Right Ventricular Failure - Anytime is a Bad Time

Eric R. Skipper, MD, FACS
Chief, Adult Cardiothoracic Surgery
Surgical Director Cardiac Transplantation
and Mechanical Assist
Sanger Heart and Vascular Institute

NCSRC Symposium 2012
34th Annual Meeting
September 28, 2012

Right Ventricular Failure - Anytime is a Bad Time

- No disclosures
- No conflicts of interest

Sanger Heart & Vascular Institute
Uncompromising Excellence. Commitment to Care.

Overview

- For decades, RV function was “under-valued”.
  - Basically..... a passive conduit for blood flow between the systemic and pulmonary circulation
- Currently, we realize:
  - incidence of RV failure approximates that of LV failure
  - RV failure can carry a worse prognosis than isolated LV failure
- Understanding both RV anatomy and physiology as well as the impact of RV dysfunction is essential in the management of these patients

Right Ventricular Anatomy / Physiology

- Receives blood from the right atrium (RA) and ejects blood into the pulmonary artery (PA)
- Divided into 2 sections
  - body or sinus - receives blood from the RA
  - outflow tract or conus (infundibulum) - funnels blood into the PA
  - Crista supraventricularis - muscular ridge separating the sinus region from the conus region

Right Ventricular Anatomy / Physiology

- Cross-sectional anatomy
  - Crescent-shaped
    - ➢ concave free wall
    - ➢ convex interventricular septum
  - Thin walled
    - ➢ 18% as much muscle mass as the LV
  - Overall design
    - ➢ accommodates increases in preload well
    - ➢ does not tolerate significant increases in afterload

Right Ventricular Anatomy / Physiology

- In contrast to the LV, the RV:
  - ➢ pumps blood under much lower pressures through a highly compliant vascular system (ie: the pulmonary vascular bed)
  - ➢ volume work, not pressure work
- RV ejection is dependent on:
  - ➢ contraction of it's free wall
  - ➢ contraction of the interventricular septum
  - ➢ twisting, corkscrew action of the LV

Causes of Right Ventricular Failure

- Normal afterload
  - RV infarction
- Increased afterload
  - PE
  - MV disease w pulmon htn
  - Congenital heart disease
  - OSA
  - ARDS
- Following cardiac or thoracic surgery
  - Inflammatory effects of CPB
  - Protamine
  - Extensive lung resection
  - LVAD
- Volume overload
  - ASD / VSD

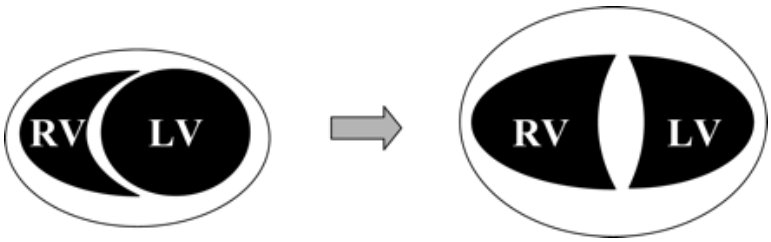
Right Ventricular Failure with Normal RV Afterload

- Myocardial Infarction - the most common senario
  - ➢RCA disease
  - ➢Left Circumflex disease (left dominant)
- Within the past decade, the high mortality in this patient population has been recognized

Consequences of Increased RV Afterload

- Opening of the pulmonary valve in systole is delayed
- RV pressure-volume curve assumes the shape of a "LV curve" -> greater oxygen consumption
- RV dilates -> increases wall stress (a major determinant of O2 demand)
- RVEDP increases -> RCA blood flow becomes restricted to a diastolic phoenomenon
- O2 supply is decreased inspite of an increasing demand
- TV annulus dilates -> TR which causes further dilation
- RV hypertrophy occurs due to increased wall stress
- Cresentric shape is lost and IVS buldges into the LV
- LV filling and function is impaired
- Systemic and coronary perfusion pressures decrease

Right Ventricular Failure - Schematic Representation



Consequences of Severe RV Failure - the avalanche.....

