Clinical question.

“For infants and children with single ventricle, s/p stage I repair, who require resuscitation from cardiac arrest or pre-arrest states (prehospital [OHCA] or in-hospital [IHCA]) (P), does any specific modification to standard practice (I) compared with standard resuscitation practice (C) improve outcome (e.g. ROSC, survival to discharge, survival with good neurologic outcome)(O)?”

Is this question addressing an intervention/therapy, prognosis or diagnosis? Intervention

State if this is a proposed new topic or revision of existing worksheet: New topic

Conflict of interest specific to this question

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet?

Dr. Hoffman has authored or co-authored several of the papers reviewed as evidence.

Search strategy (including electronic databases searched).

PubMed: ("cardiopulmonary resuscitation"[Mesh] OR "Heart Arrest"[Mesh]) AND ("Heart Defects, Congenital"[Mesh] OR “hypoplastic left heart syndrome” OR “single ventricle”) AND ("neonate" OR "infant" OR "child" OR "pediatric") 477 hits

PubMed: ("venous saturation" OR "cerebral oxygenation") AND ("Heart Defects, Congenital"[Mesh] OR “hypoplastic left heart syndrome” OR “single ventricle”) AND ("neonate" or "infant") 59 hits

EMBASE: [cardiopulmonary resuscitation.mp OR exp. *resuscitation/ OR Heart arrest.mp OR exp. *heart arrest/ ] AND [single ventricle.mp OR exp *heart single ventricle/ ] 45 hits

Cochrane database for systematic reviews or clinical trials 1 hit

Central register of controlled trials 1 hit

Also, “see related articles” in PubMed, as well as bibliographies of review articles on CPR in children

• State inclusion and exclusion criteria

Exclusion criteria; studies involving subsequent surgical repairs (Stages 2 and 3), adults, non-single ventricle repairs, case reports, review articles, editorials

• Number of articles/sources meeting criteria for further review:

For CPR

Forty two studies met the criteria for further review. None were LOE 1-3.

Of these, 3 detailed causes of death only (and were thus not evaluated, but used to refine the search), 1 was a case series detailing outcomes from CPR in univentricular and biventricular patients (LOE 4), 1 RCT examining two surgical approaches for stage 1 repair (results not yet reported) was referenced for contemporaneous outcome data.

There were 5 were animal models (LOE 5) examining effects of shunt size, alveolar gas manipulation and inotropes; all in pre-arrest states.

Six studies examined extracorporeal cardiopulmonary resuscitation (LOE 4).

Twelve studies reported use of central venous oximetry or near infra red spectroscopy in near arrest states (LOE 4-5).

Of the remainder, 6 examined varying concentrations of FIO2 and CO2 in stable neonates with univentricular circulation in the perioperative period (LOE 4-5), 3 examined prophylactic use of afterload reduction with phenoxybenzamine (LOE 4-5), 2 with other agents (LOE 5) and one was a case series used for hypothesis generation (role of SVR in late collapse) (LOE 4).

Two studies reported the role of home monitoring to reduce inter-stage death (LOE 5)
# Summary of evidence

## Evidence Supporting Clinical Question

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### Level of evidence

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

## Evidence Neutral to Clinical question

|------|---|---|---------------------------------|----------------------------------------------------------------------------------|

### Level of evidence

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

## Evidence Opposing Clinical Question

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### Level of evidence

- **A** = Return of spontaneous circulation
- **C** = Survival to hospital discharge
- **E** = Other endpoint
- **B** = Survival of event
- **D** = Intact neurological survival
- *Italics* = Animal studies
REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

The high risk nature of this patient group is demonstrated by a recent multicenter randomized controlled trial of modified BT shunt vs. RV-PA conduit (Ohye, 2009), which found an early CPR rate of 17% (three times that of other cardiac surgical patients), an early ECMO rate of 10% and a one-year mortality of 29%. The variation in center-specific mortality exceeded the variation in mortality by shunt type; however at time of writing the final results are not yet in the public domain.

