WORKSHEET for Evidence-Based Review of Science for Veterinary CPCR

1. Basic Demographics

Worksheet author(s)

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[redacted]

2. Clinical question:

In dogs and cats with cardiac arrest due to VF (P) does the use of CPR before defibrillation (I) as opposed to defibrillation first (C), improve outcome (O) (e.g. ROSC survival)?

3. Conflict of interest specific to this question:

None

4. Search strategy (including electronic databases searched):

4a. Databases

-MEDLINE via PUBMED (1950 to May 2011) (performed on May 17th 2011)
1. ventricular fibrillation
2. cardiac arrest
3. animal model
4. defibrillation
5. outcome

1 and 2: **23** relevant hits out of **5510** total hits
2 and 3: **2** additional relevant hits out of **1628** hits
3 and 4: **4** additional relevant hits out of **435** hits
4 and 5: **9** additional relevant hits out of **2318** hits

-CAB (1973 to May 2011) (performed on May 17th 2011)
1. ventricular fibrillation
2. cardiac arrest
3. animal model
4. defibrillation
5. outcome

1 and 2: **0** relevant hits out of **56** total hits
2 and 3: **0** additional relevant hits out of **4** total hits
3 and 4: **0** additional relevant hits out of **0** total hits
4 and 5: **0** additional relevant hits out of **12** total hits

4b. Other sources

-In addition all references of identified articles and in particular the references of the following relevant review articles were checked:

- Link M, Atkins D, Passman R, et al. 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Part 6: Electrical Therapies: Automated External Defibrillators, Defibrillation, Cardioversion, and Pacing
- ILCOR BLS-024A Worksheet
- Meta-analyses:
    - Meier P, Baker P, Jost D et al. Chest compressions before defibrillation for out-of-hospital cardiac arrest: A meta-analysis of randomized controlled clinical trials. *BMC Medicine* 2010, 8:52
    - Simpson P, Goodger M, Bendall J. Delayed versus immediate defibrillation for out-of-hospital cardiac arrest due to ventricular fibrillation: A systematic review and meta-analysis of randomised controlled trials. *Resuscitation* 2010, 81(8):925

4c. State inclusion and exclusion criteria for choosing studies and list number of studies excluded per criterion

Inclusion criteria

Human or animal studies, documented rhythm of ventricular fibrillation, utilization of defibrillation with CPR

Exclusion criteria

Abstracts or editorials, conference presentations, non peer reviewed publications

4d. Number of articles/sources meeting criteria for further review: Of the **38** articles identified as relevant hits, **28** articles met the above criteria for further review. Of those 28 articles, **6** were not included for review because they were LOE 6 studies of poor quality (all retrospective in nature). The **22** articles that were included for review include the following:

LOE 1

None

LOE 2

None

LOE 3

A total of **3 studies** were reviewed in the target species (dogs), all prospective randomized laboratory studies:

Niemann, J. T., Cairns, C. B., Sharma, J., & Lewis, R. J. (1992). Treatment of prolonged ventricular fibrillation. Immediate countershock versus high-dose epinephrine and CPR preceding countershock. *Circulation*, *85*(1), 281-7.

Wang, Y.-L., Zhong, J.-Q., Tao, W., Hou, X.-M., Meng, X.-L., & Zhang, Y. (2009). Initial defibrillation versus initial chest compression in a 4-minute ventricular fibrillation canine model of cardiac arrest. *Critical care medicine*, *37*(7), 2250-2.

Yakaitis, Donald W., Ewy, Gordon A, Otto Charles W., et al. (1980). Influence of time and therapy on ventricular defibrillation in dogs. *Critical care medicine*, *8*(3), 157-163

LOE 4
None

LOE 5
None

LOE 6
A total of **18** studies, further subdivided by species:

For **meta-analyses**, a total of **2** human studies were reviewed:

Meier, P., Baker, P., Jost, D., Jacobs, I., Henzi, B., Knapp, G., et al. (2010). Chest compressions before defibrillation for out-of-hospital cardiac arrest: a meta-analysis of randomized controlled clinical trials. *BMC medicine*, *8*, 52.

