VEITH 2017
Wednesday, November 15
7:55-8:00 AM
Session 32

HOW TO MANAGE RENAL DYSFUNCTION AND HYPERTENSION IN PATIENTS WITH ATHEROSCLEROTIC RENAL ARTERY STENOSIS: WHEN IS MEDICAL TREATMENT OR STENTING/BYPASS INDICATED DESPITE THE CORAL AND ASTRAL TRIALS

THOMAS SOS, MD
NYPH CORNELL
New York, NY

Potential conflicts of interest
• Royalties
  AngioDynamics, Inc.
  Cook, Inc.
• Ownership
  Confluent Medical, Inc. (NDC, Inc.)
  Venity, Inc.

CONCLUSIONS

"RENAL ARTERY STENTING DID NOT CONFER A SIGNIFICANT BENEFIT... WHEN ADDED TO COMPREHENSIVE, MULTIFACTORIAL MEDICAL THERAPY IN PEOPLE WITH ATHEROSCLEROTIC RENAL-ARTERY STENOSIS AND HYPERTENSION OR CHRONIC KIDNEY DISEASE."

DE BRUYNE K, et al, Journal of the American College of Cardiology
Volume 48, Issue 9, 7 November 2006, Pages 1851-1855

ASSESSMENT OF RENAL ARTERY STENOSIS SEVERITY BY PRESSURE GRADIENT (Pd/Pa) and RENIN PRODUCTION

84F CHF, CKD (Scr 2.9), HTN, COPD

• ADMITTED TO CCU
  – Oliguria, ANURIA, Scr 2.8 > 4.6
  – Sonogram: R kidney 6.8mm, B/L mild IRI
  – BP 180/80
  – BNP 2000 pg/mL
  – Failing diuretics
  – Decompensated CHF
  – Pulmonary edema
  – Respiratory failure > intubated
• Dx’s: AKI, CKD, 2° CARD DYSFXN

DAY AFTER ADMISSION
84F CHF, CKD (Scr 2.9), HTN, COPD

**CLINICAL COURSE**

**PRE STENT**

**POST STENT**

84F CHF, CKD (Scr 2.9), HTN, COPD

**CLINICAL COURSE**

**PRE STENT**

**POST STENT**

**CONCLUSIONS**

- **CORAL** “RENAL ARTERY STENTING DID NOT CONFER A SIGNIFICANT BENEFIT...IN PEOPLE WITH Atherosclerotic Renal Artery STENOSIS AND HYPERTENSION OR CHRONIC KIDNEY DISEASE.”
- **SOS**: THE CORAL RESULTS APPLY ONLY TO THE POPULATION STUDIED, MOST WITH HEMODYNAMICALLY INSIGNIFICANT or UNCERTAIN STENOSIS and WITHOUT CONFIRMATORY PRESSURE GRADIENTS.
- **WHITHER CMS?!**

**NEWSFLASH**
WHEN TO **EVALUATE** for RENAL ARTERY STENOSIS

CLINICAL CRITERIA

• RENAL DYSFUNCTION
  - RECENT ONSET or PROGRESSIVE
  - MODERATE TO SEVERE

• HYPERTENSION
  - DIFFICULT TO CONTROL
  - SEVERE or RECENT ONSET

• PULMONARY EDEMA
  - RECURRENT FLASH

• ?JEOPARDIZED RENAL PARENCHYMA?

WHEN TO **INTERVENE** for RENAL ARTERY STENOSIS

ANATOMIC CRITERIA

• BILATERAL/SOLITARY KIDNEY DISEASE

• ≥70% D STENOSIS (~85% XS AREA)

• COLLATERAL CIRCULATION

• POST STENOTIC DILATATION

• REDUCTION of RENAL SIZE
  - RENAL LENGTH ≤ 7-8 cm
  - LENGTH DISCREPANCY ≥ 1.5 cm
  - DOCUMENTED LENGTH ≥ 1 cm

RENAL ARTERY STENOSIS

DIAGNOSIS AND TREATMENT

CLINICAL SUSPICION, PRA WITH ACEI

- RVR ASSAY WITH ACEI
- NUCLEAR SCAN WITH ACEI
- DUPLEX ULTRASOUND
- HELICAL CONTRAST CT
- MRA WITH GADOLINIUM

CHOOSE ONLY ONE

- MEDICAL RX
- PTRA/STENT/SURGERY

ISCHEMIC NEPHROPATHY

DIAGNOSIS AND TREATMENT

CLINICAL SUSPICION: NO Hx MED. NEPHROPATHY

- MEDICAL RX
- PTRA/STENT/SURGERY

84F CHF, CKD (CR 2.8), HTN, COPD

- 2mm BALLOON
- 5mm x 2cm STENT
- 5mm x 2cm STENT

THANK YOU FOR YOUR ATTENTION
84F CHF, CKD (SCr 2.9), HTN, COPD

• PRESENTED TO ED (2x IN 1 WK)
  – CHEST TIGHTNESS & SOB x 1 WEEK
  – 3+ PILLOW ORTHOPNEA
  – T36.5 | HR 101 | BP 179/79 | RR 18 | SPO2: 97 RmAIR
  – BNP 2000 pg/mL
  – SCr 2.9

• ADMITTED FOR CONTROL OF EXACERBATION OF RI, CHF & COPD

84F CHF, CKD (SCr 2.9), HTN, COPD DAY OF ADMISSION

• RENAL DUPLEX US (C/W 2 YEARS PREVIOUSLY):
  – NEW RIGHT RENAL ATROPHY
    o RIGHT 6.8CM (PREV 9.3cm). NEW CORTICAL THINNING.
  – B/L PERSISTENT MILD NONSPECIFIC ELEVATED RI.
    o RIGHT 0.75; LEFT 0.76

