Understanding the Vasculature in Pulmonary Atresia, Ventricular Septal Defect, and Aortopulmonary Collaterals

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TOF with PA
The Basic Lesion

- Tetralogy-like intracardiac morphology
- Pulmonary valve atresia (PA)
- Highly variable pulmonary artery morphology

MAPCA

A unique lesion in which the pulmonary vascular bed is multi-compartmentalized
Unifocalization refers to the process of changing an abnormal multi-compartment pulmonary artery circulation to a normal single compartment circulation using surgical reconstruction.

What conditions allow an abnormal multi-compartment pulmonary artery circulation to form?

- During primary morphogenesis, the pulmonary artery circulation changes from the early multi-sited foregut source to the central true pulmonary arteries.
- The presence of either a patent pulmonary valve or a ductus arteriosus is necessary for this transition.
- If neither a PV or ductus is present, the foregut source persists, and the native pulmonary arteries do not form normally.

Pulmonary Artery Morphology in PA

- PA with ductus arteriosus (60%)
  - Normal pulmonary artery size and arborization

- PA with absence of ductus arteriosus (40%)
  - Pulmonary artery size and arborization abnormalities
  - Aortopulmonary collaterals (MAPCAs)

MAPCAs

- Morphology – Highly variable patterns of:
  1) Pulmonary artery size and arborization
  2) Collateral origin, number, and course
  3) Connections between the two

- Physiology – Although there is total mixing of the pulmonary and systemic circulations, there can be pulmonary overcirculation, or pulmonary undercirculation. Commonly both overcirculation and undercirculation occur simultaneously in the same patient.
MAPCAs
Unique Physiology

Whereas the duct (or shunt) dependant patient with a systemic saturation of 80% is both clinically stable AND has healthy pulmonary hemodynamics, the MAPCAs patient with a saturation of 80% is clinically stable but likely does not have healthy pulmonary hemodynamics.

- A decision to observe the first patient is appropriate; a similar decision for the second patient is not.
- Delayed stabilization of blood flow to all segments of lung leads to microvascular disease.

Principles

- The goal of surgery for TOF/PA/MAPCAs is to create a separated biventricular circulation with the lowest possible PVR and PA pressure.

**WHY?**

Importance of PA Pressure

How do we achieve a low PVR and PA pressure?

- The lowest PVR will be achieved by maximizing both the size and health the pulmonary microvascular bed.
- Including all parenchymal lung segments in the pulmonary circulation is a requirement for achieving this.
Principles

Can MAPCAs contribute to the pulmonary circulation?

All lung segments have a blood supply—sometimes it is from the native PA and sometimes it is from a MAPCA.

Sometimes a lung segment can have dual supply from both the native PA and a MAPCA, but frequently it is exclusively from one or the other.

In this disease, it is a frequent occurrence that MAPCAs will be the only source of blood flow to certain segments of the pulmonary microvascular bed.

Figure 1. Bronchopulmonary arterial anatomy in pulmonary atresia or pulmonary valve atresia with ventricular septal defect (PAVPASD) is characterized by a continuous morphologic spectrum, but one definition of major overcirculation of the pulmonary arteries (MAPCA) patients is supported by the obvious pulsed Doppler of those in the non-MAPCA group (closed circles) and those in the MAPCA group (open circles). There is a strong negative correlation ($r^2 = 0.8$, $p < 0.001$) between increasing number of bronchopulmonary segments supplied by the native pulmonary arteries and decreasing number of bronchopulmonary segments with abnormal supply. Abnormal supply = number of hypoplastic segments + number of stenosed segments + number of collateral supplied segments; PA = pulmonary artery; RTO = right ventricular outflow tract.
Spectrum of Lung Perfusion

If an individual case is here, no unifocalization is needed (only 12%)

If an individual case is here, unifocalization is necessity (23%)
65% fall between the two extremes just shown

What about here if no unifocalization? Survival? PVR?
It seems logical, even compellingly so, that in many cases, including MAPCAs in the pulmonary circulation will be beneficial. This assumes, however, that MAPCAs will remain patent, and the microvascular bed supplied by them will remain healthy.

**Observations**

MAPCAs are intrinsically unstable after birth

- **At birth**
  - All lung segments have a blood supply (true PA or MAPCA)
  - MAPCAs tend to be smooth and sinusoidal
  - Optimal health of microvasculature exists

- **Loss of lung segments occurs over time due to abnormal arterial flow and pressure**
  - Natural occlusion / stenosis in some
  - Obstructive vascular disease in others
Natural History

- 50% die by age 3-5 yrs
- 80-90% die by a decade
- Few survivors beyond 30 yrs

Goals of Management

Improve on the Natural History

Achieve a completely separated two ventricle circulation (intracardiac repair with closure of VSD and creation of RV-PA connection)

Achieve lowest possible RV pressure after repair

How is a low RV pressure best achieved?