From uncontrolled case series (excluding use of extracorporeal CPR), there does not appear to be an appreciable difference between resuscitation outcomes for children with single ventricles post Norwood 1 repair and “standard” pediatric patients (Rhodes 1999). One series (Rhodes 1999) suggested that univentricular patients had a tendency to a higher incidence of non-VF/VT arrests (12/18 versus 8/16 for biventricular); however this did not reach significance (p = 0.32), and the rhythm type did not influence survival in the overall study population.

It is important to consider the causes of death post single ventricle repair with respect to resuscitative interventions that may potentially differ from those for the “standard” pediatric patient. Causes of death post Stage 1 repair for HLHS (Bartam 1997) include: impaired coronary perfusion (27%), excessive pulmonary blood flow (19%), obstruction of pulmonary blood flow (17%), neoaortic obstruction (14%), right ventricular failure (13%), hemorrhage (7%), infection (5%), AV-valve dysfunction (5%), arrhythmia/sudden death (5%), necrotizing enterocolitis (3%), obstructed pulmonary veins (2%), others (5%). From this study, a majority of causes were mechanical and related to the surgery itself (e.g. large shunts producing over circulation, with smaller shunts being more at risk of blockage). Of note, those related to coronary artery obstruction caused death in the early post-operative phase (median 0.25 days). However, changes in surgical technique reduced many of the mechanical complications in the latter part of the series, which has subsequently been born out by a lower post operative mortality in the last decade. Examples include: not opening the ascending aorta down to the aortic root, abandoning tubular augmentation of the neoaorta, use of smaller BT shunts, Sano procedure, etc. There appears to be a relatively constant attrition between stages 1 and 2 of the repair (approximately 10 - 15%); the majority of these are sudden and the cause unclear; although shunt blockage, ventricular failure and myocardial ischemia have all been implicated (Fenton 2003, Simsic 2005).

Given that the largest combined cause of death is mechanical (occlusion/obstruction of the coronaries, pulmonary shunt or neoaorta), it is unlikely that any resuscitative measures in this setting will be successful, except for rapid institution of extracorporeal cardiopulmonary support. If extracorporeal support is instituted in the setting of a cardiac arrest (E-CPR), survival to hospital discharge appears comparable to that for other cardiac surgical neonates receiving E-CPR (Alsoufi 2007, Chan 2008, Ravishankar 2006, Raymond 2009, Tajik 2008). There may be considerable intra-group variation however, dependent upon the etiology of the arrest. One series quoted survival rates of 100% (5/5) for E-CPR following BT shunt blockage, compared to 35% (6/17) for other causes (Ravishankar 2006). The incidence of central nervous system injury after E-CPR following single ventricle operations is 16%, comparable to that for other diagnoses (Barrett 2009).

This also raises the question about heparin administration during CPR for an arrest of unknown etiology (particularly if shunt blockage is suspected). There are no data in the setting of HLHS; however following general guidelines for significant vascular occlusion, it may be worth considering administering an intravenous bolus of unfractionated heparin (dose 100 U/kg if not concurrently receiving heparin, otherwise bolus dose 50 U/kg) (based on cardiac catheter recommendations from Monagle, 2008, section 1.19.2.)

Identifying a pre-arrest state poses a major challenge in this patient group, as routine hemodynamic variables may remain normal or near normal; in addition deterioration may be rapid. The superimposition of ischemic- and hypoxic-hypoxia mechanisms makes the entire period from birth through second stage palliation a potential pre-arrest state, with typical mortality in the 0.1-0.3% per day range. The individual components of low total cardiac output, and excessive or inadequate pulmonary blood flow cannot be differentiated based upon arterial blood pressure or saturation, and require measurement or approximation of systemic venous oxygenation by an SvO2 catheter or near infra red spectroscopy (NIRS); these variables exhibit the best predictive value for a variety of adverse clinical outcomes following initial staged palliation (Charpie 2001, Hoffman (2) 2005, Johnson 2009). However, none have been evaluated prospectively in a goal directed manner.

