共通質問項目】

6. 除細動の電源を入れた状態で、無線交信をした場合にアーチファクトが出た経験はありますか？
下記に☑をお願いします。

□ある

□ない

□経験がないので分からない

【全施設共通質問項目】

7. これまでに、除細動の誤作動を経験したことはありますか？（ＡＥＤも含みます）下記に☑をお願いします

□ある・・・8へお進み下さい

□ない・・・9へお進み下さい

□経験がないので分からない・・・9へお進み下さい

8.『除細動の誤作動を経験した施設に質問です』よろしければ、どのような内容の誤作動だったでしょうか？教えていただけないでしょうか？

【全施設共通質問項目】

9.貴施設において、現場で（外因性・内因性）CPA症例に遭遇した場合に、CPRを行いながら、ヘリに乗せ、CPRを継続しながら搬送を行いますか？下記に☑をお願いします

□ CPRを行いながら搬送します・・・10へお進み下さい

□ 搬送は行わず、近隣の救急医療機関に救急車で搬送します・・・13へお進み下さい

10.『CPR を行いながら搬送します』と答えた施設に質問です。胸骨圧迫はどのような方法で行いますか？下記に☑をお願いします

□ 用手的胸骨圧迫・・・・11・12へお進み下さい

□ 自動心臓マッサージ器・・・13へお進み下さい

※用手的胸骨圧迫・自動心臓マッサージ器併用を行う施設は11へお進み下さい

11.『用手的胸骨圧迫』と答えた施設に質問です。ヘリ機内においては、どの方向から胸骨圧迫を行いますか？下記に☑をお願いします

□傷病者の頭側から胸骨圧迫を行う

□傷病者の横側から胸骨圧迫を行う

□その他（　　）

12.機内で用手的胸骨圧迫を行う際は、シートベルトは着用していますか？

下記に☑をお願いします

□ 着用して胸骨圧迫を行う。

□ 着用しないで胸骨圧迫を行う。

【全施設共通質問項目】

13.ドクターヘリ内での胸骨圧迫は効果的と思われますか？

□効果的と考える

□通常、行う胸骨圧迫より効果的ではないと考えるが、多少は効果的と考える

□効果的ではないと考える

14.貴施設は自動心臓マッサージ器（胸骨圧迫用）をヘリに搭載していますか？

下記に☑をお願いします

□ 常時搭載している・・・15・16へお進み下さい

□ 要請内容により搭載する・・・15・16へお進み下さい

□ 搭載していない・・・終了です。ご協力ありがとうございました。

15.『常時搭載している』、『要請内容により搭載する』にチェックをした施設にご質問です。

自動心臓マッサージ器の機種の名前を下記にお書き下さい

（例：日本光電社製　オートパルス）

16.ヘリ搬送で使用中に胸骨圧迫のずれが生じて、再装着をした、もしくは、病院に収容して、ずれていることに気づいた経験はありますか？

□ある

□ない

□ 経験がないので分からない

17.その他、自動心臓マッサージ器で困った点などありましたら、下記に記載をお願い致します

ご協力ありがとうございました。

平成 22 年度厚生労働科学研究費補助金
循環器疾患・糖尿病等生活習慣疾病対策総合研究事業
循環器疾患等の救命率向上に資する効果的な救急蘇生法の普及啓発に関する研究
(H21-心筋-一般-001)
(研究代表者　丸川征四郎)

平成 22 年度研究報告

分担研究報告

欧米との比較検証に基づく救急蘇生実施率向上のための研究

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救急救命九州研修所 教授

平成 23(2011)年 3 月

目　次

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(H21-心筋-一般-001)
(研究代表者　丸川征四郎)

平成22年度研究報告

研究課題A

諸外国における病院外心停止に対するバイスタンダーCPRの現状

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