- By maintaining a healthy microvascular bed in every lung segment
- That means normalizing arterial flow and pressure in every lung segment as soon as possible

How do we do that?

MAPCAs

Given the complexity and variability of this lesion, a broadly applicable surgical management protocol is needed that:

- is physiologically and morphologically driven
- provides the most good for the greatest number of patients
Surgical Priorities

- Unifocalize early and completely
- Perform intracardiac repair as soon as, but only when, a low PVR is assured

Keeping these principles in mind, the morphology and physiology do determine the specific operative approach.

1. Midline complete unifocalization with intracardiac repair
2. Midline complete unifocalization with central aortopulmonary shunt
3. Central aortopulmonary window

1: One Stage Unifocalization & Intracardiac Repair (56%)

2: One Stage Unifocalization with Shunt (18%)
3: Aortopulmonary Window (12%)

Central Mediastinal Dissection

Major Aortopulmonary Collaterals

Technique
Major Aortopulmonary Collaterals

Surgical Technique: One Stage Complete Unifocalization

Technique

Total Experience

n = 570
1992 – 2011

- Age: median 7.7 month
  range 10d - 39 yrs
  Infants: 65%

- Weight: median 5.7 Kg;
  range 1.8 – 98.7 Kg

Early Mortality

- 1999 – 2008
  1.9%
**Actuarial Survival**

- **Years After Surgery**
  - 0: N=262
  - 5: N=55
  - 10: N=5

- 30% CI

**Perioperative RV / LV Pressure**

- **Mean +/- SD**
  - 1999 – 2008
    - 0.37 +/- 0.11

**Mid-Late Follow Up**

- **RV / LV Pressure Ratio**
  - The RV / LV pressure ratio at follow up was compared to the perioperative value to determine PA and collateral growth.

  - **Ratio difference** = -0.03 +/- .32

**Cumulative Distribution for Intracardiac Repair**
Summary of Experience

- Complete One Stage Unifocalization can be achieved in most patients.
- Intracardiac repair is possible in over half of pts at first unifocalization operation, and eventually about 90% achieve intracardiac repair with low RV pressure.
- Selected patients (normal arborization and all dual supply collaterals) (about 12%) are best managed initially by surgical aortopulmonary window, rather than complete unifocalization.

What Does the Surgeon Need to Know Before Unifocalization?

- True pulmonary artery size and arborization
- Number, origin, exact course, and destination of every collateral
- Exact position and severity of all stenoses in both true pulmonary arteries and collaterals
- For every collateral, does it intercommunicate with true pulmonary artery: “isolated supply” or “dual supply”
- Relationship of collaterals to other thoracic structures: bronchial tree, pulmonary veins, esophagus
- Post stenotic pressure in collaterals
CT of true Pulmonary Arteries

CT of MAPCA intercommunicating with true pulmonary artery

CT Angiogram
Tetralogy of Fallot with Major Aortopulmonary Collaterals

Technique

Balloon Dilatation After Unifocalization
**Surgical Principles**

- Emphasis on early complete repair
- Emphasis on native tissue to tissue connections deep in lung parenchyma
- Recruit as many collaterals as possible initially
- Judicious decision making regarding VSD closure
- In staged pts: close FU and early cath to reintervene

**Mid-Late Follow Up**

- 83.6% complete, up to 12 years
- Surgical reintervention for conduit change: 5.6%
- Surgical reintervention for PA stenosis: 22.6%
- Catheter intervention for PA stenosis: 19.7%

**Morphology**

- Absence of true PAs: 23.5%
- # of MAPCAs (mean +/- sd): 3.8 +/- 1.4
- Diameter of true PAs (median): 2

**CT Angiogram**
4: Staged Thoracotomy (13%)

Intraoperative Flow Study

Monitor Mean PA pressure

Left atrium is vigorously vented

...But

Many disagree on how best to get there
7 year follow up after one stage complete repair at 4 months of life in patient with only collaterals and absent intrapericardial pulmonary arteries

RV/LV ratio 0.42 at repair
RV/LV ratio 0.36 at 7y FU

Mid-Late Mortality

- Total Experience 7.0%
- 1992 – 1998 8.3%
- 1999 – 2005 6.2%

Actuarial Survival
### Risk Analysis

**Variables Examined:**

- Age
- DiGeorge
- Weight
- GE Reflux
- MAPCAs
- Initial Operation
- True PAs
- Year of Surgery

### Early Death Risk Analysis

- By univariate testing, “year of surgery” was the only risk factor for early death. \( p = .001 \)
- Multivariate testing unrevealing

### Late Death Risk Analysis

- By univariate testing there were no risk factors for late death
- By multivariate analysis, GE reflux was barely significant, but when interactions were examined, the combination of GE reflux and DiGeorge Syndrome was highly significant

### Cumulative Distribution for Intracardiac Repair

- Total Experience

Cumulative distribution plot showing the cumulative probability of survival over time.
Summary of Experience