84F CHF, CKD (SCr 2.9), HTN, COPD

CLINICAL COURSE

• B/L RAS
  – OCCLUDED R RA, ATROPHIC KIDNEY
  – LEFT KIDNEY - PINHOLE PROXIMAL RENAL ARTERY STENOSIS

• EXTUBATED 2 DAYS POST RA STENT

• AUTO DIURESIS STARTED DURING PROCEDURE

• SCr DECREASED

84F CHF, CKD (SCr 2.8), HTN, COPD

• ECHOCARDIOGRAM:
  – CONCENTRIC LVH
  – EF 35% (70% 3 WEEKS PREVIOUSLY )

• CORONARY ARTERIOGRAM:
  – NORMAL 2 YEARS PREVIOUSLY
RENAL ARTERY STENOSIS, HYPERTENSION and RENAL INSUFFICIENCY

THE PROBLEM?

IS THE SOLUTION!

RENAL VASCULAR HYPERTENSION

RENIN/ANGIOTENSIN/ALDOSTERONE SYSTEM

ASSESSING SIGNIFICANCE

• CLINICAL
  - BP
  - RENAL FUNCTION
  - FLASH PULMONARY EDEMA

• ANATOMIC
  - DIAMETER STENOSIS ≥70% (~90% XA) (USUALLY “EYEBALL” MEASUREMENT)

• HEMODYNAMIC/PHYSIOLOGIC
  - ≥10% MEAN ARTERIAL PRESSURE GRADIENT
  - ??? DUPLEX ULTRASOUND

RENAL VASCULAR HYPERTENSION

CLINICAL CHARACTERISTICS

• RECENT ONSET
  - ATEROMA: MEN AGE ≥55
  - FMD: YOUNG WOMEN

• DIFFICULT TO CONTROL

• RETINOPATHY, END ORGAN DAMAGE

• RENAL DYSFUNCTION

• RECURRENT FLASH PULMONARY EDEMA

• CONTINUOUS ABDOMINAL BRUIT

• HISTORY OF SMOKING

• OTHER VASCULAR DISEASE

RENAL ARTERY STENOSIS

ASSESSING SIGNIFICANCE

• CLINICAL
  - BP
  - RENAL FUNCTION

• ANATOMIC
  - DIAMETER STENOSIS ≥70% (~90% XA) (USUALLY “EYEBALL” MEASUREMENT)

• HEMODYNAMIC/PHYSIOLOGIC
  - ≥10% MEAN ARTERIAL PRESSURE GRADIENT
  - ??? DUPLEX ULTRASOUND

ISCHEMIC NEPHROPATHY

CLINICAL CHARACTERISTICS

• NO INTRINSIC RENAL DISEASE

• RECENT ONSET AZOTEMIA

• PROGRESSIVE AZOTEMIA

• HYPERTENSION

• OTHER VASCULAR DISEASE

• SMOKING

• UNEQUAL KIDNEY SIZE
**RENAL ARTERY STENOSIS**

**WHEN NOT TO INTERVENE**

- **Atheroma**
  - **NO SIGNIFICANT PRESSURE GRADIENT**
  - **EASILY CONTROLLED HYPERTENSION**
  - **MILD STABLE RENAL DYSFUNCTION?**
  - **INCIDENTALLY DISCOVERED STENOSIS WITHOUT PRIOR CLINICAL EVALUATION**

→ **NO INTERVENTION**

**PHYSIOLOGIC SCREENING & CRITERIA**

- **RADIONUCLIDE SCAN**
- **DUPLEX ULTRASOUND**
- **RENAL VEIN RENIN ASSAY** / ***
- **≥10% MEAN ARTERIAL PRESSURE GRADIENT***

* UNRELIABLE IN BILATERAL DISEASE & T|Scr
** TECHNICALLY DIFFICULT & OPERATOR DEPENDENT
*** INVASIVE

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**RENAL ARTERY STENOSIS**

**PHYSIOLOGIC SCREENING & CRITERIA**

- **RADIONUCLIDE SCAN**
- **DUPLEX ULTRASOUND**
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**RENOVASCULAR HYPERTENSION**

**DIAGNOSIS AND TREATMENT**

- **CLINICAL SUGGESTION, PRA WITH ACEI**
  - **RVR ASSAY WITH ACEI**
  - **NUCLEAR SCAN WITH ACEI**
  - **DUPLEX ULTRASOUND**
  - **HEMICAL CONTRAST CT**

