



Prevention of Shunt Thrombosis Following Systemic-to-Pulmonary Artery Shunts

Publication Date: July 20, 2009

Target Population

Inclusion: Infants and children with congenital heart disease who have undergone placement of a palliative systemic-to-pulmonary artery shunt, including those as part of the Norwood operation.

Exclusion:

- Patients with a coagulopathy
- Patients with a salicylate allergy

Introduction

Patients with shunt dependent pulmonary blood flow pose a significant risk for mortality in the early postoperative period until further surgical palliation is completed (*Chang 2006 [D]*). Surgical shunts have been performed in patients with a variety of anatomic subtypes, including those individuals with single ventricles as well as those with two ventricles who have severe pulmonary stenosis or atresia. Shunts may be used as a bridge to the next palliative stage or may be temporizing until the older child is deemed amenable for complete surgical repair. Systemic-to-pulmonary shunts confer some risk to an individual by the creation of a parallel circulation. The most feared complication is fatal shunt thrombosis. Furthermore, this relatively unstable physiology may result in a volume load on the ventricle, coronary steal, pulmonary overcirculation, and serves as a potential nidus for infection. Due to the high risk for interstage mortality, efforts are being made to delineate potential etiologies specifically for thrombotic complications.

Aspirin is a nonselective cyclooxygenase inhibitor, blocking both the COX-1 and COX-2 pathways resulting in decreased platelet aggregation and inflammation, respectively. This would theoretically result in less neointimal proliferation, possibly preventing systemic-to-pulmonary artery (PA) shunt occlusion. Routine use of aspirin in shunted patients has remained controversial

with mixed results in the literature. However, a recent large multicenter prospective trial concluded that aspirin significantly decreased the risk of shunt thrombosis and its associated morbidity and mortality (*Li 2007 [C]*). To date, however, no randomized controlled trials have been performed.

The purpose of this guideline is to present scientifically based recommendations for preventing or decreasing the incidence of systemic-to-pulmonary artery shunt thrombosis.

Incidence/Risk Factors

It has been reported that approximately 14% of children who have undergone placement of aortopulmonary shunts die following hospital discharge prior to any further surgical palliation (*Fenton 2003 [D]*). This estimate may be as high as 19% in patients with single ventricle anatomy. However, the incidence of shunt occlusion due to thrombus formation ranges from 5% in children with univentricular hearts (*Fenton 2003 [D]*, *Alkhulaifi 2000 [D]*) to 12% for all shunted congenital heart lesions (*Li 2007 [C]*). The contribution of shunt thrombosis to interim mortality may be underestimated, however, due to the lack of histopathologic evidence at the time of death.

Systemic-to-pulmonary artery shunts pose a significant risk factor for mortality between one month and one year postoperatively in children undergoing cardiac surgery (*Chang 2006 [D]*). Specific risk factors for shunted patients, not all of which are statistically significant, have been elucidated. These include a weight < 2 kg at the time of surgery, preoperative mechanical ventilation (*Alkhulaifi 2000 [D]*), smaller shunt size (< 4 mm) as a predictor of > 50% shunt stenosis (*Wells 2005 [D]*), central AP shunts (*Motz 1999 [E]*), shunts performed using cardiopulmonary bypass, and those as part of the Norwood operation (*Li 2007 [C]*). The role of shunt size as a risk factor for thrombosis and sudden death remains controversial. Several published studies have demonstrated no significant relationship between shunt size and risk for occlusion (*Fenton 2004 [D]*, *Fenton 2003 [D]*, *Alkhulaifi 2000 [D]*, *Sivakumar 2001 [E]*). Furthermore, shunt size is often not a modifiable risk factor. Physiologic factors, including cyanosis associated polycythemia with increased blood viscosity, a tenuous fluid balance with a predisposition to clot formation during a state of dehydration, low cardiac output, or a coagulopathy all contribute to the likelihood of a thrombotic complication in shunted patients.

GUIDELINE RECOMMENDATIONS

References (), Evidence strengths []
(See last page for Evidence strengths)

Clinical Assessment

1. It is recommended that patients be evaluated for any of the following clinical conditions:
 - Patient or family history of coagulopathy, salicylate allergy or viral exposures
 - Physical findings suggestive of a coagulopathy.
 (Local Consensus [E])

Laboratory Assessment

2. It is recommended that, prior to initiation of aspirin therapy, the following laboratory studies be conducted:
 - CBC with platelets
 - Coagulation studies if personal/family history or physical examination are suggestive of coagulopathy.
 (Local Consensus [E])

Treatment Recommendations

3. It is recommended that a heparin infusion be started postoperatively once hemostasis has occurred and should be continued for at least 48 hours and until aspirin therapy is initiated (Sivakumar 2001 [E], Motz 1999 [E], Al Jubair 1998 [E]).

NOTE: A heparin infusion will be initiated at 15-20 units/kg/hr to maintain aPTTs in the range of 60 to 80 seconds. An aPTT value should be checked four hours after initiating therapy and rechecked four hours following any adjustments in dose. If the aPTT value is stable and no dose adjustment is necessary, then it may be monitored once daily (Hirsh 2008 [S]).

4. It is recommended that patients begin aspirin therapy once oral intake is initiated following systemic-to-pulmonary artery shunt placement, due to the significantly lower risk of shunt thrombosis and risk of death (Li 2007 [C], Sivakumar 2001 [E], Motz 1999 [E], Al Jubair 1998 [E], Tweddell 2007 [X])

NOTE: The optimal aspirin dose recommendation has not been established, but ranging from 20.25 mg to 40.5 mg (Li 2007 [C]). The occurrence of aspirin-related complications, such as Reye syndrome, is relatively low and dose-related with administration of doses greater than 40 mg/kg

(Monagle 2008 [S]). Current practice at CCHMC is to administer aspirin at a dose of 40.5 mg once daily for children below the weight of 10 kg and 81 mg of aspirin daily for children weighing greater than 10 kg.