- The combination of DiGeorge and GE Reflux is a risk factor for mid term death
- The RV pressure does not show a tendency to rise over time, implying growth of the reconstructed PAs and MAPCAs
- Reintervention on the peripheral PA system is required in about one third of patients

Who Are the Bad Actors

- There is a subgroup of pts who predictably require multiple peripheral PA operations, some of whom never achieve intracardiac septation:
  - severely cyanotic immediately at birth
  - AND neonatal angiography shows very small MAPCAs (as opposed to stenoses)

Is it worth the effort in this subgroup? There are some successes

- Single ventricle pts with MAPCAS

Observations

- Overall, about 50% of all pts are as well off as TOF pt with a conduit.
- Another 30% are not quite that good
- 15% are worse again, but better than the natural Hx
- 5% are probably no better than the natural Hx

Our Prospectively Applied Treatment Protocol
Conclusion

- Using the decision making protocol described, improved early and midterm outcomes, as defined by survival with a complete repair and low RV pressure, can be achieved.

- Early mortality is currently about 2%, however a midterm mortality of about 7% persists.

Weighted VSD Protocol

Unweighted VSD Protocol

Our Prospectively Applied Treatment Protocol
Outline

- **The theory**: first, I will present several basic physiologic principles which are the basis for advocating unifocalization of MAPCAs.

- **The evidence**: theory is nice, but evidence is convincing. Second, I will present evidence that MAPCAs can reliably contribute, and commonly in a crucial way, to reducing PVR and PA pressure.
The Theory

The goal of surgery for TOF/PA/MAPCAs is to create a separated biventricular circulation with the lowest possible PVR and PA pressure.

WHY?

Principles

How do we achieve a low PVR and PA pressure?

- The lowest PVR will be achieved by maximizing both the size and health the pulmonary microvascular bed
- Including all parenchymal lung segments in the pulmonary circulation is a requirement for achieving this.
Principles

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Sometimes a lung segment can have dual supply from both the native PA and a MAPCA, but frequently it is exclusively from one or the other

In this disease, it is a frequent occurrence that MAPCAs will be the only source of blood flow to certain segments of the pulmonary microvascular bed

Relationship Between Native PA and MAPCA Distribution To The Lung

Spectrum of Lung Perfusion

Figure 1. Bronchopulmonary arterial anatomy in pulmonary arteries associated with ventricular septal defect (PA/ASD). It is characterized by a continuous morphologic spectrum, but our definition of early arterio-pulmonary collateral arteries (MAPCA) permits is supported by the absence of pulmonary hypertension. If there is no MAPCA, group labeled healthy; if there is MAPCA, group labeled abnormal. The data points for the normal and abnormal groups are represented by solid and open circles, respectively. The red line is the linear regression line. The correlation coefficient is $R^2 = 0.8, p < 0.001$, between increasing number of bronchopulmonary segments supplied by the native pulmonary arteries and decreasing number of bronchopulmonary segments with abnormal supply. Abnormal supply = number of dual supplied segments + number of unilaterally supplied segments + number of collateral supplied segments. PA = pulmonary artery; RVOT = right ventricular outflow tract.

If an individual case is here, no unifocalization is needed (only 12%).
Spectrum of Lung Perfusion

If an individual case is here, unifocalization is necessity (23%)

65% fall between the two extremes just shown
Spectrum of Lung Perfusion

65% fall between the two extremes just shown

What about here? If no unifocalization, only 80% of lung is perfused. Survival, but not ideal PVR

What about here if no unifocalization? Survival? PVR?

Real Live Weighted Spectrum of Lung Perfusion

PA and MAPCA Distribution in 482 Cases

Mixed 65%
All 18 segs from PA 12%
All 18 segs from MAPCAs 23%
It seems logical, even compellingly so, that in many cases, including MAPCAs in the pulmonary circulation will be beneficial. This assumes, however, that MAPCAs will remain patent, and the microvascular bed supplied by them will remain healthy.

The Evidence

Total Experience

- n = 482
- (currently over 500 cases)

Morphology

- Absence of true PAs: 23.5%
- # of MAPCAs (mean +/- sd): 3.8 +/- 1.4
- Diameter of true PAs (median): 2
113 patients with absent native PAs underwent unifocalization.

I will focus on this subset because outcomes in this subgroup cannot be attributed to any positive influence from native PAs.

**Early Mortality**

- 1999 – 2008: 1.9%

**Survival**

1999-2005

**Perioperative RV / LV Pressure**

- 1999 – 2005: 0.37 +/- .11
  - The great majority are under 0.5, and the vast majority are under 0.6

By our treatment protocol we do not attempt intracardiac repair unless we expect an RV/LV pressure ratio of < 0.5.

Mid-Late Follow Up
83.6% complete, up to 12 years

Mid-Late Follow Up
RV / LV Pressure Ratio

- The RV / LV pressure ratio at follow up was compared to the perioperative value to determine PA and collateral growth.

