Apoptotic activity is increased in brain cortex infarct after hypothermic circulatory arrest in a porcine model.

https://arctichealth.org/en/permalink/ahliterature57253

Author: A. Mennander
P. Pääkkö
J. Hirvonen
V. Anttila
J. Rimpiläinen
M. Pokela
V. Vainionpää
K. Kiviluoma
P. Romsi
F. Biancari
T. Juvonen

Author Affiliation: Department of Surgery, University of Oulu, Oulu, Finland.


Date: Aug-2002

Language: English

Publication Type: Article

Keywords: Animals
Apoptosis
Brain Infarction - complications - pathology
Brain Ischemia - complications - pathology
Cold
Disease Models, Animal
Hypothermia - complications
In Situ Nick-End Labeling
Shock - complications
Statistics, nonparametric
Survival Rate
Swine
Time Factors
OBJECTIVE: It has been shown that apoptosis contributes to neuronal cell death after ischemia, and we evaluated the degree of apoptotic activity occurring in brain cortex of pigs after hypothermic circulatory arrest (HCA).

DESIGN: Thirty-one pigs underwent 75 min of HCA at 20 degrees C. Histological examination of the brain was performed, and slides of brain cortex were evaluated for apoptotic activity by the TUNEL method. RESULTS: Ten animals died during the first postoperative day and 21 survived until the seventh postoperative day. Brain cortex infarcts were found in animals that survived 7 days and these were included in this study. The median histopathological score among animals that died on the first postoperative day was 3.0 (range, 2-4), whereas it was 4.0 (range, 2-4) among survivors (p = 0.019). The apoptotic index was particularly high in the area of the infarct, whereas only a few TUNEL-stained cells were observed in noninfarcted areas. The apoptotic index was nil in all pigs that died in the first postoperative period, whereas it was 2.0 (range, 0-6) among the animals that survived until the seventh postoperative day (p

Cold retrograde cerebral perfusion improves cerebral protection during moderate hypothermic circulatory arrest: A long-term study in a porcine model.

https://arctichealth.org/en/permalink/ahliterature57276

Author: V. Anttila
K. Kiviluoma
M. Pokela
J. Rimpiläinen
M. Mäkiranta
V. Jäntti
J. Hirvonen
T. Juvonen

Author Affiliation: Department of Surgery Oulu University Hospital, Oulu, Finland.


Date: Nov-1999

Language: English

Publication Type: Article
Keywords: Animals, Behavior, Animal, Brain - blood supply, Cerebrovascular Circulation - physiology, Cold, Electroencephalography, Female, Heart Arrest, Induced, Hypothermia, Induced, Monitoring, Intraoperative, Perfusion - methods, Random Allocation, Reperfusion Injury - prevention & control, Research Support, Non-U.S. Gov't, Rewarming, Swine

Abstract: BACKGROUND: Deep hypothermic circulatory arrest is an effective method of cerebral protection, but it is associated with long cardiopulmonary bypass times and coagulation disturbances. Previous studies have shown that retrograde cerebral perfusion can improve neurologic outcomes after prolonged hypothermic circulatory arrest. We tested the hypothesis that deep hypothermic retrograde cerebral perfusion could improve cerebral outcome during moderate hypothermic circulatory arrest. METHODS: Twelve pigs (23-29 kg) were randomly assigned to undergo either retrograde cerebral perfusion (15 degrees C) at 25 degrees C or hypothermic circulatory arrest with the head packed in ice at 25 degrees C for 45 minutes. Flow was adjusted to maintain superior vena cava pressure at 20 mm Hg throughout retrograde cerebral perfusion. Hemodynamic, electrophysiologic, metabolic, and temperature monitoring were carried out until 4 hours after the start of rewarming. Daily behavioral assessment was performed until elective death on day 7. A postmortem histologic analysis of the brain was carried out on all animals. RESULTS: In the retrograde cerebral perfusion group, 5 (83%) of 6 animals survived 7 days compared with 2 (33%) of 6 in the hypothermic circulatory arrest group. Complete behavioral recovery was seen in 4 (67%) animals after retrograde cerebral perfusion but only in 1 (17%) animal after hypothermic circulatory arrest. Postoperative levels of serum lactate were higher, and blood pH was lower in the hypothermic circulatory arrest group. There were no significant hemodynamic differences between the study groups. CONCLUSIONS: Cold hypothermic retrograde cerebral perfusion during moderate hypothermic circulatory arrest seems to improve neurologic outcome compared with moderate hypothermic circulatory arrest with the head packed in ice.