- **CHOSE ONLY ONE**

**MEDICAL RX**

**PTRA/STENT/SURGERY**

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**ISCHEMIC NEPHROPATHY**

**DIAGNOSIS AND TREATMENT**

**NEPHROGENIC/ISCHEMIC FIBROSIS??**

- **RENAL SIZE ASYMMETRY**
- **RENAL ARTERY STENOSIS**
- **?INCREASED RESISTIVE INDEX?**

**IA DSA & PRESSURE GRADIENT**

**MEDICAL RX**

**PTRA/STENT/SURGERY**

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**FMD CLASSIFICATION**

**PATHOLOGY**

- **INTIMAL FIBROPLASIA**
  - 1–2%
- **MEDIAL FIBROUS DYSPLASIA**
  - 60–70%
- **IMMEDIATE HYPERPLASIA**
  - 5–15%

**FREQUENCY**

**PATHOLOGY**

- **POSSIBLE HYPERPLASIA**
- **PERIMEDIAL FIBROPLASIA**
- **ADVENTITIAL FIBROPLASIA**

**FREQUENCY**

- 15–25%
- 5–10%
- <1%
**BP RESULTS of PTRA**

<table>
<thead>
<tr>
<th>AUTHOR</th>
<th>PTS. n</th>
<th>1º SUCC. n (%)</th>
<th>CURED n (%)</th>
<th>IMPR. n (%)</th>
<th>F/U Mos MEAN (RANGE)</th>
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<tbody>
<tr>
<td>SOS</td>
<td>31</td>
<td>27 (87)</td>
<td>16 (59)</td>
<td>9 (33)</td>
<td>16 (4-40)</td>
</tr>
<tr>
<td>TEGTMeyer</td>
<td>27</td>
<td>27 (100)</td>
<td>10 (37)</td>
<td>17 (83)</td>
<td>NA (2-51)</td>
</tr>
<tr>
<td>GEYSKES</td>
<td>21</td>
<td>21 (100)</td>
<td>10 (48)</td>
<td>10 (48)</td>
<td>NA (12-48)</td>
</tr>
<tr>
<td>MARTIN, L</td>
<td>20</td>
<td>20 (100)</td>
<td>5 (25)</td>
<td>12 (60)</td>
<td>16 (3-36)</td>
</tr>
<tr>
<td>MARTIN, E</td>
<td>11</td>
<td>8 (73)</td>
<td>5 (63)</td>
<td>1 (13)</td>
<td>13 (NA)</td>
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<tr>
<td>GRIM</td>
<td>10</td>
<td>9 (90)</td>
<td>5 (56)</td>
<td>4 (44)</td>
<td>10 (1-14)</td>
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<tr>
<td>TOTAL</td>
<td>120</td>
<td>112 (93)</td>
<td>51 (46)</td>
<td>53 (47)</td>
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</tbody>
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**ATHEROMATOUS RENAL ARTERY STENOSIS (ARAS) PREVALENCE**

- In hypertensive population: 5.0%
- In pts with clinically manifest chronic renal disease: 5.5%
- In pts with ESRD: 2.1-16.5%
- In cardiac cath pts with (> 50-70% RA stenosis): 6-8%
- In autopsy of CVA deaths (> 75% RA stenosis): 10%

**HEMODYNAMICALLY SIGNIFICANT RENAL ARTERY STENOSIS CARDIOVASCULAR EFFECTS**

- Angiotensin II release
  - Vasoconstriction
  - Hypertension
  - Aldosterone release
  - Cellular hypertrophy
  - Proliferation of vascular smooth muscle
  - Vascular wall and LV hypertrophy
  - Accelerated atherosclerosis
  - Glomerular sclerosis
HEMODYNAMICALLY SIGNIFICANT RENAL ARTERY STENOSIS
CARDIOVASCULAR EFFECTS (cont.)

• ESRD DUE to ARAS
  – MEDIAN SURVIVAL 25 MONTHS
  – 5 YEAR SURVIVAL 18%
• INCREASED NITRIC OXIDE PRODUCTION
• INCREASED INTRARENAL PROSTAGLANDIN CONCENTRATION
• INCREASED SYMPATHETIC NERVE ACTIVITY

RENAL ARTERY ANGIOPLASTY ANATOMIC INDICATIONS

• PRIMARY
  – NON OSTIAL ATEROMATOUS STENOSSES
  – ALL NON ATEROMATOUS STENOSSES, EXCEPT RENAL TRANSPLANT ARTERY ANASTOMoses
• SECONDARY
  – POST ANGIOPLASTY RECURRENCE
  – POST STENT RECURRENCE

RENAL ARTERY STENTING ANATOMIC INDICATIONS

• PRIMARY
  – ATEROMATOUS OSTIAL STENOSIS
  – TRANSPLANT RENAL ARTERY STENOSIS
  – DISSECTING ANEURYSM
• SECONDARY
  – RESTENOSIS POST PTRA
  – OCCLUSIVE COMPLICATIONS OF PTRA
  – UNSUCCESSFUL / INADEQUATE PTRA
  • RESIDUAL STENOSIS ≥50% DIAMETER
  • RESIDUAL GRADIENT ≥10% MEAN ARTERIAL PRESSURE

RENAL ARTERY STENTING

Cr, RENAL FUNCTIONAL RESERVE (GFR) AND RISK OF INTERVENTION

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<th>PRIMARY</th>
<th>SECONDARY</th>
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<td>NON OSTIAL ATEROMATOUS STENOSSES</td>
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  • RESIDUAL GRADIENT ≥10% MEAN ARTERIAL PRESSURE

Renal Transplant Artery Stenting

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<th>Renal Function Reserve (GFR)</th>
<th>High Risk</th>
<th>Int. Risk</th>
<th>Low Risk</th>
</tr>
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<tbody>
<tr>
<td>Normal Serum Cr</td>
<td>25</td>
<td>50</td>
<td>75</td>
</tr>
<tr>
<td>% Renal Functional Reserve (GFR)</td>
<td>100</td>
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**CHOLESTEROL EMBOLIZATION**

**AORTA - MOST HOSTILE ENVIRONMENT FOR ENDOVASCULAR THERAPY!**

**RENO ARTERY STENTING**

**CAN WE REDUCE THE RISKS?**

- **APPROPRIATE PATIENT SELECTION**
- **REDUCE IODINATED CONTRAST**
- **METICULOUS TECHNIQUE with MINIMAL MANIPULATION**
- **LOWER PROFILE STENTS?**
- **EMBOLIC PROTECTION??**

---

**APPROPRIATE PATIENT SELECTION**

**REDUCE IODINATED CONTRAST**

**METICULOUS TECHNIQUE with MINIMAL MANIPULATION**

**LOWER PROFILE STENTS?**

**EMBOLIC PROTECTION??**

---

**RENO ARTERY STENTING**

**CONTRAST SAVING STRATEGIES**

**TOTAL CONTRAST USED/PROCEDURE**

- **1/3 – 1/2 DILUTE IODINATED CONTRAST (ml)**
  - DIAGNOSTIC AORTOGRAM 10
  - STENT POSITIONING ANGIO 5
  - COMPLETION AORTOGRAM 5
  - TOTAL 1/3-1/2 DILUTE 20
  - TOTAL “FULL STRENGTH” 7-10