As up to 19% of deaths involve an element of excessive pulmonary blood flow, it is worth considering strategies that may manipulate the balance of pulmonary to systemic flow (Qp:Qs) in the pre-arrest state. The two major strategies to manipulate Qp/Qs are manipulation of alveolar gas concentrations and the use of systemic vasodilators, particularly
alpha-adrenergic blockade. No data directly address resuscitation from cardiac arrest. To date, the small body of evidence comes from animal models, corroborated by similar manipulations in stable univentricular patients.

Manipulation of the inspired concentration of both oxygen and carbon dioxide gave reproducible effects on Qp:Qs in two animal models (Reddy (2) 1996, Riordan (1) 1996). Of the two strategies, increasing inspired carbon dioxide concentration to 2.7-3.0% to achieve a PaCO2 of approximately 50 - 60 mmHg appears to produce more favorable effects than inspired hypoxia (17%) on global and cerebral oxygen delivery in mechanically ventilated pre-operative (Tabbutt 2001, Ramamoorthy 2002) and post-operative HLHS patients (Bradley (2) 2001). However the global benefit seems to arise predominantly from increased cerebral venous saturation at the expense of splanchnic venous desaturation (Li 2008). Raising the PaCO2 produces an increase in Qs (and hence DO2) secondary to a decrease in SVR, without a change in Qp (Li 2008). One study (Bradley (1) 2004) showed that the converse, namely neither hyperoxia nor hyperventilation (PaCO2 = 31 mmHg) produced an appreciable effect, in direct contrast to animal studies. It seems reasonable therefore, to conclude that short-term use of high FIO2 is unlikely to be harmful; however given the known adverse effects of hypocarbia on the cerebral circulation and Qp:Qs, hyperventilation should be avoided. In addition, the use of hypoxic gas mixtures should be considered only when systemic arterial and venous oxygen monitoring is continuously available.

However, all of the above studies manipulating alveolar gas concentrations were limited to short term use (10 - 30 minutes) only, and it is not known if tachyphylaxis ensues. Of note, in an animal model, the effect of both inspired oxygen and carbon dioxide on manipulation of Qp:Qs was completely lost when a large pulmonary BT shunt, defined as having a diameter in mm greater than 1.1 times body weight (in kg) was inserted (Kitaichi 2003). The type of pulmonary shunt may also be important. Use of a right ventricle to pulmonary artery conduit (Sano procedure) may increase likelihood of return of spontaneous circulation compared to a traditional modified BT shunt (Graham 2006). In this case series, the Sano was associated with a greater return of spontaneous circulation (8/12 versus 3/15 for a BT shunt, p = 0.02), this did not translate into better survival to hospital discharge (58% versus 20%, p = 0.1), but was likely limited by reduced power from the small study size. The two surgical approaches are currently under evaluation in a RCT.

Manipulation of Qp:Qs by lowering SVR pharmacologically with phenoxybenzamine has been evaluated in the early postoperative period. One retrospective cohort study (Tweddell 2002) showed improved survival to stage 2 repair. Another (Hoffman 2004) demonstrated an association between phenoxybenzamine and a higher SvO2, and an improved Qp:Qs compared to non-use when the arterial saturations were >80%. A third (De Oliveira 2004) showed a decreased risk of post-operative circulatory collapse, regardless of whether there was an operative technical issue with the surgical repair. All these studies involved prophylactic administration on cardiopulmonary bypass with a reduced incidence of postoperative instability, but none has examined acute administration to improve hemodynamics in a pre-arrest situation.