PubMed ID: 10534701 View in PubMed

Immediate and 5-year outcome after coronary artery bypass surgery in very high risk patients (additive EuroSCORE = 10).
https://arctichealth.org/en/permalink/ahliterature135627
Abstract: We have evaluated the outcome after coronary artery bypass surgery in very high risk patients (additive EuroSCORE = 10). The impact of beating heart coronary artery bypass surgery (BHCAB) on their outcome has been evaluated.

Retrospective study including 160 consecutive patients with additive EuroSCORE = 10. The overall survival rates at 30-day, 1-year, 3-year and 5-year were 83.8%, 76.0%, 72.4% and 66.8%, respectively. Baseline cardiac index (O.R. 0.20, 95%C.I. 0.08-0.53), preoperative inotropic support (O.R. 4.55, 95%C.I. 1.41-14.73) and preoperative resuscitation (O.R. 3.937, 95%C.I. 1.02-15.26) were independent predictors of 30-day mortality. Baseline cardiac index (R.R. 0.48, 95%C.I. 0.28-0.85), left ventricular ejection fraction (P=0.032), preoperative use of intraaortic balloon pump (R.R. 3.22, 95% C.I. 1.50-6.93), preoperative tracheal intubation (R.R. 3.44, 95%C.I. 1.37-8.68) and creatinine (R.R. 1.004, 95%C.I. 1.00-1.01) were independent predictors of late death. OPCAB/BHCAB was associated with somewhat lower 30-day mortality rate (16.2% vs. 18.0%, P=0.73), stroke (2.0% vs. 4.9%, P=0.37), red blood cells transfusion (3.4 vs. 5.4 units, P=0.004) and combined adverse outcome (43.4% vs. 50.8%, P=0.42). OPCAB/BHCAB surgeons compared with surgeons with a prevalent conventional approach achieved slightly better the 30-day mortality rate (16.7% vs. 27.9%, P=0.15) and stroke rate (2.8% vs. 4.7%, P=0.60) and 5-year survival rate (65.3% vs. 57.4%, P=0.35).

Despite their poor immediate postoperative outcome, 5-year survival of these high risk patients is satisfactory and supports efforts in the treatment of this very high risk population. A more confident approach toward OPCAB/BHCAB is also suggested in these patients.

PubMed ID: 21460778 View in PubMed
Intermittent retrograde cerebral perfusion during prolonged period of hypothermic circulatory arrest: a study in a chronic porcine model.

https://arctichealth.org/en/permalink/ahliterature57270

Author: V. Anttila
M. Pokela
K. Kiviluoma
J. Rimpiläinen
V. Vainionpää
J. Hirvonen
T. Juvonen

Author Affiliation: Department of Surgery, University of Oulu, Finland.


Date: 2000

Language: English

Publication Type: Article

Keywords: Animals
Brain - blood supply
Heart Arrest, Induced
Hypothermia, Induced
Random Allocation
Reperfusion - methods
Research Support, Non-U.S. Gov't
Swine
Time Factors

Abstract: Previous studies have shown that although retrograde cerebral perfusion (RCP) improves cerebral outcome during hypothermic circulatory arrest (HCA), RCP exposes the brain to subsequent edema. In this study, we have compared intermittent RCP (I-RCP) with continuous RCP (C-RCP) and HCA alone to determine whether the rate of fluid sequestration can be decreased without losing the beneficial effects of RCP. Eighteen pigs were randomly assigned to undergo 75 min of I-RCP, C-RCP or HCA at 20 degrees C. Hemodynamic and metabolic measurements were carried out for up to 20 h. Behavioral assessments were examined until day 7, when histopathologic analysis of the brain was performed. The median amount of fluid sequestered was 145 ml after C-RCP and -50 ml after I-RCP (p = 0.04). The mean brain weight of the animals that died within the first postoperative day was significantly higher than that in electively sacrificed animals in the C-RCP group (p = 0.04). These data suggest that if RCP is implemented intermittently, the rate of cerebral edema can be decreased, without compromising the benefits of this strategy.