---

**# 1: PRIMUM NON NOCERE**

**OR**

**THOU SHALT NOT SCREW AROUND**

- **INTERVENE ONLY WHEN INDICATED**
- **THINK THROUGH THE CASE BEFORE YOU START**
  - EQUIPMENT, TECHNIQUE, APPROACH
  - ALTERNATE CHOICES
  - BE PREPARED FOR THE WORST
- **WORK FAST, BUT CAREFULLY**

---

**# 2: LIMIT CONTRAST**

- **THE IODINATED PARTICLE IS TOXIC**
- **USE 150 mg I/ml (30% I) CONTRAST**
- **FOR AORTOGRAM USE 10 cc/s X 1 s**
- **USE NON REFLUX FLUSH CATHETER**
- **USE CO2 or GAD?**
- **NO/LIMIT TEST INJECTION**
- **NO/LIMIT SELECTIVE ARTERIOGRAM**
- **FENOLDOPAM & n-ACETYL CYSTEINE?**
- **HYDRATION & SODIUM BICARBONATE**

---

**# 3: PROPER OBLIQUITY**

**CT: 160 PTS (320 RA's) AGES 1-92**

- **RRA 30° ± 19°**
- **LRA ± -6° ± 15°)**

**KIM PA, KHLINNAI NM, TROST DW, SOS TA, LEE L.**

**J VASC INTERV RADIOL. 1999 JAN;10(1):37-9**
# 3: PROPER OBLIQUITY

**AXIAL MRA or CTA**

- TO SELECT PROPER OBLIQUITY FOR AORTOGRAM and INTERVENTION
- TO IDENTIFY PRECISELY:
  - THE OSTIUM
  - THE LOCATION OF STENOSIS
  - THE AORTIC ORIGIN ("NUBBIN") OF THE OCCLUDED RENAL ARTERY

# 3: CORRECT OBLIQUITY

**RENAL ARTERY IMAGING and STENTING**

- **AP**
  - AORTIC WALL
- **LAO**
  - AORTIC WALL
  - CORRECT STENT PLACEMENT

# 2: LIMIT CONTRAST

**FLUSH CATHETERS**

- **4 F PIGTAIL**
- **4 F OMNIFLUSH™**

- 1:75 sec
- 30% Iodine 10cc @ 10cc/sec

# 5a: CROSSING STENOSES

**THE "SOS FLICK"**

- SOFTVU™ SOS OMNI SELECTIVE™ and BENTSON™

THE “NO TOUCH TECHNIQUE

**CROSSING RENAL ARTERY STENOSIS**

- 0.014” WIRE
- 0.035” WIRE

**CRITICAL DEGREE OF RENAL ARTERIAL STENOSIS THAT CAUSES HYPERTENSION IN DOGS**

MASAHTO IMANISHI, SATOSHI AKABANE, MAKOTO TAKAMIYA, MINORU KAWAMURA, YOHKAZU MATSUSHIMA, MORIO KURAMOCHI AND TERUO OMAE

“CRITICAL RENAL ARTERIAL STENOSIS OF 70-75 % OF THE DIAMETER ...LEADS TO THE DEVELOPMENT OF RENIN-DEPENDENT RENOVASCULAR HYPERTENSION”

Angiology 1992; 43; 833
CRITICAL STENOSIS IN PATIENTS WITH Atherosclerotic RENOVASCULAR DISEASE APPEARS TO BE 80% OR GREATER.

*CRITICAL STENOSIS IN PATIENTS WITH Atherosclerotic RENOVASCULAR DISEASE APPEARS TO BE 80% OR GREATER.*

**INTER-OBSERVER VARIABILITY IN THE ANGIOGRAPHIC ASSESSMENT OF RENAL ARTERY STENOSIS.**

**INTER-OBSERVER VARIABILITY IN THE ANGIOGRAPHIC ASSESSMENT OF RENAL ARTERY STENOSIS.**


**PHYSIOLOGIC SCREENING & CRITERIA**

- **RENAL ARTERY STENOSIS**
- **WHEN TO INTERVENE**
- **PHYSIOLOGIC SCREENING & CRITERIA**

- **RADIONUCLIDE SCAN**
- **DUPLEX ULTRASOUND**
- **RENAL VEIN RENIN ASSAY**
- **≥10% MEAN ARTERIAL PRESSURE GRADIENT**

* UNRELIABLE IN BILATERAL DISEASE & \( \uparrow \) Scr
** TECHNICALLY DIFFICULT & OPERATOR DEPENDENT
*** INVASIVE

**CONCLUSION:**

ONE SIDE WOULD INTERVENE IN ANY PATIENT WHO HAS AT LEAST A 50% STENOSIS, WHETHER OR NOT THE PATIENT HAS CLINICAL SYMPTOMS. THE OTHER SIDE WOULD NOT INTERVENE IN ANY RENAL ARTERY STENOSIS, REGARDLESS OF THE PRESENCE AND SEVERITY OF THE SYMPTOMS, HYPERTENSION TO SEVERE RENAL DYSFUNCTION...PHYSICIANS WHO WOULD TAKE THE MIDDLE GROUND WOULD TRY TO FIND SOME REASONABLE CRITERIA FOR INTERVENTION...THE APPROPRIATENESS OF RENAL ARTERY STENTING HAS YET TO BE SUFFICIENTLY RESOLVED. THE BEST HOPE SO FAR IS CORAL, BUT I FEAR ITS RESULTS MAY NOT YIELD THE CLARITY WE ALL SEEK.