Use of epinephrine may also affect Qp:Qs. In one animal model (Reddy 1996 (1)), an arrest dose of epinephrine (5 mcg/kg), when given in a non-arrest state, produced a deleterious effect on Qp:Qs, by increasing systemic vascular resistance 856%, while at the same time reducing pulmonary vascular resistance by 18%, producing a net increase in Qp:Qs of 584%. Although this was not administered during a pre-arrest state, and no interventional human trial exists, pharmacologic control of SVR is a rational target based on theoretical models, interventional animal data, and observational human data..

There is a consistent mortality of approximately 10-15% between hospital discharge after stage 1 repair and subsequent stage 2 operation. The causes are ill defined, although shunt blockage is implicated in a percentage of these deaths. Early reports suggest a role for aggressive home monitoring programs in reducing inter-stage mortality (Ghanayem 2003; Furck 2009 (2)).

**Acknowledgements:**

Nil
Citation List


LOE 4, fair, neutral. Single centre experience with E-CPR. Hospital survival for patients with single ventricle physiology was 44%, compared to 27% for 2-ventricle physiology; however details of outcomes for post stage 1 patients are not given.


FOR REFERENCE ONLY. LOE 5, excellent animal model and study design. Supports deep hypothermia and defines CPB flow rates at various temperatures (using pH stat) to reduce cerebral injury post hypothermic low flow CPB. Supports NIRS to detect conditions associated with neurologic injury, but not included as therapy evaluated was type of cardiopulmonary bypass.


LOE 4, quality good, neutral. ELSO registry analysis of factors related to CNS insult during E-CPR. The overall incidence was 22%, and for single ventricle patients was 16%.


FOR REFERENCE ONLY. LOE 5, quality good. This case series documents autopsy-evaluated causes of death following stage 1 repair for HLHS. As such, it provides a basis for evaluation of therapies that may help with resuscitation. Of note, the majority of deaths was associated with technical issues resulting in obstruction to flow (occlusion obstruction of the coronaries, pulmonary shunt or neoaorta), thus it is unlikely that any resuscitative measures in this setting will be successful. However as up to 19% of deaths involve an element of excessive pulmonary blood flow, it is worth considering strategies that may manipulate the balance of pulmonary to systemic flow (Qp:Qs) in the pre-arrest state.


LOE 5, quality good, opposing. Randomized crossover trial of effects of inspired hyperoxia (FIO2=100%) and hypocarbia (PCO2 = 31 mmHg) post-op Norwood (n = 14). Endpoints involved hemodynamics, A-V difference and oxygen excess factor, NOT PRE-ARREST. Neither hyperoxia nor hyperventilation produced appreciable effects on blood pressure or A-V saturation difference (because arterial and venous saturations rose in tandem). Hyperoxia improved oxygen excess factor.


LOE 5, quality fair, supporting. Non-randomized crossover trial of inhaled CO2 with and without changes in minute ventilation post-op Norwood I (n = 17). Endpoints hemodynamics, SvO2 and A-V sat difference, NOT PRE-ARREST. No change in hemodynamics, but rise in CO2 produced favorable change in SvO2 and A-V sat difference.


LOE 4, quality good, neutral. ELSO database analysis of factors affecting outcome from E-CPR. Although patients with single ventricle physiology fared worse than others, the analysis included those with non-surgical conditions (cardiac muscle disease). The hospital survival for RACHS-1 class 6 patients (which are predominantly Norwood I) was 28% (22/78).

LOE 4, quality fair, neutral. Observational only. Patients who require extracorporeal support post stage 1 repair for HLHS demonstrate marked derangements in DO2:VO2 ratio as monitored by the oxygen excess factor. No intervention evaluated.


LOE 4, quality good, supporting. Before and after retrospective case series examining use of phenoxybenzamine in a cohort of neonates undergoing Norwood 1 repair (n = 105). Endpoints were prevention of circulatory collapse (cardiopulmonary arrest or failure to wean from bypass). Good use of statistics (bootstrap bagging in the multivariable model). Model showed phenoxybenzamine use was associated with decreased risk of circulatory collapse, regardless of whether there was an operative technical issue.