5. It is recommended that alternative forms of anticoagulation, such as enoxaparin, be considered in cases where there is significant patient or family history of coagulopathy or any contraindication to the administration of aspirin (Monagle 2008 [S]). For those patients in whom enoxaparin is used, an initial prophylactic dose of 0.75 mg/kg subcutaneously (SQ) every 12 hours for infants less than 2 months of age and 0.5 mg/kg SQ every 12 hours for infants greater than 2 months of age can be administered (Cincinnati Children's Hospital Medical Center 2009 [S]). An antifactor-Xa level should be monitored 4 to 6 hours following SQ injection with the goal prophylactic range of 0.1 to 0.3 antifactor-Xa units/mL as extrapolated from adult data (Monagle 2008 [S]).
6. It is recommended that non-steroidal anti-inflammatory drugs, such as ibuprofen and ketorolac, be avoided in shunted patients due to their competitive inhibition of aspirin's antiplatelet effects (Gengo 2008 [B], Gladding 2008 [B], Hong 2008 [B], Catella-Lawson 2001 [B], MacDonald 2003 [D]).

Early Identification

7. It is recommended that all patients be discharged from the hospital with home surveillance, consisting of daily weights, oxygen saturation checks and feeding records performed by the parent or legal guardian (Ghanayem 2004 [D]). The goal of the home monitoring program is to identify early, individuals who are at increased risk for interstage morbidity and mortality.
8. It is recommended to avoid dehydration in infants with systemic-to-pulmonary shunts due to the critical increased risk of life-threatening shunt thrombosis (Local Consensus [E]).

Future Research Agenda

9. Compare incidence of shunt thrombosis in patients pre and post guideline implementation.
10. Evaluate incidence of adverse events related to antithrombotic therapy.

References

Note: When using the electronic version of this document,  indicates a hyperlink to the PubMed abstract. A hyperlink following this symbol goes to the article PDF when the user is within the CCHMC network.

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All Team Members and Clinical Effectiveness support staff listed above have declare conflict of interest and none were found.

Development Process

The process by which this guideline was developed is documented in the Guideline Development Process Manual; a Team Binder maintains minutes and other relevant development materials. The recommendations contained in this guideline were formulated by an interdisciplinary work group which performed systematic and critical literature reviews, using the grading scale that follows, and examines current local clinical practices.

To select evidence for critical appraisal by the group the Medline, EmBase and the Cochrane databases were searched. Evidence from 1998 to the present were reviewed to generate an unrefined, "combined evidence" database using a search strategy focused on answering clinical questions relevant to systemic-to-pulmonary shunts and employing a combination of Boolean searching on human-indexed thesaurus terms (MeSH headings using an OVID Medline interface) and "natural language searching on words in the title, abstract, and indexing terms. The citations were reduced by: eliminating duplicates, non-English articles, and adult articles. The resulting abstracts were reviewed by a methodologist to eliminate low quality and irrelevant citations. During the course of the guideline development, additional clinical questions were generated and subjected to the search process, and some relevant review articles were identified.

Appropriate companion documents have been developed to assist in the effective dissemination and implementation of the guideline. Once the guideline is in place for four years, the development team reconvenes to explore the continued validity of the guideline. This phase can be initiated at any point that evidence indicates a critical change is needed.

Evidence Grading Scale			
A	Randomized controlled trial: large sample	S	Review article
B	Randomized controlled trial: small sample	M	Meta-analysis
C	Prospective trial or large case series	Q	Decision analysis
D	Retrospective analysis	L	Legal requirement
E	Expert opinion or consensus	O	Other evidence
F	Basic laboratory research	X	No evidence

Recommendations are formulated by a consensus process directed by best evidence, patient and family preference and clinical expertise. During formulation of these recommendations, the team members have remained cognizant of controversies and disagreements over the management of these patients. They have tried to resolve controversial issues by consensus where possible and, when not possible, to offer optional approaches to care in the form of information that includes best supporting evidence of efficacy for alternative choices.

The guidelines have been reviewed and approved by clinical experts not involved in the development process, distributed to senior management, and other parties as appropriate for their intended purposes. The guideline was developed without external funding.

Copies of this Evidence-based Care Guideline (EBCG) and its companion documents are available online and may be distributed by any organization for the global purpose of improving child health outcomes. Website address:

<http://www.cincinnatichildrens.org/svc/alpha/h/health-policy/ev-based/default.htm> Examples of approved uses of the EBCG include the following:

- copies may be provided to anyone involved in the organization's process for developing and implementing evidence based care guidelines;
- hyperlinks to the CCHMC website may be placed on the organization's website;
- the EBCG may be adopted or adapted for use within the organization, provided that CCHMC receives appropriate attribution on all written or electronic documents; and
- copies may be provided to patients and the clinicians who manage their care.

Notification of CCHMC at HPCEInfo@cchmc.org for any EBCG, or its companion documents, adopted, adapted, implemented or hyperlinked by the organization is appreciated.

NOTE: These recommendations result from review of literature and practices current at the time of their formulations. This guideline does not preclude using care modalities proven efficacious in studies published subsequent to the current version of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this guideline is voluntary. The physician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.

For more information about this guideline, its supporting evidences and the guideline development process, contact the guideline team members at 513-636-4200 or thc@cchmc.org.