**The Renal Stenting Debate**

BY THOMAS A. SOS, MD

ENDOVASCULAR TODAY JANUARY 2006

**STAR STUDY 2009**

NO GRADIENTS MEASURED!
The ASTRAL Investigators
NEJM 361:1953-1962 November 12, 2009 Number 20

Revascularization versus Medical Therapy for Renal-Artery Stenosis

TRIAL DESIGN LIMITATIONS

• PATIENT SELECTION (CONT.)
  - "PATIENTS WERE NOT ELIGIBLE IF THEY REQUIRED SURGICAL REvascularIZATION OR WERE CONSIDERED TO HAVE A HIGH LIKELiHOOD OF REvascularIZATION WITHIN 6 MONTHS"
  - "THERE IS A CONSENSUS, WHICH IS NOT EVIDENCE-BASED, THAT CERTAIN GROUPS OF PATIENTS WITH SEVERE RENAL-ARTERY STENOSIS (E.G., THOSE PRESENTING WITH ACUTE KIDNEY INJURY OR "FLASH" PULMONARY EDEMA) SHOULD BE TREATED WITH REvascularIZATION, AND SUCH PATIENTS WERE UNLIKELY TO HAVE BEEN INCLUDED IN OUR TRIAL"
Revascularization versus Medical Therapy for Renal-Artery Stenosis
The ASTRAL Investigators
NEJM 361:1953-1962 November 12, 2009 Number 20

VERY SEVERE ANATOMICAL DISEASE
BILATERAL RENAL-ARTERY STENOSIS >70% (N=103) OR RENAL ARTERY
STENOSIS >70% IN A SOLITARY FUNCTIONING KIDNEY (N=60)*

THERE IS A CONSENSUS, WHICH IS NOT EVIDENCE-BASED, THAT CERTAIN
GROUPS OF PATIENTS WITH
SEVERE RENAL-ARTERY STENOSIS
(E.G., THOSE
PRESENTING WITH
ACUTE KIDNEY INJURY OR "FLASH" PULMONARY EDEMA
SHOULD BE TREATED WITH REVASCULARIZATION,
AND
SUCH PATIENTS WERE
UNLIKELY TO HAVE BEEN INCLUDED IN OUR TRIAL

November 18, 2013, at NEJM.org.

SLOW SITE and PATIENT RECRUITMENT
CORAL
NEEDED CHANGE!

RELAX INCLUSION CRITERIA
STOP STUDY

REVISIONS TO STUDY DESIGN

INCLUSION CRITERIA
• HYPERTENSION ≥ 155 mmHg ON 2 OR MORE ANTIHYPERTENSIVE MEDICATIONS
• ONE OR MORE RENAL ARTERY STENOSIS
• ≥ 80% - <100% BY ANGIOGRAPHY
• ≥ 60% - < 80% BY ANGIOGRAPHY WITH ≥ 20 mmHg SYSTOLIC PRESSURE GRADIENT OPTIONAL

PROTOCOL
• ONLY US SITES
• MANDATORY USE OF DPD

IT’S THE GRADIENT, STUPID!!

THE CARDIOVASCULAR OUTCOMES WITH RENAL
ATHEROSCLEROTIC LESIONS (CORAL) STUDY:
Background and Methods
BY DESIGN (“NEED SURGERY or LIKELY TO NEED
REVASCULARIZATION IN 6 MONTHS, VERY SEVERE STENOSES”)
THANK YOU
FOR YOUR ATTENTION

PREDICTION OF HYPERTENSION IMPROVEMENT AFTER STENTING OF RENAL ARTERY STENOSIS: COMPARATIVE ACCURACY OF TRANSLATIONAL PRESSURE GRADIENTS, INTRAVASCULAR ULTRASOUND, AND ANGIOGRAPHY

77 y.o. WOMAN
BILAT RA DISEASE, HYPERTENSION, CRI, SJÖGREN’S

77 y.o. WOMAN
BILAT RA DISEASE, HYPERTENSION, CRI, SJÖGREN’S

# 2: LIMIT CONTRAST
OMNIFLUSH™ RECURE TYPE
FLUSH CATHETER for AORTOGRAM

# 9: COMPLETION AORTOGRAM

PRE INTERVENTION Gad MRA

HYPERTENSION x 15 yrs
CHF x 2
SEVERE R RAS L RA OCOL Dx by MRA
BILAT RAS LEFT RENAL ATROPHY Dx by US
ACUTE AFF

SCr mg/dl

5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0

5/5/16
5/7/16
5/9/16
5/11/16
5/13/16
5/15/16
5/17/16
5/19/16
5/21/16
5/23/16
5/25/16
5/27/16
5/29/16
5/31/16
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6/4/16
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1/3 DILUTE I, 5 cc @ 7 cc/sec
What Is The Role Of Renal Artery Stenting After The CORAL, [STAR] and ASTRAL Trials

THOMAS SOS, MD
NYPH CORNELL
New York, NY

References

TRIAL DESIGN LIMITATIONS

• PATIENT SELECTION

- "Patients were eligible to participate if they had substantial anatomical atherosclerotic stenosis in at least one renal artery that was considered potentially suitable for endovascular revascularization and if the patient’s doctor was uncertain that the patient would definitely have a worthwhile clinical benefit from revascularization…"
A Critical Analysis Of The Renal STENT [Angioplasty] Data

THOMAS SOS, MD
NYPH CORNELL
New York, NY

AIM Symposium
2014
New York City

STENTING “NOT SUPERIOR” to MEDICAL RX
OVERALL STUDY DESIGN

• PROTOCOL - MAN
• STATISTICAL - ADEQUATE
• CLINICAL - MOST LIKELY TO BENEFIT FROM INTERVENTION MAY NOT HAVE BEEN EXCLUDED
• UNFORTUNATELY, THE RESULTS PROBABLY DO NOT REPRESENT “REAL WORLD” EXPERIENCE

ASTRAL and STAR
WHY STENTING “FAILED” vs MEDICAL RX
STUDY DESIGN

• STATISTICAL - UNDERPOWERED
• CLINICAL - PATIENTS MOST LIKELY TO BENEFIT WERE EXCLUDED (PATIENT and/or MD PREFERENCE FOR INTERVENTION)

ASTRAL and STAR
WHAT HAVE WE LEARNED?