Ratio difference = -0.03 +/- 0.32

The crucial questions are:

“Do the MAPCAs matter?”

and

“Would we get the same outcomes if no unifocalization of MAPCAs had been performed?”
Follow up in Patients with Absent Native PAs

- Case study
- 7 year follow up
- after one stage unifocalization and simultaneous complete repair at 4 months of life
- in patient with only MAPCAs and absent native pulmonary arteries

RV/LV Ratio and angiography at Follow Up

- RV/LV ratio 0.42 at repair
- RV/LV ratio 0.36 at 7y FU

This is one case

Are there important statistical differences between patients with absent PAs and those with PAs?

Risk Analysis

Variables Examined:

<table>
<thead>
<tr>
<th>Age</th>
<th>DiGeorge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>GE Reflux</td>
</tr>
<tr>
<td>#MAPCAs</td>
<td>Initial Operation</td>
</tr>
<tr>
<td>Native PAs(+-)</td>
<td>Year of Surgery</td>
</tr>
</tbody>
</table>
Early Death Risk Analysis

- univariate testing: Native PA(+/−) was not a factor
- Multivariate testing: Native PA(+/−) was not a factor

Late Death Risk Analysis

- univariate testing: Native PA(+/−) was not a factor
- Multivariate testing: Native PA(+/−) was not a factor

Summary

- 90% of all cases can be septated:
  - with an RV/LV pressure ratio of < 0.5
  - that stays low over time
  - with a surgical mortality risk of < 2%
  - with no apparent differences among pts with absent native PAs

Inferences

- It is unequivocal that unifocalizing MAPCAs matters when native PAs are absent
- The absent PA group demonstrates that unifocalized MAPCAs are upstanding and contributing members of (lung) society
- And that they have growth potential and staying power
- Can it really be argued that unifocalizing MAPCAs is not beneficial in the great majority of the other 65% of cases that range the spectrum of mixed blood supply from native PAs and MAPCAs? Not convincingly
- The relatively small subset of patients with dual supply to all segments (12%), or the occasional patient with 90% native PA and 10% MAPCA distribution, may be the exception
RV/LV Ratio at Follow Up

- 7 year follow up after one stage complete repair at 4 months of life in patient with only collaterals and absent intrapericardial pulmonary arteries

RV/LV ratio 0.42 at repair

RV/LV ratio 0.36 at 7y FU

Actuarial Survival

<table>
<thead>
<tr>
<th>Years After Surgery</th>
<th>1 yr</th>
<th>5yr</th>
<th>10yr</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>93.7 (93.1-94.3)</td>
<td>85.5 (84.7-86.8)</td>
<td>85.5 (79.8-88.5)</td>
</tr>
</tbody>
</table>

30% CI
Complete One Stage Unification can be achieved in most patients.

Intracardiac repair is possible in over half of pts at first unification operation, and eventually about 90% achieve intracardiac repair with low RV pressure.

Selected patients (about 25%) are best managed initially by staged thoracotomy or surgical APW, rather than complete unification.

The combination of DiGeorge and GE Reflux is a risk factor for midterm death.

The RV pressure does not show a tendency to rise over time, implying growth of the reconstructed PAs and MAPCAs.

Reintervention on the peripheral PA system is required in about one third of patients.
Who Are the Bad Actors
Is Anyone Inoperable?

- There is a subgroup of pts who predictably require multiple peripheral PA operations, some of whom never achieve intracardiac septation:
  - severely cyanotic immediately at birth
  - AND neonatal angiography shows very small MAPCAs (as opposed to stenoses)

Is it worth the effort in this subgroup? There are some successes

- Single ventricle pts with MAPCAS

Observations

- Overall, about 50% of all pts are as well off as TOF pt with a conduit.
- Another 30% are not quite that good
- 15% are worse again, but better than the natural Hx
- 5% are probably no better than the natural Hx
Conclusion

- Using the decision making protocol described, improved early and midterm outcomes, as defined by survival with a complete repair and low RV pressure, can be achieved.
- Early mortality is currently about 2%, however a midterm mortality of about 7% persists.

The Basic Lesion

- Tetralogy-like intracardiac morphology
- Pulmonary valve atresia
- Highly variable pulmonary artery morphology

MAPCAs

The Challenges

- Morphology – Highly variable patterns of:
  1) pulmonary artery size and arborization
  2) collateral origin, number, and course
  3) connections between the two

- Physiology – Although there is total mixing of the pulmonary and systemic circulations, there can be pulmonary overcirculation, or pulmonary undercirculation. *Commonly both overcirculation and undercirculation occur simultaneously in the same patient.*

MAPCAs

Unique Physiology

Whereas the duct (or shunt) dependant patient with a systemic saturation of 80% is both clinically stable AND has healthy pulmonary hemodynamics, the MAPCAs patient with a saturation of 80% is clinically stable but likely does not have healthy pulmonary hemodynamics.