Simpson, P. M., Goodger, M. S., & Bendall, J. C. (2010). Delayed versus immediate defibrillation for out-of-hospital cardiac arrest due to ventricular fibrillation: A systematic review and meta-analysis of randomised controlled trials. *Resuscitation*, *81*(8), 925-31.

For **human randomized controlled studies**, a total of **4** studies were reviewed:

Baker, P. W., Conway, J., Cotton, C., Ashby, D. T., Smyth, J., Woodman, R. J., et al. (2008). Defibrillation or cardiopulmonary resuscitation first for patients with out-of-hospital cardiac arrests found by paramedics to be in ventricular fibrillation? A randomised control trial. *Resuscitation*, *79*(3), 424-31.

Jacobs, I. G., Finn, J. C., Oxer, H. F., & Jelinek, G. A. (2005). CPR before defibrillation in out-of-hospital cardiac arrest : A randomized trial. *Emergency Medicine*, 39-45.

Jost, D., Degrange, H., Verret, C., Hersan, O., Banville, I. L., Chapman, F. W., et al. (2010). DEFI 2005: a randomized controlled trial of the effect of automated external defibrillator cardiopulmonary resuscitation protocol on outcome from out-of-hospital cardiac arrest. *Circulation*, *121*(14), 1614-22.

Wik L., Hansen T.B., Fylling F., et al. (2003). Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation. A randomized trial. *J Am Med Assoc*, *289*(11), 1389-1395.

For **human observational studies,** a total of **6** studies were reviewed:

Bradley, S. M., Gabriel, E. E., Aufderheide, T. P., Barnes, R., Christenson, J., Davis, D. P., et al. (2010). Survival increases with CPR by Emergency Medical Services before defibrillation of out-of-hospital ventricular fibrillation or ventricular tachycardia: observations from the Resuscitation Outcomes Consortium. *Resuscitation*, *81*(2), 155-62.

Cobb, L. a, Fahrenbruch, C. E., Walsh, T. R., Copass, M. K., Olsufka, M., Breskin, M., et al. (1999). Influence of cardiopulmonary resuscitation prior to defibrillation in patients with out-of-hospital ventricular fibrillation. *JAMA : the journal of the American Medical Association*, *281*(13), 1182-8.

Kellum, M. J., Kennedy, K. W., & Ewy, G. a. (2006). Cardiocerebral resuscitation improves survival of patients with out-of-hospital cardiac arrest. *The American journal of medicine*, *119*(4), 335-40.

Skogvoll, E., & Nordseth, T. (2008). The early minutes of in-hospital cardiac arrest: shock or CPR? A population based prospective study. *Scandinavian journal of trauma, resuscitation and emergency medicine*, *16*, 11.

Spearpoint, K. G., McLean, C. P., & Zideman, D. a. (2000). Early defibrillation and the chain of survival in "in-hospital" adult cardiac arrest; minutes count. *Resuscitation*, *44*(3), 165-9.

Vilke, G. M., Chan, T. C., Dunford, J. V., Metz, M., Ochs, G., Smith, A., et al. (2005). The three-phase model of cardiac arrest as applied to ventricular fibrillation in a large, urban emergency medical services system. *Resuscitation*, *64*(3), 341-6.

For **swine randomized laboratory studies**, a total of **5** studies were reviewed:

Berg, R. (2002). Precountershock cardiopulmonary resuscitation improves ventricular fibrillation median frequency and myocardial readiness for successful defibrillation from prolonged ventricular fibrillation: A randomized, controlled swine study. *Annals of Emergency Medicine*, *40*(6), 563-570.

Berg, R. a, Hilwig, R. W., Ewy, G. a, & Kern, K. B. (2004). Precountershock cardiopulmonary resuscitation improves initial response to defibrillation from prolonged ventricular fibrillation: A randomized, controlled swine study*. *Critical Care Medicine*, *32*(6), 1352-1357.

Indik, J. H., Hilwig, R. W., Zuercher, M., Kern, K. B., Berg, M. D., & Berg, R. a. (2009). Preshock cardiopulmonary resuscitation worsens outcome from circulatory phase ventricular fibrillation with acute coronary artery obstruction in swine. *Circulation. Arrhythmia and electrophysiology*, *2*(2), 179-84.