• UNFORTUNATELY, THE RESULTS PROBABLY DO NOT REPRESENT “REAL WORLD” EXPERIENCE

• OPTIMAL MEDICAL THERAPY IS EASIER TO STANDARDIZE
• LARGE SINGLE CENTER STUDIES MAY PRODUCE BEST RESULTS ACHIEVABLE

ASTRAL and STAR
PREDICTION OF HYPERTENSION IMPROVEMENT AFTER STENTING OF RENAL ARTERY STENOSIS: COMPARATIVE ACCURACY OF TRANSLESIONAL PRESSURE GRADIENTS, INTRAVASCULAR ULTRASOUND, AND ANGIOGRAPHY

Massoud A. Leesar, Jai Varma, Adam Shapira, Ibrahim Fahsah, Seyed T. Raza, Ziad Elghoul, Anthony C. Leonard...

STUDY DESIGN

• ANATOMIC/HEMODYNAMIC/PHYSIOLOGIC - BOTH
  - MANY STENOSES ≥ 70%; NO ANGIO CORELAB
  - NO PRESSURE GRADIENT MEASURED

• STATISTICAL - BOTH
  - UNDERPOWERED

• CLINICAL - ASTRAL
  - PATIENTS MOST LIKELY TO BENEFIT WERE EXCLUDED (“NEED SURGERY or LIKELY TO NEED REVASCULARIZATION IN 6 MONTHS, VERY SEVERE STENOSES”)

• TECHNICAL/OPERATOR - INEXPERIENCE?
  - VERY FEW CASES DONE BY MOST CENTERS
  - HIGH COMPLICATION RATE
  - MEDICAL THERAPY EASIER TO STANDARDIZE and ADMINISTER

OVERALL STUDY DESIGN

• ANATOMIC/HEMODYNAMIC/PHYSIOLOGIC - INCLUDED ANGIO CORELAB
  - BUT, IGNORED ITS DATA FOR ESSENTIAL CALCULATIONS!!!
  - DIAMETER STENOSIS THRESHOLD ≥ 60% !?
  - DISTRIBUTION OF % STENOSIS (e.g. HISTOGRAM) NOT SHOWN
  - NO PRESSURE GRADIENTS MEASURED IN MOST PATIENTS
  - NO PRESSURE GRADIENT/STENOSIS/OUTCOME CORRELATIONS

• PROTOCOL - MANY SUBSTANTIAL CHANGES DURING STUDY
• STATISTICAL - ADEQUATELY POWERED (JUST!)
• CLINICAL - PATIENTS MOST LIKELY TO BENEFIT FROM INTERVENTION MAY HAVE BEEN UNINTENTIONALLY “EXCLUDED” (PATIENT and/or MD PREFERENCE FOR INTERVENTION)

WHAT HAVE WE LEARNED?

• THE DUTCH SHOULD NOT DO TRIALS or write editorials!?
CRITERIA FOR INTERVENTION

• **HEMODYNAMIC/PHYSIOLOGIC**
  - > 25% MEAN ARTERIAL PRESSURE GRADIENT

• **CLINICAL**
  - CHRONIC RENAL FAILURE STAGE III (SCr ~ 3)
  - ACUTE PULMONARY EDEMA x 2
  - HYPERTENSION x 15 yrs, ACCELERATED (200 SYST) x 3 mos ON 3 MEDS
  - CREST SYNDROME

• **ANATOMIC**
  - > 80% RIGHT RENAL ARTERY STENOSIS
  - LEFT RENAL ARTERY OCCLUSION
  - ATROPHIC LEFT KIDNEY

• **HEMODYNAMIC/PHYSIOLOGIC**
  - > 25% MEAN ARTERIAL PRESSURE GRADIENT

TREATMENT OPTIONS

• **RENAL ARTERY STENT**
  - 1-2% RISK OF CHOLESTEROL EMBOLI
  - LOW PROCEDURAL (OCCLUSION) RISK
  - LOW SEDATION RISK

• **HEPATO RENAL BYPASS**
  - LOW RISK OF CHOLESTEROL EMBOLI
  - MODERATE SURGICAL/ANESTHESIA RISK

77 y.o. WOMAN

BILAT RA DISEASE, HYPERTENSION, CRI, SJÖGREN’S SYNDROME

89 y.o. WOMAN

BILAT RA DISEASE, HYPERTENSION, CRI

PRE INTERVENTION Gad MRA

89 y.o. WOMAN

BILAT RA DISEASE, HYPERTENSION, CRI

SCr (mg/dl)