- High CVP and low systemic arterial pressure
  - ➢ impaired end organ perfusion
  - ➢ renal hypoperfusion with decrease UO and Cr clearance
  - ➢ tissue hypoperfusion with elevated serum lactate
  - ➢ hepatic hypoperfusion with elevated LFT's and coagulation abnormalities
  - ➢ eventual circulatory failure with MOSF and death

RV Failure - Evaluation of RV Dysfunction

- High index of suspicion
- Clinical signs
- ECG
- CXR
- Invasive monitors
  - CVP
  - SG catheter
    - ➢ TPG = mean PAP - PCWP
    - ➢ PVR = TPG / CO

RV Failure
- Evaluation of RV Dysfunction

- ECHO
  - clues
    - dilation
    - hypertrophy
    - contractility
    - septal shift
    - TR
  - Specifically
    - RV free wall motion
    - free wall thickness (>15 mm)
    - dilation
    - TR
    - tissue doppler tricuspid annular velocity
    - hepatic venous flow pattern

Right Ventricular Failure
- Perioperative Management

- Optimize preload
- Maintain AV synchrony (ie: NSR)
- Attn to factors that can alter PVR
  - PaO2
  - PCO2
  - pH
  - PCWP (LAP)
  - airway pressure
  - preload
    - » reduce with nitrates, diuretics, etc
  - BP - not too low, not too high....just right

Right Ventricular Failure- Perioperative Management - When the Above Fails.....

- Inotropes
- inhaled Nitric Oxode (iNO)
- inhaled Prostacyclin (iProstacyclin)
- Sildenafil
- Ventricular-Assist options
- “Creative Ventilator Tricks”
  - Collaboration is key
    - ➢ Respiratory Therapist
    - ➢ Pulmonary / Critical Care

Right Ventricular Failure - Inotropes

- Dobutamine
  - ➢ Beta 1 agonist with limited alpha 1 activity
- Phenylephrine / Norepinephrine
  - ➢ If arterial BP is low, vasoconstrictors may be beneficial
- Isoprenaline
  - ➢ pulmonary vasodilator
  - ➢ use is limited by tachycardia
- Phosphodiesterase inhibitors
  - ➢ cAMP pathway
  - ➢ vascular smooth muscle vasodilator

Right Ventricular Failure - Inhaled Nitric Oxide

- iNO activates guanylate cyclase
  - ➢ increased levels of cGMP
  - ➢ vasodilation
  - – excess NO binds to Hgb thus minimal systemic effect
- excellent in reducing PVR
- no documented survival benefit
- can be problematic in the setting of acute LV decompensation
- can cause an increase in PaO2 due to improved perfusion of ventilated areas
- can be associated with rebound pulmonary htn upon cessation of therapy
- usual starting dose is 20-40 ppm
- expensive

Right Ventricular Failure - Inhaled Prostacyclin

- iProstacyclin
  - binds to specific receptors in the pulmonary vascular bed resulting in vasodilation
    - ➢ comparable potency to iNO
  - rebound pulmonary hypertension can occur upon cessation of therapy
  - can be problematic in the setting of acute LV decompensation
  - usual starting dose is 2-4 ng/kg/min; range 2-16 ng/kg/min
  - less expensive than iNO
    - ➢ ~ 1/10th as much

Right Ventricular Failure - Sildenafil

- Sildenafil inhibits phosphodiesterase-5
  - ➢ the predominant isoform in pulmonary vascular smooth muscle
  - oral agent
  - usual dose 20-40 mg po q 8 hrs
  - can have a synergistic effect with iNO and iProstacyclin
  - rapid onset of action
  - a long-term treatment option

Right Ventricular Failure - Mechanical Circulatory Support

- RVAD
  - ➢ temporary
    - » percutaneous, transvenous (ie: Tandem)
    - » open (ie: Biomedicus, Centromag, etc)
  - ➢ long-term
    - » Thoratec
- LVAD
  - ➢ temporary
    - » percutaneous (Impella 2.5; Tandem)
    - » open (Impella 5.0; Biomedicus, Centromag, etc)
  - ➢ long-term
    - » Thoratec
- ECMO
  - ➢ Veno-arterial (VA)

Right Ventricular Failure - "Creative Ventilator Tricks"

- Goals
  - reduce RV afterload
  - improve pulmonary blood flow
  - augment cardiac output

Right Ventricular Failure Complicating Cardiac Surgery

- RV ischemia / infarct
  - native CAD
  - graft problem
- Air embolus
  - RCA is in vulnerable position
- Preexisting pulmonary htn worsened by:
  - mechanical ventilation
  - atelectasis
  - pleural effusion(s)
  - hypoxemia
  - hypercarbia
- Protamine
  - generates thromboxane A2
    - » pulmonary vasoconstriction
- Inadequate RV protection with cardioplegia
- Post cardiac transplant or VAD

Case #1

- 48 yo female
  - MVC
  - Surgery for open femur fracture right LE
  - Sudden intraop hypoxemia and hypotension
  - TEE --> RV strain; RV dilation; mild PI; thrombus at PA bifurcation
  - Continued hemodynamic deterioration - sys BP ~ 70; HR 140
  - Strategies:
    - ➢ IV primacor and levophed
    - ➢ Emergent operative pulmonary artery embolectomy
      - » not candidate for lytics
    - ➢ Consider iNO or iFlolan ??