Menegazzi, J. (2003). Immediate defibrillation versus interventions first in a swine model of prolonged ventricular fibrillation. *Resuscitation*, *59*(2), 261-270.

Rittenberger, J. C., Suffoletto, B., Salcido, D., Logue, E., & Menegazzi, J. J. (2008). Increasing CPR duration prior to first defibrillation does not improve return of spontaneous circulation or survival in a swine model of prolonged ventricular fibrillation. *Resuscitation*, *79*(1), 155-60.

For **swine observational laboratory studies,** a total of **1** study was reviewed:

Niemann, J. T., Cruz, B., Garner, D., & Lewis, R. J. (2000). Immediate countershock versus cardiopulmonary resuscitation before countershock in a 5-minute swine model of ventricular fibrillation arrest. *Annals of emergency medicine*, *36*(6), 543-6.

For **murine randomized laboratory studies**, a total of **1** study was reviewed:

Kolarova, J., Ayoub, I. M., Yi, Z., & Gazmuri, R. J. (2003). Optimal timing for electrical defibrillation after prolonged untreated ventricular fibrillation. *Critical care medicine*, *31*(7), 2022-8.

5. Summary of evidence

Evidence Supporting Clinical Question

Good			Niemann 1992; A			*Berg 2002; A, E=cardiac output* *Berg 2004; A, D, E=24 hr survival* *Kolorova 2003; A* *Menegazzi 2003; A*
Fair						*Bradley 2010; C* *Cobb 1999; C, D*
Poor						*Kellum 2006; C, D* *Vilke 2005; C*
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival *Italics = Non-target species studies*

Evidence Neutral to Clinical question

Good			Wang 2009; A, E=24 hr survival			*Baker 2008; A, C, D* *Jacobs 2005; A, C* *Meier 2010; A, C, D, E=1 year survival* *Wik 2003, A, C, E= 1 year survival* *Simpson 2010, C*
Fair						*Jost 2010; A, B, C* *Rittenburger 2008; A*
Poor						
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival *Italics = Non-target species studies*

Evidence Opposing Clinical Question

Good			Yakaitis 1980; A			*Indik 2009; B, D* *Niemann 2000; A, E=first shock success rate, number of shocks required to terminate VF*
Fair						*Spearpoint 2000; A, C*
Poor						*Skogvoll 2008; A, C*
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival *Italics = Non-target species studies*

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

In recent human literature, there is greater understanding for what is now known as the three-phase model of cardiac arrest, with each phase having a different optimal therapeutic approach. The initial "electrical phase" is characterized by minimal ischemic injury. Rapid restoration of a perfusing rhythm (through use of defibrillation) appears to be most important during this time. After approximately 4 minutes, the "circulatory phase" is entered and consists of the accumulation of toxic metabolites, depletion of high-energy phosphate stores, and the initiation of ischemic cascades. During this phase, a period of CPR may be indicated prior to defibrillation, in an effort to deliver substrate (i.e. oxygen) to the myocardial cells and potentially flush out toxic metabolites. Finally, the "metabolic phase" begins approximately 10 minutes following arrest, resulting in irreversible cellular injury. Return of circulation may result in reperfusion injury. During this latest phase, these is no proven efficacious therapy. (Vilke 2005).

As a result of the development of the three-phase model, the timing from onset of ventricular fibrillation to intervention (either defibrillation or CPR) is very important. Most studies reviewed in this worksheet identified which "phase" of arrest that was likely being treating, and many studies also acknowledged that different therapies might be required for different phases. The general consensus from available human literature is that when response time is quick, then defibrillation should be attempted immediately. Conclusions from those studies are as follows:

> Human meta-analyses (Meier, Simpson) and RCTs (Baker, Jacobs, Jost, Wik): There is no obvious benefit of providing CPR prior to defibrillation. Wik found that if response time is > 5 minutes, consider providing 3 minutes CPR first prior to defibrillation. This was also mentioned in the conclusion of meta-analysis by Meier. In the Jost article, it was difficult to interpret the effect of precountershock CPR on outcome, because other changes to the protocol were simultaneously being performed.
>
> Human observational studies (Bradley, Cobb, Kellum, Skogvoll, Spearpoint, Vilke): Two studies (Spearpoint, Skogvoll) emphasized that defibrillation should be prioritized in the first 2-3 minutes of ventricular fibrillation. Two studies (Cobb, Vilke) found that for patients with time since collapse > 4 minutes, performing CPR prior to defibrillation improved survival. In the Cobb study, 90 seconds of CPR was performed prior to defibrillation. In the Kellum study, the effects of CPR-first were studied in combination with a number of other variables, and although survival was improved, it is difficult to discern how much CPR-first contributed to the overall effect. In the Bradley study, between 46-195 seconds of EMS CPR prior to defibrillation was weakly associated with improved survival, and this effect was more pronounced in patients with a longer time to EMS unit arrival. Also, the benefit of CPR before defibrillation was reduced when the duration of CPR exceeded 195 seconds.

There are no randomized controlled clinical trials or clinical studies regarding this question in our species of question (dogs or cats). There are a total of three experimental laboratory studies in the target species (dog) that would qualify as LOE 3 (Niemann 1992, Wang, Yakitis). Conclusions from these studies are as follows:

> In these studies, ventricular fibrillation was electrically induced and then left untreated for varying amounts of time (Niemann- 7.5 minutes, Wang- 4 minutes, Yakaitis- 1, 3, 5, or 9 minutes). Intervention was with either immediate defibrillation, or CPR prior to defibrillation. When performed, duration of CPR also varied (Niemann- 3 to 5 minutes, Wang- 200 chest compressions, Yakaitis- 1 minute) Additionally, epinephrine was also administered in the Niemann (0.08 mg/kg) and Yakaitis (1 mg) studies. In the Yakitis study, the administration of epinephrine had no effect on

the dose needed for conversion, but it became increasingly important for restoration of circulation after 2 minutes of fibrillation. Recommendations from these studies include immediate countershock for episodes of fibrillation limited to 3 minutes (Yakatis), but defibrillation versus CPR first was found to be equivocal if duration of fibrillation is around 4 minutes (Wang). CPR first may be helpful if duration of ventricular fibrillation is closer to 7.5 minutes (Niemann 1992).

Laboratory studies in swine have also been performed (Berg 2002, Berg 2004, Indik, Menegazzi, Rittenberger, Niemann 2000). All were randomized except one (Niemann). Conclusions from these studies are as follows:

Most studies had at least 8 minutes of untreated vfib, with 2 studies having only 5 minutes of untreated vib (Rittenburger, Niemann). Important to note on the Rittenburger study, there was no control group that had immediate defibrillation. One study suggested shocking first provided better 24-hour survival (Indik), and 3 studies supported using 1.5-3 minutes of compressions first to improve ROSC (Berg 2002 and 2004, Menegazzi). In these 3 studies, swine were fibrillating for at least 8 minutes. In the only study where fibrillation lasted 5 minutes and immediate defibrillation was provided as an intervention (Niemann), providing CPR prior to countershock negatively impacted the cardiac resuscitation rate.

7. CONCLUSION:

Consensus on Science statement:

Evidence from 3 laboratory studies in dogs (LOE 3) and 0 studies in cats, in addition to additional studies in non-target species (LOE 6 studies consisting of 2 meta-analyses, 4 randomized controlled trials, 6 observational studies and 7 laboratory studies) indicate that defibrillation should be performed immediately if time since onset of ventricular fibrillation is $\leq$ 4 minutes, because this is most consistent with the electrical phase of cardiac arrest. In cases where response time is longer (> 4 minutes) and the arrest has transitioned into the circulatory phase, a brief period of CPR lasting 90 seconds to 3 minutes may be performed prior to defibrillation.

Treatment recommendation:

In cases of witnessed arrest with rapid detection of ventricular fibrillation, defibrillation should be performed immediately. If the time of arrest and/or duration of ventricular fibrillation is unknown but suspected to be > 4 minutes, it is reasonable to perform a brief period of CPR prior to defibrillation.