LOE 5, quality fair, neutral. Observational radiological study demonstrated moderate relationship between low post-operative cerebral NIRS saturation, expressed as time-below-threshold, and new ischemic injury by MRI (and early post-op neurological status). Clinical endpoint not in study design. Supports post-op NIRS monitoring, but no therapy evaluated to prevent low NIRS values: thus evidence neutral.

Fenton KN, Lessman K, Glogowski K, Fogg S, Duncan KF. Cerebral oxygen saturation does not normalize until after stage 2 single ventricle palliation Ann Thorac Surg. 2007 Apr;83(4):1431-6. (1)

FOR REFERENCE ONLY. LOE 5, poor. Small sample size, basic statistics. No therapy evaluated. Not included for further review. Sample size.


FOR REFERENCE ONLY. LOE 5, quality good. Another article examining late causes of death after stage 1 repair.


LOE 5, quality poor, neutral. Uncontrolled observational study, with no attempt at multivariable analyses. Almost all patients received a type of afterload reducing agent (e.g. enoximone), but the patients who also received alpha-adrenergic blockade with phentolamine had improved outcomes and slightly lower arterial blood pressure.


FOR REFERENCE ONLY. LOE 5, quality fair. Not included in analysis, as (a) duplicate patient pop to Furck (1), and (b) no specific therapy evaluated. However the study did report the virtual elimination of interstage mortality with initiation of a home monitoring program.

FOR REFERENCE ONLY. LOE 5, quality fair, neutral. Uncontrolled, observational, mixed population (neonate and infants, various surgeries). CPR not studied. Not included for further review..


LOE 5, quality good, supporting. Non-randomised, before-and–after study (introduction of home monitoring post stage 1). Extended electronic monitoring post hospital discharge was associated with reduced mortality.


LOE 4, quality poor, neutral. Uncontrolled case series documenting outcome from CPR (ROSC and survival to hospital discharge) in a small cohort of infants with either modified BT shunt (n = 15) or Sano (n = 12). In this case series, the Sano was associated with a greater return of spontaneous circulation (8/12 versus 3/15 for a BT shunt, p = 0.02), this did not translate into better survival to hospital discharge (58% versus 20%, p = 0.1), but was likely limited by reduced power from the small study size. There was no adjustment for confounders and patients having multiple arrests were treated as separate episodes.


FOR REFERENCE ONLY. LOE 5, quality poor. Examined correlation between base excess and SvO2 post stage 1 repair. Change in base excess defined as “anaerobic threshold” without taking into account confounding variables for base excess (hyperchloremia, albumin, etc) No other endpoint evaluated; thus not included for further review.


LOE 4, quality good, supporting. Small sample (n=13), but late (4 year) neurological outcome evaluated thoroughly. Great use of statistics, demonstrating interaction effect between SvO2 and dichotomised length of DHCA on neurological outcome. A similar detrimental effect of hypocarbia was also seen. Other hemodynamics not predictive. CPR not tested. Strategies to elevate SvO2 not tested.


LOE 5, quality good, supporting. Prospective cohort study examining the effect of phenoxybenzamine on the relationship between arterial and central venous oxygen saturations and Qp:Qs following Norwood 1 repair (n = 71), thus ENDPOINT NOT PRE-ARREST. Method of selection of controls not receiving phenoxybenzamine (n = 9) was not reported. Phenoxybenzamine use was associated with a more favorable SvO2 overall, and also a better Qp:Qs at higher levels of SaO2 (>80%).


FOR REFERENCE ONLY. LOE 5, quality fair. Observational study (mixed population: post uni- and biventricular repair) examining time course of cerebral and somatic NIRS, post sternal closure. In univentricular group neither cerebral nor somatic NIRS changed after sternal closure. No endpoints relevant to the question, so not evaluated further.