- A decision to observe the first patient is appropriate; a similar decision for the second patient is not.
- Delayed stabilization of blood flow to all segments of lung leads to microvascular disease.
At birth, all lung segments have a blood supply (true PA or MAPCA). MAPCAs tend to be smooth and sinusoidal. Optimal health of microvasculature exists.

Loss of lung segments occurs over time due to abnormal arterial flow and pressure. Natural occlusion/stenosis in some, obstructive vascular disease in others.

Observations

- MAPCAs are intrinsically unstable after birth

Natural History

- 50% die by age 3-5 yrs
- 80-90% die by a decade
- Few survivors beyond 30 yrs

Goals of Management

- Improve on the Natural History
- Achieve a completely separated two ventricle circulation (intracardiac repair with closure of VSD and creation of RV-PA connection)
- Achieve lowest possible RV pressure after repair

Most people agree on these goals.
...But

Many disagree on how best to get there

How is a low RV pressure best achieved?

- By maintaining a healthy microvascular bed in every lung segment
- That means normalizing arterial flow and pressure in every lung segment as soon as possible

How do we do that?

MAPCAs

Given the complexity and variability of this lesion, a broadly applicable surgical management protocol is needed that:

- is physiologically and morphologically driven
- provides the most good for the greatest number of patients

Surgical Priorities

- Unifocalize early and completely
- Perform intracardiac repair as soon as, but only when, a low PVR is assured

Keeping these principles in mind, the morphology and physiology do determine the specific operative approach
Surgical Priorities

1. Midline complete unifocalization with intracardiac repair
2. Midline complete unifocalization with central aortopulmonary shunt
3. Central aortopulmonary window
4. Thoracotomies with staged unilateral unifocalizations

1: One Stage Unifocalization & Intracardiac Repair (56%)

2: One Stage Unifocalization with Shunt (18%)

3: Aortopulmonary Window (12%)
**Surgical Principles**

- Emphasis on early complete repair
- Emphasis on native tissue to tissue connections deep in lung parenchyma
- Recruit as many collaterals as possible initially
- Judicious decision making regarding VSD closure
- In staged pts: close FU and early cath to reintervene

**Major Aortopulmonary Collaterals**

**Technique**

A

B
Major Aortopulmonary Collaterals

Intraoperative Flow Study

Monitor Mean PA pressure

Left atrium is vigorously vented

Roller pump

MID-LATE MORTALITY

- Total Experience 7.0%
- 1992 – 1998 8.3%
- 1999 – 2005 6.2%

WEIGHTED VSD PROTOCOL

VSD

Subarterial

Muscular

Conoventricular

Size

Small

Large

AI

Single

Multiple

Small

Large

Observe

Repair

PAD

PAB

Acute Lung Injury

PAE
The Data 3: RV/LV

Delta for early to follow-up RV/LV Ratio
Mean -0.03 +/- .32

Breakdown of initial operations
56.4% uni + intracardiac repair
17.5% uni + shunt or conduit
13.2% AP Window
12.9% thoracotomy
Follow-up 83.6%

Management of Major Aortopulmonary Collateral Arteries

Frank L Hanley, Olaf Reinhartz, Sam Suleman, David B Gremmels, Stanton B Perry, Jeffrey A Feinstein, V Mohan Reddy

Follow-up RV / LV Delta

Delta for early to follow-up RV/LV Ratio:
Mean -0.03 +/- .32

Correlation between RV/LV & Age

Age at Repair, Years
The Data: Mortality

Early mortality 17/286  5.9%
Halves
1/2  11.9%
2/2  2.3%
Thirds
1/3  12.7%
2/3  6.6%
3/3  2.4%

Late mortality 20/286  7.0%
Halves
1/2  8.3%
2/2  6.2%
Thirds
1/3  12.7%
2/3  5.7%
3/3  5.6%
The Data 2

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
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<tbody>
<tr>
<td>Reop Rate for conduit</td>
<td>5.6%</td>
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<tr>
<td>Reop Rate for PA</td>
<td>22.6%</td>
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<tr>
<td>reconstruction:</td>
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<td>Recath rate for PA</td>
<td>19.7%</td>
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<td>intervention:</td>
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<td>TOF Anatomy</td>
<td>84.4%</td>
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<tr>
<td>Absent PA</td>
<td>23.5%</td>
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<tr>
<td>MAPCA</td>
<td>Mean 3.83 ± 1.43</td>
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<tr>
<td>Size of True PAs</td>
<td>Mean 2.36 ± 1.42</td>
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<td></td>
<td>Median 2</td>
</tr>
</tbody>
</table>

Management of Major Aortopulmonary Collateral Arteries

Frank L Hanley

Surgical Priority

- Normalize hemodynamics in every lung segment as soon as possible

How can this best be achieved?