8. ACKNOWLEDGEMENTS:

None

9. CITATION LIST:

Baker, P. W., Conway, J., Cotton, C., Ashby, D. T., Smyth, J., Woodman, R. J., et al. (2008). Defibrillation or cardiopulmonary resuscitation first for patients with out-of-hospital cardiac arrests found by paramedics to be in ventricular fibrillation? A randomised control trial. *Resuscitation*, *79*(3), 424-31.

- Human RCT consisting of 202 patients
- Those in ventricular fibrillation with an ambulance response time of > 5 minutes
- Compared immediate defibrillation to 3 minutes of CPR prior to defibrillation
- Primary outcome was survival to hospital discharge

- Secondary outcomes were neurological status at discharge, ROSC
- No difference between groups in survival to hospital discharge, or ROSC
- Conclusion was that there is no evidence to support the use of 3 minutes of CPR prior to first defibrillation

Berg, R. (2002). Precountershock cardiopulmonary resuscitation improves ventricular fibrillation median frequency and myocardial readiness for successful defibrillation from prolonged ventricular fibrillation: A randomized, controlled swine study. *Annals of Emergency Medicine*, *40*(6), 563-570.

- Swine randomized laboratory study involving 32 pigs
- All had 10 minutes of untreated ventricular fibrillation
- Groups either received immediate countershock (Group 1), CPR for 3 minutes followed by countershock (Group 2), or CPR for 3 minutes + epinephrine followed by countershock (Group 3)
- All countershocks were stacked
- Primary endpoint was ROSC
- ROSC was 0/10 for Group 1, 5/10 for Group 2, and 6/12 for Group 3
- Cardiac output posr-resuscitation was worse in Group 1, compare to Groups 2 & 3
- Conclusion was that epi did not provide much of a benefit, but precountershock CPR did provide substantial physiologic benefit

Berg, R. a, Hilwig, R. W., Ewy, G. a, & Kern, K. B. (2004). Precountershock cardiopulmonary resuscitation improves initial response to defibrillation from prolonged ventricular fibrillation: A randomized, controlled swine study*. *Critical Care Medicine*, *32*(6), 1352-1357.

- Swine randomized laboratory study involving 30 pigs
- All had 8 minutes of untreated ventricular fibrillation
- Groups either received immediate countershock, or CPR for 90 seconds prior to countershock
- All countershocks were stacked
- Endpoint were ROSC, 24 hours survival, neurologic outcome at 24 hours
- Conclusion was that higher ROSC if CPR provided first, no difference in ultimate outcomes between the two groups (24 hours survival or neurologic outcome at 24 hours)

Bradley, S. M., Gabriel, E. E., Aufderheide, T. P., Barnes, R., Christenson, J., Davis, D. P., et al. (2010). Survival increases with CPR by Emergency Medical Services before defibrillation of out-of-hospital ventricular fibrillation or ventricular tachycardia: observations from the Resuscitation Outcomes Consortium. *Resuscitation*, *81*(2), 155-62.

- Prospective observational study involving 1638 human patients in ventricular fibrillation
- Duration of EMS CPR prior to first shock was divided into < 45 seconds, 46-195 seconds, and > 195 seconds
- Endpoint was survival to hospital discharge
- Performing 46-195 seconds of CPR was weakly associated with improved survival compared to < 45 seconds
- The benefit of performing CPR before defibrillation was reduced when the duration of CPR exceeded 195 seconds
- The evidence for increased survival when performing 46-195 seconds of CPR was greatest amongst patients when time to EMS arrival was > 5 minutes

Cobb, L. a, Fahrenbruch, C. E., Walsh, T. R., Copass, M. K., Olsufka, M., Breskin, M., et al. (1999). Influence of cardiopulmonary resuscitation prior to defibrillation in patients with out-of-hospital ventricular fibrillation. *JAMA : the journal of the American Medical Association*, *281*(13), 1182-8.