PubMed ID: 10872695 View in PubMed

Is maintained cranial hypothermia the only factor leading to improved outcome after retrograde cerebral perfusion? An experimental study with a chronic porcine model.

https://arctichealth.org/en/permalink/ahliterature57271
BACKGROUND: Previous studies have shown that retrograde cerebral perfusion can improve neurologic outcome after prolonged hypothermic circulatory arrest. Here we have compared two temperatures of retrograde cerebral perfusion (15 degrees C and 25 degrees C) with hypothermic circulatory arrest at systemic hypothermia of 25 degrees C to clarify whether the possible benefit of retrograde cerebral perfusion may only be due to improved cooling effect. METHODS: Eighteen pigs (23-27 kg) were randomly assigned to undergo 15 degrees C retrograde cerebral perfusion at systemic hypothermia of 25 degrees C, 25 degrees C retrograde cerebral perfusion at 25 degrees C systemic hypothermia, or hypothermic circulatory arrest at 25 degrees C for 40 minutes. Flow was adjusted to maintain superior vena cava pressure at 20 mm Hg during retrograde cerebral perfusion. Hemodynamic, electrophysiologic, metabolic, and temperature monitoring were performed until 4 hours after the start of rewarming. Daily behavioral assessment was done until death or until the animals were killed on day 7. Histopathologic analysis of the brain was carried out on all animals. RESULTS: Epidural temperatures were lower in the 15 degrees C retrograde cerebral perfusion group during the intervention (P
porcine model.

https://arctichealth.org/en/permalink/ahliterature57269

Author: V. Anttila
J. Rimpiläinen
M. Pokela
K. Kiviluoma
M. Mäkiranta
V. Jäntti
V. Vainionpää
J. Hirvonen
T. Juvonen

Author Affiliation: Departments of Surgery and Anesthesiology and the Laboratory of Clinical Neurophysiology, Oulu University Hospital, Oulu, Finland.


Date: Aug-2000

Language: English

Publication Type: Article

Keywords: Analysis of Variance
Animals
Behavior, Animal - drug effects - physiology
Brain Ischemia - pathology - physiopathology - prevention & control
Calcium Channel Blockers - pharmacology
Cardiopulmonary Bypass
Disease Models, Animal
Electroencephalography
Female
Heart Arrest, Induced
Hemodynamic Processes
Hypothermia, Induced
Nerve Growth Factors
Neuroprotective Agents - pharmacology
Research Support, Non-U.S. Gov't
S100 Proteins - blood
Statistics, nonparametric
Swine
Triazines - pharmacology
Abstract: BACKGROUND: Glutamate excitotoxicity has an important role in the development of brain injury after prolonged hypothermic circulatory arrest. The goal of the present studies was to determine the potential efficacy of lamotrigine, an Na(+) channel blocker, to mitigate cerebral injury after hypothermic circulatory arrest. METHODS: Sixteen pigs (21-27 kg) were randomly assigned to receive lamotrigine (20 mg/kg) or placebo in a blinded fashion before a 75-minute period of hypothermic circulatory arrest (20 degrees C). Hemodynamic, electroencephalographic, and metabolic monitoring were carried out. S-100beta protein was determined up to the first postoperative morning. Daily behavioral assessment was performed until the animal died or was put to death on day 7. Histologic analysis of the brain was carried out in all animals. RESULTS: Complete behavioral recovery was seen in 5 of 8 (63%) animals after lamotrigine administration, compared with 1 of 8 (13%) in the placebo group (P = .02). Among the animals that survived for 7 days, the median behavioral score was higher in the lamotrigine group (8 vs 7, P = .02). The medians of recovered electroencephalographic bursts in the lamotrigine group were higher than those in the placebo group 4 1/2 hours after the start of rewarming (P = .01). The median S-100beta level was lower in the lamotrigine group (0.01 microg/L) than in placebo controls (0.1 microg/L) 20 hours after the start of rewarming (P = .01). The median of total histopathologic score was 5.5 in the lamotrigine group and 7.5 in the placebo group (P = .06). CONCLUSIONS: The present data suggest that lamotrigine improves neurologic outcome after a prolonged period of hypothermic circulatory arrest.