MAPCAs

Unique Physiology

Assessment of pulmonary blood flow by usual clinical criteria is misleading

Example:

- In duct dependent PA, the PA system represents a single compartment and all lung segments are exposed to the same hemodynamic conditions.
  - A systemic oxygen saturation of 80% tells you something

- In PA with MAPCAs, the PA system is multi compartmentalized, with some lung segments that may be over circulated and others that are under circulated, simultaneously
  - A systemic oxygen saturation of 80% tells you nothing
TOF / PA / MAPCAs
Management Protocols

In reality all-inclusive management protocols are complex even for relatively simple lesions

Example: VSD
How do you manage VSDs?

VSD
- Small: Observe
- Large: Repair

Given the complexity and variability of this lesion, and the numerous management options that have been proposed over the years, there is a need for a broadly applicable surgical management protocol that:
- is physiologically and morphologically driven
- provides the most good for the greatest number of patients

Goals of Management
- Improve on the Natural History
- Achieve completely repaired two ventricle circulation
- Achieve lowest possible RV pressure

Observations
- At Birth
  - All lung segments have a blood supply
  - There is optimal surgical accessibility to source of PBF
  - The pulmonary microvasculature is at its healthiest
- Loss of Lung segments overtime
  - Natural occlusion / stenosis
  - Pulmonary hypertension
  - Iatrogenic stenosis / occlusion of collaterals
Hypothesis

- Normalizing hemodynamics in every lung segment, as soon as possible, is the best way to optimize the size and health of the pulmonary microvascular bed.

Late Death Risk Analysis

Multivariable logistic regression

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<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>p Value</th>
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<tr>
<td>Weight</td>
<td>0.81 (0.60 – 1.10)</td>
<td>0.180</td>
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<tr>
<td>GE Reflux</td>
<td>8.36 (1.05 - 66.55)</td>
<td>0.045*</td>
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<tr>
<td>Year of Surgery</td>
<td>1.64 (0.31 – 8.72)</td>
<td>0.56</td>
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Late Death Risk Analysis

Risk factor Interactions

<table>
<thead>
<tr>
<th>DiGeorge NO</th>
<th>DiGeorge YES</th>
</tr>
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<tbody>
<tr>
<td>GE Reflux</td>
<td>% late death</td>
</tr>
<tr>
<td>No</td>
<td>6.8% (10/148)</td>
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<tr>
<td>Yes</td>
<td>0.0% (0/5)</td>
</tr>
<tr>
<td>No</td>
<td>0.0% (0/40)</td>
</tr>
<tr>
<td>Yes</td>
<td>40.0% (2/5)</td>
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</table>
The Data 3: RV/LV

Delta for early to follow-up RV/LV Ratio
Mean -0.03 +/- .32

Breakdown of initial operations
56.4% uni + intracardiac repair
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<table>
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<tr>
<th></th>
<th>MAPCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reop Rate for conduit</td>
<td>5.6%</td>
</tr>
<tr>
<td>Reop Rate for PA reconstruction</td>
<td>22.6%</td>
</tr>
<tr>
<td>Recath rate for PA intervention</td>
<td>19.7%</td>
</tr>
<tr>
<td>TOF Anatomy</td>
<td>84.4%</td>
</tr>
<tr>
<td>Absent PA</td>
<td>23.5%</td>
</tr>
<tr>
<td>MAPCA Mean</td>
<td>3.83 ± 1.43</td>
</tr>
<tr>
<td>Size of True PAs Mean</td>
<td>2.36 ± 1.42</td>
</tr>
<tr>
<td>Median</td>
<td>2</td>
</tr>
</tbody>
</table>

Management of Major Aortopulmonary Collateral Arteries

Frank L Hanley

Surgical Priority

- Normalize hemodynamics in every lung segment as soon as possible

How can this best be achieved?

MAPCAs Unique Physiology

Assessment of pulmonary blood flow by usual clinical criteria is misleading

Example:
- In duct dependent PA, the PA system represents a single compartment and all lung segments are exposed to the same hemodynamic conditions.
  - A systemic oxygen saturation of 80% tells you something

- In PA with MAPCAs, the PA system is multi compartmentalized, with some lung segments that may be over circulated and others that are under circulated, simultaneously
  - A systemic oxygen saturation of 80% tells you nothing
In reality all-inclusive management protocols are complex even for relatively simple lesions.

Example: VSD
How do you manage VSDs?

**VSD**

- Small
  - Observe

- Large
  - Repair

**Goals of Management**

- Improve on the Natural History
- Achieve completely repaired two ventricle circulation
- Achieve lowest possible RV pressure

**Observations**

- **At Birth**
  - All lung segments have a blood supply
  - There is optimal surgical accessibility to source of PBF
  - The pulmonary microvasculature is at its healthiest

- **Loss of Lung segments overtime**
  - Natural occlusion / stenosis
  - Pulmonary hypertension
  - Iatrogenic stenosis / occlusion of collaterals
Hypothesis

- Normalizing hemodynamics in every lung segment, as soon as possible, is the best way to optimize the size and health of the pulmonary microvascular bed.