- Prospective observational study involving 478 human patients in ventricular fibrillation
- 90 seconds of CPR was performed in all patients prior to stacked countershock
- Historical controls used to compare this group to those that had immediate defibrillation
- Patients in the current study were divided into early (< 4 minutes) and late (> 4 minutes) response intervals
- Endpoints were survival and neurologic status at hospital discharge
- Conclusion was that in patients with later response time (> 4 minutes), 90 seconds of CPR prior to defibrillation was associated with increased survival and a more favorable neurologic recovery

Indik, J. H., Hilwig, R. W., Zuercher, M., Kern, K. B., Berg, M. D., & Berg, R. a. (2009). Preshock cardiopulmonary resuscitation worsens outcome from circulatory phase ventricular fibrillation with acute coronary artery obstruction in swine. *Circulation. Arrhythmia and electrophysiology*, *2*(2), 179-84.

- Swine randomized laboratory study involving 26 pigs
- All had 8 minutes of untreated ventricular fibrillation
- Groups were then treated with up to 3 stacked defibrillation shocks, or 3 minutes of chest compression before shock
- Primary endpoint was 24-hour survival and favorable neurological status
- Outcome was more favorable in those where defibrillation was performed first without preceding chest compressions

Jacobs, I. G., Finn, J. C., Oxer, H. F., & Jelinek, G. A. (2005). CPR before defibrillation in out-of-hospital cardiac arrest : A randomized trial. *Emergency Medicine*, 39-45.

- Human RCT consisting of 256 patients
- Patients received either 90 seconds of CPR prior to defibrillation, or immediate defibrillation
- Primary endpoint was survival to hospital discharge
- Secondary endpoints were ROSC and 1 year survival
- No difference between groups in any of the endpoints
- Conclusion was that 90 seconds of CPR prior to defibrillation does not improve overall survival

Jost, D., Degrange, H., Verret, C., Hersan, O., Banville, I. L., Chapman, F. W., et al. (2010). DEFI 2005: a randomized controlled trial of the effect of automated external defibrillator cardiopulmonary resuscitation protocol on outcome from out-of-hospital cardiac arrest. *Circulation*, *121*(14), 1614-22.

- Human RCT consisting of 845 patients
- Compared Group 1 (based on 2000 CPR guidelines- sequence of up to 3 stacked countershocks) and Group 2 (based on 2005 CPR guidelines- 1 minute of CPR before the first countershock, shorter CPR interruptions before and after each shock, and no stacked shocks)
- Primary endpoint was survival to hospital discharge
- This study did not find a significant difference between groups

Kellum, M. J., Kennedy, K. W., & Ewy, G. a. (2006). Cardiocerebral resuscitation improves survival of patients with out-of-hospital cardiac arrest. *The American journal of medicine*, *119*(4), 335-40.

- Prospective, observation human study of 33 patients
- Evaluated newer guidelines established in 2004, including minimizing interruption of chest compressions, 200 uninterrupted chest compressions prior to defibrillation, single rather than stacked shocks, and elimination of post shock rhythm and pulse checks
- Historical controls were used for comparison
- There was improved survival and improved neurologic function
- The use of precountershock CPR was not separately evaluated for its effect on outcome

Kolarova, J., Ayoub, I. M., Yi, Z., & Gazmuri, R. J. (2003). Optimal timing for electrical defibrillation after prolonged untreated ventricular fibrillation. *Critical care medicine*, *31*(7), 2022-8.

- Murine randomized laboratory study involving 70 rats
- Ventricular fibrillation was induced for 10 minutes
- Rats were then randomized to receive immediate countershock or 2, 4, 0r 6 minutes of CPR prior to countershock, shocks could be stacked
- Pertinent endpoint included ROSC
- Conclusion was that improved outcome after prolonged ventricular fibrillation may result from strategies that provide chest compression before attempting defibrillation
- This study also found that 6 minutes was the minimum amount of time that should be spent on chest compressions before attempting defibrillation

Meier, P., Baker, P., Jost, D., Jacobs, I., Henzi, B., Knapp, G., et al. (2010). Chest compressions before defibrillation for out-of-hospital cardiac arrest: a meta-analysis of randomized controlled clinical trials. *BMC medicine*, *8*, 52.