LOE 5, quality fair, supporting. Prospective observational study evaluating NIRS use pre stage 1 repair. Choice of institution of NIRS guided by monitor availability, so time effect likely. Overall, use of NIRS associated with fewer invasive interventions (e.g. need for intubation, hypoxic gas mix, etc). In essence, NIRS associated with lower likelihood of instituting unnecessary pre-arrest therapies (e.g. mechanical ventilation).


FOR REFERENCE ONLY. LOE 5, quality fair. Examined correlation between somatic NIRS trends and SvO2 and lactate levels in univentricular and biventricular circulation; other clinical endpoint not studied; not subsequently analyzed.


LOE 5, quality poor, opposing. Prospective case series of effect of inhaled CO2 when added to hypoxic FIO2 (15 - 18%) pre- (n = 12) and post-op Norwood I (n = 8). Endpoint was a rise in systolic BP > 10mmHg, with CO2, NOT PRE-ARREST. Positive effect only seen pre-op.


LOE 5, quality good, supporting. Animal model examining effect of FIO2 and CO2 on Qp:Qs at various sizes of surgical shunt. Of note, the effect of both inspired oxygen and carbon dioxide on manipulation of Qp:Qs was completely lost when a large pulmonary BT shunt, defined as having a diameter in mm greater than 1.1 times body weight (in kg) was inserted.


LOE 5, quality fair, supporting. Non-randomized crossover trial of sequential increase (30 min periods) in inhaled CO2 post-op Norwood I (n = 7). Endpoints hemodynamics, cerebral and splanchnic SvO2and A-V sat difference, NOT PRE-ARREST. Addition of CO2 produced a dose-dependent increase in oxygen delivery and Qs (via a decrease in SVR), as well as cerebral SvO2, but a decrease in splanchnic SvO2.


FOR REFERENCE ONLY. LOE 5, quality good. Guidelines for antithrombotic therapy, used to inform role and dose for heparin administration in suspected acute shunt thrombosis, thus not included in evidence grid.


FOR REFERENCE ONLY. LOE 5, quality fair. Not single ventricle patients; examined correlation of NIRS and SvO2; thus not subsequently analyzed.


FOR REFERENCE ONLY. Not graded in table because to date, only presented in abstract for. Provides contemporaneous outcome data for patients requiring stage 1 repair.

LOE 4, quality poor, supporting. Observational study evaluating relationship between NIRS and adverse outcome (prolonged ICU stay, need for ECMO, hospital mortality) post stage 1 repair. Problems with composite endpoints, also AUC for ROC analysis not given. Adverse outcomes associated with lower NIRS overall, but no therapeutic intervention altering NIRS evaluated.


LOE 5, quality good, supporting. Randomized crossover trial of effects of inspired hypoxia (FIO2=17%) and CO2 (FICO2 = 3%) pre-op Norwood (n = 15). Endpoint involved hemodynamics and cerebral ScO2, NOT PRE-ARREST. Of the two therapies, CO2 appeared beneficial. Some of the patient population may also be included in Tabbutt 2001.


LOE 4, quality good, neutral. Case series detailing experience with ECMO after stage I repair. Survival to hospital discharge in the cohort requiring E-CPR was 11/22 (50%), although this differed according to the reason for E-CPR: for shunt thrombosis, survival was 5/5 (100%) versus 6/17 (35%) for others.


FOR REFERENCE ONLY. LOE 5, quality good. National Registry analysis of E-CPR outcomes for all-comers, used as a baseline for comparison of studies detailing E-CPR after stage 1 Norwood repair. Thus not included in the summary of evidence table.


LOE 5, quality poor, supporting. Although part of a randomized crossover study in an animal model of single ventricle evaluating effects of inotropes at standard doses on hemodynamics, the study also involved giving an arrest dose of epinephrine to all animals when not in cardiac arrest or pre-arrest. This showed an undesirable effect on Qp:Qs, by increasing systemic vascular resistance 856%, while at the same time reducing pulmonary vascular resistance by 18%, producing a net increase in Qp:Qs of 584%. This suggests that boluses doses to human infants in pre-arrest due to excessive Qp:Qs could be deleterious.