Late Death Risk Analysis

Multivariable logistic regression

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>0.81 (0.60 – 1.10)</td>
<td>0.180</td>
</tr>
<tr>
<td>GE Reflux</td>
<td>8.36 (1.05 - 66.55)</td>
<td>0.045*</td>
</tr>
<tr>
<td>Year of Surgery</td>
<td>1.64 (0.31 – 8.72)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Late Death Risk Analysis

Risk factor Interactions

<table>
<thead>
<tr>
<th></th>
<th>DiGeorge NO</th>
<th>DiGeorge YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>GE Reflux</td>
<td>% late death</td>
<td>% late death</td>
</tr>
<tr>
<td>No</td>
<td>6.8% (10/148)</td>
<td>0.0% (0/40)</td>
</tr>
<tr>
<td>Yes</td>
<td>0.0% (0/5)</td>
<td>40.0% (2/5)</td>
</tr>
</tbody>
</table>

Central Mediastinal Dissection
Controversy

- When is the optimal time for intervention?

The Basic Lesion

- Tetralogy-like intracardiac morphology
- Pulmonary valve atresia
- Highly variable native pulmonary artery morphology
- Highly variable MAPCA morphology
- Raw material for PA reconstruction = native PAs and MAPCAs

Observation #1

MAPCAs are intrinsically unstable after birth

- At birth
  - All lung segments have a blood supply (true PA or MAPCA)
  - MAPCAs tend to be smooth and sinusoidal
  - Optimal health of microvasculature exists

- Loss of lung segments occurs over time due to abnormal arterial flow and pressure
  - Natural occlusion / stenosis in some
  - Obstructive vascular disease in others
Observation #2

- In TOF/PA with MAPCAs, the native pulmonary arteries do not grow after birth
- These two observations support early intervention:
  - waiting causes degeneration of MAPCAs
  - waiting causes involution of native PAs

Controversy

- What do we do surgically with the raw material—PAs and MAPCAs?

MY ANSWER: Use all the raw material, and use it early

Support for the Position to Use All of the Raw Material in Reconstruction

- The theory: first, I will present several basic physiologic principles which are the basis for advocating unifocalization of MAPCAs.
- The evidence: theory is nice, but evidence is convincing. Second, I will present evidence that MAPCAs can reliably contribute, and commonly in a crucial way, to reducing PVR and PA pressure.
The Theory

The Evidence

Total Experience

n = 570
1992 – 2011

Morphology

(n=482)

- Absence of true PAs 23.5%
- # of MAPCAs (mean +/- sd) 3.8 +/- 1.4
- Diameter of true PAs (median) 2
113 patients with absent native PAs underwent unifocalization.

I will focus on this subset because outcomes in this subgroup cannot be attributed to any positive influence from native PAs.

Is the outcome different (worse) in this subgroup compared to the larger group of patients with native PAs?

### Early Mortality

**All Patients**

- 1999 – 2011: 1.9%

### Survival

- Mean +/- sd
- 0.37 +/- 0.11

The great majority are under 0.5, and the vast majority are under 0.6.

By our treatment protocol we do not attempt intracardiac repair unless we expect an RV/LV pressure ratio of < 0.5. Therefore, by protocol, the RV/LV pressure ratio is a constant and the % of patients that achieve complete repair becomes the variable of interest for measuring success.
Mid-Late Follow Up

RV / LV Pressure Ratio

- The RV / LV pressure ratio at follow up was compared to the perioperative value to determine PA and collateral growth.

- Ratio difference = -0.03 +/- .32

Mid-Late Follow Up
83.6% complete, up to 12 years

The crucial questions are:

“Do the MAPCAs matter?”

and

“Would we get the same outcomes if no unifocalization of MAPCAs had been performed?”
Follow up in the Subgroup of Patients with Absent Native PAs

- Case study
- 7 year follow up
- after one stage unifocalization and simultaneous complete repair at 4 months of life
- in patient with only MAPCAs and absent native pulmonary arteries

RV/LV Ratio and angiography at Follow Up

RV/LV ratio 0.42 at repair
RV/LV ratio 0.36 at 7y FU

Risk Analysis

Variables Examined:

- Age
- DiGeorge
- Weight
- GE Reflux
- #MAPCAs
- Initial Operation
- Native PAs(+/-)
- Year of Surgery

This is one case

Are there important statistical differences between the subgroup of patients with absent native PAs, and the larger group of those patients with native PAs?
Early Death Risk Analysis

• univariate testing: Native PA(+/−) was not a factor
• Multivariate testing: Native PA(+/−) was not a factor

Late Death Risk Analysis

• univariate testing: Native PA(+/−) was not a factor
• Multivariate testing: Native PA(+/−) was not a factor

Summary

• 90% of all cases can be septated:
  - with an RV/LV pressure ratio of < 0.5
  - that stays low over time
  - with no apparent differences among pts with absent native PAs