- Meta-analysis of four human RCTs enrolling 1503 patients
- Found no difference between chest compressions-first or defibrillation-first in regard to ROSC, survival to hospital discharge, or favorable neurologic outcome
- For 1-year survival or in cases of prolonged fibrillation, chest compressions first might possibly be more favorable
- Conclusion was that current evidence does not support chest compressions prior to defibrillation, both approaches seem to be equivalent

Menegazzi, J. (2003). Immediate defibrillation versus interventions first in a swine model of prolonged ventricular fibrillation. *Resuscitation*, *59*(2), 261-270.

- Swine randomized laboratory study involving 60 pigs
- Ventricular fibrillation was induced for 8, 11, or 14 minutes
- Additionally, groups received combinations of immediate countershock, CPR for 3 minutes prior to countershock, or CPR for 3 minutes + epi (0.1mg/kg) prior to countershock
- All countershocks would be stacked up to 3 times
- The group with the shortest amount of time in ventricular fibrillation (8 minutes) that then had 3 minutes CPR + epi had the highest rate of first-shock success and ROSC

Niemann, J. T., Cairns, C. B., Sharma, J., & Lewis, R. J. (1992). Treatment of prolonged ventricular fibrillation. Immediate countershock versus high-dose epinephrine and CPR preceding countershock. *Circulation*, *85*(1), 281-7.

- Canine randomized laboratory study involving 28 dogs
- 7.5 minutes of ventricular fibrillation prior to any treatment
- Group 1 was immediate countershock, Group 2 was CPR for 5 minutes + epinephrine (0.08 mg/kg) before countershock
- Usually used 1-2 successive countershocks
- Endpoint was a spontaneous perfusing rhythm
- 3/14 (group 1) versus 9/14 (group 2) had a perfusing rhythm restored
- Recommend a brief period of CPR prior to countershock in prolonged ventricular fibrillation

Niemann, J. T., Cruz, B., Garner, D., & Lewis, R. J. (2000). Immediate countershock versus cardiopulmonary resuscitation before countershock in a 5-minute swine model of ventricular fibrillation arrest. *Annals of emergency medicine*, *36*(6), 543-6.

- Swine laboratory study involving 11 pigs
- Observational study with historical controls (20 pigs)
- Ventricular fibrillation was induced for 5 minutes
- Pigs received either immediate countershock (historical controls), or CPR for 90 seconds preceding countershock
- Countershock could be up to 3 stacked shocks
- Endpoints were first shock success rate, the number of shocks required to terminate VF, and the cardiac resuscitation rate
- The conclusion was that providing CPR before countershock did not improve any of the outcome parameters, and in fact significantly lowered the cardiac resuscitation rate

Rittenberger, J. C., Suffoletto, B., Salcido, D., Logue, E., & Menegazzi, J. J. (2008). Increasing CPR duration prior to first defibrillation does not improve return of spontaneous circulation or survival in a swine model of prolonged ventricular fibrillation. *Resuscitation*, *79*(1), 155-60.

- Swine randomized laboratory study involving 45 pigs
- Ventricular fibrillation was induced for either 5 or 8 minutes
- All pigs CPR prior to defibrillation, duration of CPR was either 90, 180, or 300 seconds
- There was no immediate countershock group
- Endpoints were ROSC and survival (sustained ROSC for 20 minutes)
- There was no difference in ROSC or survival between groups, regardless of duration of fibrillation or duration of CPR. Authors did not recommend 300 seconds of CPR unless a defibrillator was unavailable

Simpson, P. M., Goodger, M. S., & Bendall, J. C. (2010). Delayed versus immediate defibrillation for out-of-hospital cardiac arrest due to ventricular fibrillation: A systematic review and meta-analysis of randomised controlled trials. *Resuscitation*, *81*(8), 925-31.

- Meta-analysis of three human RCTs enrolling 658 patients

- Found no benefit from providing CPR prior to defibrillation compared to immediate defibrillation for survival or hospital discharge. Either strategy is acceptable, and duration of defibrillation until intervention did not seem to matter

Skogvoll, E., & Nordseth, T. (2008). The early minutes of in-hospital cardiac arrest: shock or CPR? A population based prospective study. *Scandinavian journal of trauma, resuscitation and emergency medicine*, *16*, 11.