R RENAL A STENT
IN STENT RESTENOSIS R RENAL A RE-STENT

89 y.o. WOMAN

TREATMENT OPTIONS

• **MEDICAL**
  - FAILED 3 MEDS, RENAL FUNCTION
  - CHF, PULM EDEMA x 2

• **HEPATO RENAL BYPASS**
  - LOW RISK OF CHOLESTEROL EMBOLI
  - MODERATE SURGICAL/ANESTHESIA RISK

• **RENAL ARTERY STENT**
  - 1-2% RISK OF CHOLESTEROL EMBOLI
  - LOW PROCEDURAL (OCCLUSION) RISK
  - LOW SEDATION RISK

77 y.o. WOMAN

BILAT RA DISEASE, HYPERTENSION, CRI, SJÖGREN’S SYNDROME

89 y.o. WOMAN

BILAT RA DISEASE, HYPERTENSION, CRI, SJÖGREN’S SYNDROME

89 y.o. WOMAN

TREATMENT OPTIONS

• **MEDICAL**
  - FAILED 3 MEDS, RENAL FUNCTION
  - CHF, PULM EDEMA x 2

• **HEPATO RENAL BYPASS**
  - LOW RISK OF CHOLESTEROL EMBOLI
  - MODERATE SURGICAL/ANESTHESIA RISK

• **RENAL ARTERY STENT**
  - 1-2% RISK OF CHOLESTEROL EMBOLI
  - LOW PROCEDURAL (OCCLUSION) RISK
  - LOW SEDATION RISK

89 y.o. WOMAN

BILAT RA DISEASE, HYPERTENSION, CRI

PRE INTERVENTION Gad MRA

89 y.o. WOMAN

BILAT RA DISEASE, HYPERTENSION, CRI
PRE INTERVENTION Gad MRA

# 2: LIMIT CONTRAST
OMNIFLUSH™ RECURE TYPE
FLUSH CATHETER for AORTOGRAM
½ DILUTE I, 10 cc @ 10 cc/sec

RENAL ARTERY STENOSIS
WHEN TO INTERVENE
PHYSIOLOGIC SCREENING & CRITERIA

- **RADIONUCLIDE SCAN**
- **DUPLEX ULTRASOUND**
- **RENAL VEIN RENIN ASSAY**
- ≥10% MEAN ARTERIAL PRESSURE GRADIENT

* UNRELIABLE IN BILATERAL DISEASE & Scr
** TECHNICALLY DIFFICULT & OPERATOR DEPENDENT
*** INVASIVE

89 y.o. WOMAN
BILAT RA DISEASE, HYPERTENSION, CRI

77 y.o. WOMAN
BILAT RA DISEASE, HYPERTENSION, CRI, CREST SYNDROME

CRITERIA FOR INTERVENTION

- **CLINICAL**
  - CHRONIC RENAL FAILURE STAGE III (Scr ~ 3)
  - HYPERTENSION ON 3 MEDS
  - CREST SYNDROME
- **ANATOMIC**
  - > 90% RIGHT RENAL ARTERY STENOSIS
  - > 90% LEFT RENAL ARTERY OCCLUSION
  - BILATERAL RENAL ATROPHY L>R
- **HEMODYNAMIC/PHYSIOLOGIC**
  - ≥25% MEAN ARTERIAL PRESSURE GRADIENT

89 y.o. WOMAN
BILAT RA DISEASE, HYPERTENSION, CRI

TREATMENT OPTIONS

- **MEDICAL**
  - BILATERAL SEVERE RA DISEASE
  - CRI
  - HYPERTENSION
  - BILATERAL RENAL ATROPHY L>R
  - CHF
  - FAILED 3 MEDS, RENAL FUNCTION
- **HEPATO RENAL BYPASS**
  - LOW RISK OF CHOLESTEROL EMBOLI
  - MODERATE SURGICAL/ANESTHESIA RISK
- **RENAL ARTERY STENT**
  - 1-2% RISK OF CHOLESTEROL EMBOLI
  - LOW PROCEDURAL (OCCLUSION) RISK
  - LOW SEDATION RISK
PRE and POST STENT

1/3 DILUTE I 5 cc @ 7 cc/sec

IN STENT RESTENOSIS @ 1 YR

4mm x 12mm DES post dilated to 4.5mm

HYPERTENSION EPIDEMIOLOGY

- SINGLE LARGEST CONTRIBUTOR TO DEATH WORLDWIDE
- EVERY 20/10 MMHG INCREASE IN BP CORRELATES WITH A DOUBLING OF 10-YEAR CARDIOVASCULAR MORTALITY
- DRAMATICALLY INCREASES RISK OF STROKE, HEART ATTACK, HEART FAILURE, & KIDNEY FAILURE
- ONLY HALF OF ALL TREATED HYPERTENSIVES ARE CONTROLLED TO ESTABLISHED BP TARGETS
- HIGH PREVALENCE:
  - AFFECTS 1 IN 3 ADULTS
  - 1B PEOPLE (WORLD) → 1.6 B BY 2025

RENAL VASCULAR HYPERTENSION

RENIN/ANGIOTENSIN/ALDOSTERONE SYSTEM

VASOCONSTRICTIVE RENIN MEDIATED HYPERTENSION

VOLUME MEDIATED HYPERTENSION

EMBOLIC PROTECTION AND PLATELET INHIBITION DURING RENAL ARTERY STENTING

"THE LACK OF EFFICACY OF THE EPD IN IMPROVING GFR, CAPTURE DEBRIS, DECREASE DEBRIEF RESISTANCE, & IMPROVE THE POSITIVE PRESSURE AFTER ABDOMINAL AORTA FOR AN ALTERNATIVE MECHANISM OF RENAL INJURY: PREVENTION OF ATHROEMBOLIZATION."


CORRELATION BETWEEN TRANSLESIONAL PRESSURE GRADIENTS AND PERCENT DIAMETER STENOSIS AT QUANTITATIVE ANGIOGRAPHY

CLINICAL CRITERIA

WHEN TO INTERVENE

- RENAL DYSFUNCTION
  - RECENT ONSET OR PROGRESSIVE
  - MODERATE TO SEVERE
- HYPERTENSION
  - SEVERE OR DIFFICULT TO CONTROL
- PULMONARY EDEMA
  - RECURRENT FLASH
- ?JEOPARDIZED RENAL PARENCHYMA?