LOE 5, quality good, supporting. Randomized crossover trial of effects of 100% O2, NO, hypoxia (FIO2 10%) and CO2 (FICO2 = 5%) in a fetal lamb model of univentricular circulation, pre and post cardiopulmonary bypass with DHCA (n = 11). Endpoints were Qp:Qs, and hemodynamics, NOT PRE-ARREST. Hypoxia and hypercarbia both improved Qp:Qs; however systemic arterial pressure was decreased with hypoxia but unchanged with hypercarbia. Similar effects were seen pre- and post-bypass.

LOE 4, quality good, neutral. Retrospective cohort study documenting outcomes from cardiac arrest in a single centre, cardiac ICU. This is the only study to provide baseline outcome data for univentricular in comparison to other cardiac patients. The overall survival was 44% (8/18) for univentricular patients compared to 38% (6/16) for those with a biventricular physiology. Univentricular patients had a tendency to a higher incidence of non-VF/VT arrests (12/18 versus 8/16 for biventricular); however this did not reach significance (p = 0.32), and the rhythm type did not influence survival in the overall study population.


LOE 5, quality good, supporting. Randomized crossover trial of effects of variable FIO2 (FIO2=100 to 15%), CO2 (FICO2 = 5%) and PEEP (0 – 15cm) in a neonatal pig univentricular model (n = 6). Endpoint involved Qp:Qs and DO2, NOT PRE-ARREST. Qp:Qs decreased predictably as FIO2 was decreased. DO2 was optimized at FIO2 of 50%, and Qp:Qs of approximately 0.7. The effect of CO2 on Qp:Qs was attenuated when FIO2 was 21% versus 100%. PEEP decreased Qp:Qs, mainly via actions on PVR, but at a cost of reduced DO2.


LOE 4, quality poor, neutral. Neonatal piglet (n = 6) model of HLHS, examining effects on hemodynamics and Qp:Qs of various inotropes. Ventilation performed at an FIO2 of either 100% or 50%, thereby limiting conclusions (of note effects were blunted at FIO2 50%, compared to 100%). Not included in analysis.


FOR REFERENCE ONLY. LOE 5, quality good. Another article examining late causes of death after stage 1 repair.


LOE 5, quality poor, neutral. Case series examining risk factors for outcome post stage 1 repair. Poor use and reporting of multivariable adjustments.


LOE 5, quality good, supporting. Randomized crossover trial of effects of inspired hypoxia (FIO2=17%) and CO2 (FICO2 = 2.7%) pre-op Norwood 1 (n = 10). Endpoint involved Qp:Qs, hemodynamics and cerebral ScO2, NOT PRE-ARREST. Of the two therapies, CO2 appeared beneficial on all endpoints.


LOE 4, quality good, neutral. Meta-analysis of English language articles 1990-2007. Appendix B detailed hospital outcome from cardiac anatomical subgroups: that for left heart lesions (including HLHS), other single ventricles and heterotaxies was 22/60 (37%), comparable to other type of lesion


FOR REFERENCE ONLY. LOE 5, quality fair. Not related to study population (no post Stage 1 patients), so not further evaluated.

LOE 5, quality good, supporting. Retrospective cohort study examining the effect of management changes, including phenoxybenzamine use, on outcome after stage 1 HLHS repair (n = 115). This ENDPOINT NOT PRE-ARREST. However phenoxybenzamine use was associated with improved survival to stage 2 repair.


LOE 4, quality poor, neutral. Case series of 5 patients post HLHS 1 repair who decompensated in-hospital (PRE ARREST). The constellation of hemodynamic and laboratory data suggested to the authors that raised systemic vascular resistance was the primary problem; however this was not confirmed by invasive measurement.