Notes: Comment In: J Thorac Cardiovasc Surg. 2001 Mar;121(3):597-8;11241102

PubMed ID: 10917938 View in PubMed

Leukocyte filtration improves brain protection after a prolonged period of hypothermic circulatory arrest: A study in a chronic porcine model.

https://arctichealth.org/en/permalink/ahliterature57268

Author: J. Rimpiläinen
M. Pokela
K. Kiviluoma
V. Anttila
V. Vainionpää
J. Hirvonen
P. Ohtonen
A. Mennander
E. Remes
T. Juvonen

Author Affiliation: Departments of Surgery and Anaesthesiology, the Laboratory of Clinical Neurophysiology, Oulu University Hospital, University of Oulu, Oulu, Finland.


Date: Dec-2000

Language: English

Publication Type: Article
Abstract: BACKGROUND: Ischemic cerebral injury follows a well-attested sequence of events, including 3 phases: depolarization, biochemical cascade, and reperfusion injury. Leukocyte infiltration and cytokine-mediated inflammatory reaction are known to play a pivotal role in the reperfusion phase. These events exacerbate the brain injury by impairing the normal microvascular perfusion and through the release of cytotoxic enzymes. The aim of the present study was to determine whether a leukocyte-depleting filter (LeukoGuard LG6, Pall Biomedical, Portsmouth, United Kingdom) could improve the cerebral outcome after hypothermic circulatory arrest.

METHODS: Twenty pigs (23-30 kg) were randomly assigned to undergo cardiopulmonary bypass with or without a leukocyte-depleting filter before and after a 75-minute period of hypothermic circulatory arrest at 20 degrees C. Electroencephalographic recovery, S-100beta protein levels, and cytokine levels (interleukin 1beta, interleukin 8, and tumor necrosis factor alpha) were recorded up to the first postoperative day. Postoperatively, all animals were evaluated daily until death or until electively being put to death on day 7 by using a quantitative behavioral score. A postmortem histologic analysis of the brain was carried out on all animals. RESULTS: The rate of mortality was 2 of 10 in the leukocyte-depletion group and 5 of 10 in control animals. The risk for early death in control animals was 2.5 (95% confidence interval, 0.63-10.0) times higher than that of the leukocyte-depleted animals. The median behavioral score at day 7 was higher in the leukocyte-depletion group (8.5 vs 3.5; P = .04). The median of total histopathologic score was 8.5 in the leukocyte-depletion group and 15.5 in the control group (P = .005). CONCLUSION: A leukocyte-depleting filter improves brain protection after a prolonged period of hypothermic circulatory arrest.