Case #2

- 78 yo female
- CAD, Htn, DM, DLE, COPD with bronchospasm, Asthma, large right pleural effusion, Obesity, PAD, prior right CEA.....
- CABG x 3 and mitral valve repair
- POD #1
  - pO2 60 / pCO 50 on FiO2 .60 and 12 PEEP
  - sys BP 100; CVP 25; CI 1.9
  - UO 5-15 ml/hr
  - HGB 8.5
  - IV primacor and dopamine
- Strategies
  - ➢ Reduce peep; increase FiO2; increase vent rate
  - ➢ IV levophed or vasopressin; optimize IV primacor
  - ➢ CXR / TEE
  - ➢ Consider iNO or iFlolan

Case #3

- 40 yo male
- Ascending aortic aneurysm involving aortic root; 3+ AI; LVEF 35%; dilated, moderately HK RV; small RCA; small LCx PDA branch
- Repair of asc ao aneur with valve-sparing aortic root replacement
  - Small RCA orifice - preserved
  - Nongraftable RCA br's and LCx PDA
  - No change in RV fxn on TEE
- Progressive pressor / vasoconstr requirements over 1st two POD's
  - Elevated CVP; normal PAP's
  - Low or borderline UO
  - Rising creatinine and LFT's
  - TEE --> dilated, HK (near AK) RV; dilated RA; no effusion
- Strategies
    - ➢ iNO or iFlolan
    - ➢ off-load / rest RV --> temporary RVAD

Case # 4

- 37 yo male
- NICM with LVEF 10%; home IV primacor therapy; Htn; DLE; Obesity (BMI 40); Severe pulmonary htn; Deconditioned
- Admitted with low output state - CI 1.0; PAP's 90/40; CVP 35
- IV Dobuta added; CI 1.3
- Diuretic tx --> CVP 28
- Strategies
    - ➢ Sildenafil
    - ➢ iNO; iFlolan
    - ➢ temporary lvad
    - ➢ long-term lvad
        - » bridge-to-decision; possible OhTx

Thank you

Questions?

STATE OF ART: ISHLT SUMMARY STATEMENT

World Health Organization Pulmonary Hypertension Group 2: Pulmonary hypertension due to left heart disease in the adult—a summary statement from the Pulmonary Hypertension Council of the International Society for Heart and Lung Transplantation

James C. Fang, MD,[a] Teresa DeMarco, MD,[b] Michael M. Givertz, MD,[c] Barry A. Borlaug, MD,[d] Gregory D. Lewis, MD,[e] J. Eduardo Rame, MD, Mphil,[f] Mardi Gomberg-Maitland, MD, MSc,[g] Srinivas Murali, MD,[h] Robert P. Frantz, MD,[i] Dana McGlothlin, MD,[j] Evelyn M. Horn, MD,[k] and Raymond L. Benza, MD[l]

Sanger Heart & Vascular Institute
Uncompromising Excellence. Commitment to Care.