Inferences

• It is unequivocal that unifocalizing MAPCAs matters when native PAs are absent
• The absent PA group demonstrates that unifocalized MAPCAs function as PAs over the long term
• Can it really be argued that unifocalizing MAPCAs is not beneficial in the great majority of the other 65% of cases that range the spectrum of mixed blood supply from native PAs and MAPCAs? Not convincingly
Observations

- Overall, about 50% of all pts are as well off as TOF pt with a conduit.
- Another 30% are not quite that good
- 15% are worse again, but better than the natural Hx
- 5% are probably no better than the natural Hx

Can We Identify the Poor Outcome Patients Ahead of Time
Is Anyone Inoperable?

- There are 2 subgroups of pts who predictably require multiple peripheral PA operations, some of whom never achieve intracardiac septation:
  1. severely cyanotic immediately at birth
  2. “The 12% group”, or AP Window group (centrally confluent native PAs with normal arborization of native PAs and dual supply MAPCAs)

  Is it worth the effort in these subgroups?

  There are many successes

- Single ventricle pts with MAPCAS

Our Prospectively Applied Treatment Protocol

- MAPCAs
- TOF/PA
- OTHER
- Single Ventricle
- Two Ventricle
- MAPCAs have segmental level stenosis
- MAPCAs have abnormal or absent PAs

- Single Lung Unifocalization
- Simultaneous Intracardiac Repair
- Midline Complete Unifocalization
- Intraoperative Flow Study

- High PA Pressure
- Low PA Pressure
- Shunt
- Staged Intracardiac Repair
- Staged Intracardiac Repair
- Single Unifocalization
- Midline Single Unifocalization

- 12% 68%
- 13% 75%
- 56% 18%
Summary of Experience

- Complete One Stage Unifocalization can be achieved in most patients
- Intracardiac repair is possible in over half of pts at first unifocalization operation, and eventually about 90% achieve intracardiac repair with low RV pressure
- Selected patients (about 25%) are best managed initially by staged thoracotomy or surgical APW, rather than complete unifocalization

Summary of Experience

- The combination of DiGeorge and GE Reflux is a risk factor for mid term death
- The RV pressure does not show a tendency to rise over time, implying growth of the reconstructed PAs and MAPCAs
- Reintervention on the peripheral PA system is required in about one third of patients

Conclusion

- Using the decision making protocol described, improved early and midterm outcomes, as defined by survival with a complete repair and low RV pressure, can be achieved
- Early mortality is currently about 2%, however a midterm mortality of about 7% persists

MAPCAs

The Challenges

- Morphology – Highly variable patterns of:
  1) pulmonary artery size and arborization
  2) collateral origin, number, and course
  3) connections between the two
- Physiology – Although there is total mixing of the pulmonary and systemic circulations, there can be pulmonary overcirculation, or pulmonary undercirculation. Commonly both overcirculation and undercirculation occur simultaneously in the same patient.
MAPCAs
Unique Physiology

Whereas the duct (or shunt) dependant patient with a systemic saturation of 80% is both clinically stable AND has healthy pulmonary hemodynamics, the MAPCAs patient with a saturation of 80% is clinically stable but likely does not have healthy pulmonary hemodynamics.

- A decision to observe the first patient is appropriate; a similar decision for the second patient is not.
- Delayed stabilization of blood flow to all segments of lung leads to microvascular disease.

Natural History

- 50% die by age 3-5 yrs
- 80-90% die by a decade
- Few survivors beyond 30 yrs

PA. VSD. MAPCAS

Goals of Management

- Improve on the Natural History
- Achieve a completely separated two ventricle circulation (intracardiac repair with closure of VSD and creation of RV-PA connection)
- Achieve lowest possible RV pressure after repair

Most people agree on these goals

...But

Many disagree on how best to get there
How is a low RV pressure best achieved?

- By maintaining a healthy microvascular bed in every lung segment
- That means normalizing arterial flow and pressure in every lung segment as soon as possible

How do we do that?

MAPCAs

Given the complexity and variability of this lesion, a broadly applicable surgical management protocol is needed that:

- is physiologically and morphologically driven
- provides the most good for the greatest number of patients

Surgical Priorities

- Unifocalize early and completely
- Perform intracardiac repair as soon as, but only when, a low PVR is assured

Keeping these principles in mind, the morphology and physiology do determine the specific operative approach

Surgical Priorities

1. Midline complete unifocalization with intracardiac repair
2. Midline complete unifocalization with central aortopulmonary shunt
3. Central aortopulmonary window
4. Thoracotomies with staged unilateral unifocalizations
Surgical Principles

- Emphasis on early complete repair
- Emphasis on native tissue to tissue connections deep in lung parenchyma
- Recruit as many collaterals as possible initially
- Judicious decision making regarding VSD closure
- In staged pts: close FU and early cath to reintervene