PubMed ID: 11088037 View in PubMed

The N-methyl-D-aspartate antagonist memantine has no neuroprotective effect during hypothermic
BACKGROUND: Glutamate excitotoxicity has an important role in the development of brain injury after prolonged hypothermic circulatory arrest. The goal of the present study was to determine the potential efficacy of memantine, an N-methyl-D-aspartate receptor antagonist, to mitigate cerebral injury after hypothermic circulatory arrest. METHODS: Twenty pigs (23-33 kg) were randomly assigned to receive memantine (5 mg/kg) or placebo in a blinded fashion before a 75-minute period of hypothermic circulatory arrest at 20 degrees C. Hemodynamic, electroencephalographic, and metabolic monitoring were carried out. The intracerebral concentrations of glucose, lactate, glutamate, and glycerol were measured by means of enzymatic methods on a microdialysis analyzer. Daily behavioral assessment was performed until the animals died or were put to death on day 7. Histologic analysis of the brain was carried out in all animals. RESULTS: In the memantine group, 5 of 10 animals survived 7 days compared with 9 of 10 in the placebo group. The median behavioral score at day 7 was 3.5 in the memantine group and 7.5 in the placebo group (P >.2). Among the surviving animals, medians were 9.0 and 8.0 on day 7 (P >.2), respectively. The medians of recovered electroencephalographic bursts were equal in both groups. The median of total histopathologic score was 16 in the memantine group and 14 in the placebo group (P >.2). There was a negative correlation between glutamate levels and electroencephalographic burst recovery (tau = -0.377, P =.043). A positive correlation was found between the highest individual glutamate value and histopathologic score (tau = 0.336, P =.045). CONCLUSIONS: The present study demonstrates that memantine has no neuroprotective effect after hypothermic circulatory arrest in the pig. In addition, we have shown the accuracy of cerebral glutamate measurements to predict histopathologic injury after hypothermic ischemia.
Abstract: OBJECTIVE: To evaluate whether and which of the cerebral microdialysis parameters are predictive of postoperative outcome after an experimental 75-min period of hypothermic circulatory arrest (HCA) in a chronic porcine model. DESIGN: Seventy-four juvenile female pigs underwent a 75-min period of HCA at 20 degrees C. A microdialysis catheter was placed into the cortex gray matter and brain extracellular concentrations of glucose, lactate, glycerol and glutamate were measured throughout the experiment by enzymatic methods using a microdialysis analyzer. Surviving animals were sacrificed on the 7th postoperative day and histopathological examination of the brain was performed. RESULTS: Brain glucose concentrations were higher in animals that survived (p = 0.017), especially from the 90-min until the 7-h interval after the start of rewarming. The blood venous concentrations of glucose were also higher among survivors, and correlated significantly with the brain glucose levels at 2-h and 4-h intervals after the start of rewarming. Higher concentrations of brain lactate, glycerol and glutamate were observed throughout the study among animals that died postoperatively. Brain glutamate and glycerol concentrations were significantly, negatively correlated with brain glucose concentrations. The lactate/glucose ratio was significantly lower among survivors during the postoperative period (p=0.014). Furthermore, brain glucose concentrations were higher and brain glycerol concentrations lower among the animals that did not develop brain infarction, but such differences did not reach statistical significance. CONCLUSION: Cerebral microdialysis is a useful tool for cerebral monitoring during experimental HCA. Low brain glucose concentrations and high brain lactate/glucose ratios after HCA are strong predictors of postoperative death. Brain glucose concentrations are negatively correlated with brain glycerol and glutamate concentrations.
OBJECTIVE: Serum S-100beta protein is suggested to be a neurobiochemical marker of brain injury after cardiac and aortic arch surgery. The aim of the present study was to investigate the predictive value of S-100beta protein with respect to histopathological analysis of the brain after a prolonged period of hypothermic circulatory arrest (HCA). METHODS: Eighteen pigs (21 to 31 kg) underwent a 75 min period of HCA at 20 degrees C. Serum concentrations of S-100beta were assayed in mixed venous blood before and 2, 4, 7 and 20 h after HCA. A semiquantitative post-mortem histopathological analysis scoring all main regions of the brain was carried out in every animal. RESULTS: All animals were stable during and after cardiopulmonary bypass (CPB) and survived at least to the first postoperative day. Ten of the 18 animals survived 7 days after surgery and were electively sacrificed. Animals with severe histopathological injury showed higher serum S-100beta protein levels at every time point after HCA. The strongest correlation between the total histopathologic score and serum S-100beta levels was found at 7 h after HCA (tau = 0.422 and p = 0.023). CONCLUSION: Serum S-100beta protein levels correlate with histopathological injury after a prolonged period of HCA in pigs. This finding supports the results of previous studies suggesting the potential accuracy of S-100beta in the prediction of brain injury after cardiac surgery.