Trial	Subjects	Drug	Inclusion criteria	Primary end-point	Study	Comments
FIRST	471	Epoprostenol: 4.0 ng/kg/min (median)	EF < 25%, NYHA III-IV, mPAP > 25 mm Hg	Survival	Negative	Acute—improvements in mPAP, mPCWP, and PVR Chronic—no improvement in 6MWT, QOL, or morbidity
RITZ-1	669	Tezosentan: 25 mg/h IV × 1 hr; then 50 mg 24–72 hrs	Acute hospitalization	Symptoms at 24 hrs	Negative	Time to death or worsening CHF in 24 hrs also not significantly different
RITZ-2	215	Tezosentan 50 or 100 mg/h IV	Acute hospitalization, CI < 2.5 liters/min/m2 L2 and PCWP < 15 mm Hg	CI at 6 hrs	Positive	Improvement of 0.37 to 0.38 liters/min/m2 L2 with decreased in PCWP pressure
RITZ-5	84	Tezosentan: 50–100 mg/h × 24 hrs	Acute pulmonary edema: oxygen, furosemide, morphine, isosorbide dinitrate background	Change in arterial oxygen saturation	Negative	No change in saturation, death, recurrent pulmonary edema, mechanical ventilation, and myocardial infarction
ENABLE	1613	Bosentan: 125 mg bid, 9 mos	EF < 35%, NYHA IIIB-IV	All cause mortality + CHF hospitalization	Negative	Primary end point reached: 321/808—placebo: 312/805—bosentan: worsening CHF on bosentan
REACH-1	370	Bosentan: 250 mg bid, 6 mos	LVEF < 35%, NYHA III-IV, 6MWT < 375 m	Change in clinical status	Negative	Early termination due to liver function abnormalities
HEAT-1	179	Darusentan: dose range, 3 wks: 30, 100, 300 mg	EF < 35%, NYHA III PCWP > 12 mmHg, CL < 2.6 liters/min/m2	Change in PCWP/CI	Negative	Increased CI and reduced SVR vs placebo. No significant change in PCWP, mPAP, PVR, RAP, HR, and MAP. Worsening heart failure with high dose
EARTH-2	642	Darusentan: dose range, 24 wks: 10, 25, 50, 100, 300 mg	LVEF < 35%, NYHA II-IV	Change in LV end-systolic volume measured by MRI	Negative	No significant effect on remodeling of the heart or dirical symptoms

Trial	Subjects	Drug	Inclusion criteria	Primary end-point	Secondary end-points	Study	Results
PROMISE	1,088	Milrinone: 10 mg po qid	NYHA III-IV on conventional therapy; LFEF ≤ 35%	All cause mortality	CV mortality, # hospitalizations, addition of vasodilators, symptoms, adverse reactions	Negative	Increased mortality 28% (95% CI, 1%–61%; p = 0.016), worse in sicker pts: 53% mortality, more hospitalizations hypotension, syncope
ESSENTIAL I + II	1,854	Enoximone: 50-150 mg tid	LVEF ≤ 30%; NYHA III-IV, 1 hospitalization or 2 clinic visits (1 yr), LVEDD > 3.2 cm/m^2	Co-primary: All-cause mortality or, cardiovascular hospitalization	6MWD, QOL	Negative	No difference in HF, 0.97 (95% CL, 0.86, 1.12); safe but ineffective
Sildenafil/ placebo in Chronic Heart Failure	46	Sildenafil: 6 mos, 50 mg tid	<65 yrs, NYHA II-III; cardiomyopathy, LVEF < 45%	Change in ex capacity, ventilation efficiency, + symptoms	QOL	Positive	Improved exercise ventilation and aerobic efficiency
Sildenafil/ placebo in Chronic Heart Failure	34	Sildenafil: 12 wks, 25–75 mg tid	≥ 18 yrs; NYHA II-IV on conventional therapy LFEF ≤ 40%; mPAP > 25 mm Hg	Peak Vo_2	6MWD, hemodynamics, QOL, RV/LV performance, NT-proBNP	Positive	Improved peak Vo_2, 6MWD, and QOL; decreased CHF hospitalizations
RELAX	190 (est.)	Sildenafil: 12 wks 20 mg tid, followed by 12 wks 60 mg tid	60+ yrs, NYHA II-IV, EF > 50%, NT-proBNP > 400 pg/ml	Peak Vo_2	Change in sub-max exercise capacity, change in a composite score reflective of clinical status	Ongoing	Ongoing

Inhaled nitric oxide after left ventricular assist device implantation: A prospective, randomized, double-blind, multicenter, placebo-controlled trial

Evgenij Potapov, MD, PhD,[a] Dan Meyer, MD,[b] Madhav Swaminathan, MD,[c] Michael Ramsay, MD,[d] Aly El Banayosy, MD,[e] Christoph Diehl, MD,[f] Bryan Veynovich, DO,[g] Igor D. Gregoric, MD,[h] Marian Kukucka, MD,[a] Tom W. Gromann, MD,[a] Nandor Marczin, MD, PhD,[i] Kanti Chittuluru, MD,[j] James S. Baldassarre, MD,[j] Mark J. Zucker, MD,[k] and Roland Hetzer, MD, PhD[a]

Sanger Heart & Vascular Institute
Uncompromising Excellence. Commitment to Care.