- Prospective, observational study involving 221 patients with cardiac arrest, 90 of which had VF/VT
- For those with ventricular fibrillation, authors compared immediate defibrillation with CPR
- Outcomes were ROSC and survival to discharge
- There was a clear association between early defibrillation and survival to discharge, indicating that defibrillation should have priority in the first 3-4 minutes of VF/VT. After this period, CPR in conjunction with defibrillation improved survival

Spearpoint, K. G., McLean, C. P., & Zideman, D. a. (2000). Early defibrillation and the chain of survival in "in-hospital" adult cardiac arrest; minutes count. *Resuscitation*, *44*(3), 165-9.

- Prospective, observational study involving 102 human patients
- Groups were either delayed defibrillation, rapid defibrillation, or rapid defibrillation with ventilation &/or chest compression
- Delayed defibrillation was defined as > 2 minutes before intervention, nothing was performed during this time
- Rapid defibrillation was defined as > 2 minutes, and then groups were compared to determine if concurrent CPR made a difference in hospital discharge (those with rapid defibrillation alone were more likely to be discharged)
- Conclusion of this study was that rapid defibrillation prior to any other resuscitation intervention is associated with increased survival
- This study did not directly compare compressions-first versus counter-shock first, but it did highlight the importance of early defibrillation

Vilke, G. M., Chan, T. C., Dunford, J. V., Metz, M., Ochs, G., Smith, A., et al. (2005). The three-phase model of cardiac arrest as applied to ventricular fibrillation in a large, urban emergency medical services system. *Resuscitation*, *64*(3), 341-6.

- Prospective, observational study involving 272 human patients
- Patients were stratified by time since collapse (< 4, 4-10, >10 minutes and unknown)
- Outcome parameters were survival and neurological outcome
- Survival was highest amongst patients with < 4 minutes of collapse
- In patients with > 4 minutes of collapse, survival was significantly higher with the performance of bystander CPR prior to defibrillation. This effect was not observed in patients with < 4 minutes of collapse

Wang, Y.-L., Zhong, J.-Q., Tao, W., Hou, X.-M., Meng, X.-L., & Zhang, Y. (2009). Initial defibrillation versus initial chest compression in a 4-minute ventricular fibrillation canine model of cardiac arrest. Critical care medicine, 37(7), 2250-2

- Canine randomized laboratory study involving 24 dogs

- 4 minutes of ventricular fibrillation prior to any treatment
- Group 1 was immediate countershock, Group 2 was 200 chest compressions before countershock
- Only a single countershock was used
- Endpoints were ROSC and 24 hour survival
- 12/12 (group 1) versus 11/12 (group 2) had ROSC
- 10/12 (group 1) versus 9/12 (group 2) had 24 hour survival
- Conclusion was the order of initial chest compressions or initial defibrillation does not affect cardiac resuscitation

Wik L., Hansen T.B., Fylling F., et al. (2003). Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation. A randomized trial. *J Am Med Assoc*, *289*(11), 1389-1395.

- Human RCT enrolling 200 patients
- Patients received either immediate defibrillation or CPR for 3 minutes prior to defibrillation
- Primary endpoint was survival to hospital discharge
- Secondary endpoints were ROSC, 1-year survival, and neurological outcome
- Conclusion was that CPR prior to defibrillation offered no advantage in improving outcomes when ambulance time is < 5 minutes, but if ambulance response will be > 5 minutes, providing CPR prior to defibrillation resulted in improved outcomes

Yakaitis, Donald W., Ewy, Gordon A, Otto Charles W., et al. (1980). Influence of time and therapy on ventricular defibrillation in dogs. *Critical care medicine*, *8*(3), 157-163.

- Canine laboratory study involving 90 dogs
- Ventricular fibrillation induced for 1, 3, 5, or 9 minutes prior to any treatment
- Group 1 was CPR, Group 2 was CPR + epinephrine (1 mg IV), Group 3 was immediate countershock only
- Successive countershocks were used
- Endpoint was ROSC
- Conclusions were that energy requirement for conversion was directly proportional to the duration of fibrillation, and that using immediate countershock was effective for episodes of fibrillation limited to approximately 3 minutes