ANATOMIC DIAGNOSIS and CRITERIA

- ≥ 70% D STENOSIS (~85% XS AREA)
- POST STENOTIC DILATATION
- COLLATERAL CIRCULATON
- ?REDUCTION OF RENAL SIZE?
  - LENGTH DISCREPANCY ≥ 1.5 cm
  - DOCUMENTED 1 LENGTH ≥ 1cm
- ?RENAL LENGTH > 7-8 cm

CORRELATION BETWEEN TRANSLESIONAL PRESSURE GRADIENTS AND PERCENT DIAMETER STENOSIS AT QUANTIT. ANGIO.

84F CHF, CKD (CR 2.8), HTN, COPD.

CLINICAL COURSE

Revascularization versus Medical Therapy for Renal-Artery Stenosis
The ASTRAL Investigators
NEJM 361:1953-1962 November 12, 2009 Number 20

Very severe anatomic disease
No change in renal function over 5 years

In femoral group
84F CHF, CKD (CR 2.8), HTN, COPD.

07/14/2015 US KIDNEY

CLINICAL STATEMENT: Elevated creatinine.
Question abnormal imaging outside institution.

TECHNIQUE: A sonogram of the kidneys was performed assessing gray scale appearance and color Doppler flow.

IMPRESSION:
No hydronephrosis or shadowing calculus.
New atrophy with cortical thinning of the right kidney.
Persistent, nonspecific mild elevation of the resistive indices bilaterally.
Partially imaged bilateral pleural effusions.

Relationship of Albuminuria and Renal Artery Stent Outcomes: Results from the CORAL Study

Timothy P. Murphy, M.D., Full Professor, Research Track, Department of Diagnostic Imaging, Alpert Medical School at Brown University, Director, Vascular Disease Research Center, Rhode Island Hospital; co-authors: Christopher J. Cooper, M.D., Karol M. Pencina, Ph.D., Ralph D’Agostino, Ph.D., Karol M. Pencina, Ph.D., William Henrich, M.D., Joseph I. Shapiro, M.D., Katherine R. Tuttle, M.D., David J. Cohen, M.D., Michael Steffes, M.D., Qi Gao, M.S., D. Christopher Metzger, M.D., William B. Abimanyu, M.D., Stephen C. Textor, M.D., John Briguglio, M.D., Alan T. Hirsch, M.D., Sheldon Toia, M.D., Lance D. Dawkins, M.D.
Methods

• Principal Component Analysis (PCA) to examine all baseline variables
• Dichotomize population based on any variables positive to p<.05 by PCA based on the median value, re-run the primary and secondary analyses in CORAL on each subset

Results

• Baseline urine albumin/creatinine ratio (uACR) was strongly positive by PCA
  – Known linear effect on cardiovascular risk
• Test for interaction between treatment group and uACR on the time to the composite primary endpoint (p=.02)
• Of 931 evaluable patients in CORAL, there were 826 with; 105 with missing baseline Uacrb

COROLLARY (CORALII) Study

• Cardiovascular and Renal Outcomes with Low Levels of urine Albuminuria and Renal Artery Stenting
  • www.corollarystudy.org
  • tmurphy@lifespans.org

Results

• Data set dichotomized based on median uACR (22.5 mg/g)(n=413 in each group)
• In the lower uACR cohort, “Cohort 1”, there was a lower incidence of primary endpoints than Cohort 2 (180/413 (44%) vs. 110/413, (27%), and also lower prevalence of diabetes mellitus, higher eGFR, and lower baseline systolic blood pressure

• B/L RAS
  – OCCLUDED RI RA, ATROPHIC KIDNEY
  – LEFT KIDNEY W/ PINHOLE PROXIMAL RENAL ARTERY STENOSIS
• EXTUBATED 2 DAYS POST RA STENT
• AUTO DIURESIS STARTED DURING PROCEDURE
• SCr DECREASED
MY PERSPECTIVES AND DO WE REALLY NEED CORAL II (COROLLARY)?

- CORAL WAS DEEPLY FLAWED
  - STENOSIS SEVERITY ≥ 60%
  - NO GRADIENTS MEASURED
  - SERIOUS CHANGES IN PROTOCOL and SITES MIDSTREAM
- CORAL II (COROLLARY)
  - MAY NOT START FOR SEVERAL YEARS (? AT ALL?????)
  - COMPLETE PROTOCOL NOT AVAILABLE
  - MEASURING GRADIENTS NOT MANDATORY

C3 2016
Session: Innovation in Vascular Medicine
Thursday, June 30, 2016
11:45 AM - 11:55 AM

C3 Flash Presentation: State of Renal Artery Stenting:
MY PERSPECTIVES AND DO WE REALLY NEED CORAL II (COROLLARY)?

Cr, RENAL FUNCTIONAL RESERVE (GFR) AND RISK OF INTERVENTION

RENAL ARTERY STENOSIS, HYPERTENSION and RENAL INSUFFICIENCY

RENAL FUNCTIONAL RESERVE (GFR)

NORMAL

HIGH RISK

INT. RISK

LOW RISK

% RENAL FUNCTIONAL RESERVE (GFR)

25 50 75 100

ISCHEMIC NEPHROPATHY

RENAL VASCULAR HYPERTENSION and ISCHEMIC NEPHROPATHY

RENAL ARTERY STENOSIS

HYERTENSION

RENAL INSUFFICIENCY

RENAL VASCULAR HYPERTENSION

RENAL VASCULAR HYPERTENSION

RENAL VASCULAR HYPERTENSION

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