UCSF Department of Surgery

Lipophilic Statins: A Potential Novel Risk Factor for Paraplegia After Branched Endovascular Aortic Aneurysm Repair: What is the Mechanism?

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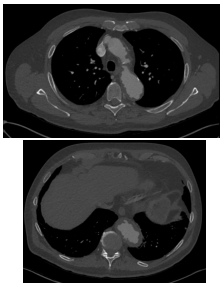
Disclosures

- None relevant

Risk Factors For Spinal Cord Ischemia (SCI)

- Extensive aortic coverage
- Compromised collateral perfusion
  - Vertebral artery
  - Subclavian artery
  - Hypogastric arteries
- "Shaggy" aorta
- Symptomatic/contained rupture
  - Hypotension
  - Anemia



SCI and TAAA Repair: Preventative Strategies

- Staged Repair
- Management of hemodynamic parameters
- Cerebrospinal fluid drainage
- Segmental artery embolization

Preoperative	
Adjunctive Procedures	TEVAR Iliofemoral Conduit Carotid to Subclavian Bypass
1-2 Days Prior to Procedure	
Permissive Hypertension	Hold Blood Pressure Medications (Except beta blockers, ACE/ARB)
Day Before Procedure	
Prophylactic CSF Drainage	Place under CT-guidance

SCI and TAAA Repair: Intraoperative Maneuvers

Early Lower Extremity and Pelvic Perfusion	Removal of Delivery System After Deployment of Branched Device
Management of Hemodynamic Parameters	SBP>140 or MAP >85 mmHg After Placement of Final Branch
Blood Product Transfusion	Hgb≥10 g/dL
CSF Drain Management	5mL Every 2 Hours to Keep Drain Open 10 mL After Placement of Final Branch

SCI and TAAA Repair: Postoperative Care

- Postoperative Care
  - ICU for q1 hour neurovascular monitoring
  - SBP>140 mmHg or MAP>85 mmHg
  - Hgb≥10 g/dL for 72 hours
  - Prophylactic CSF drain: 10 mL/hour; clamp at 24 hours if normal LE exam
  - Insulin drip to maintain blood glucose ≤ 120 mg/dL
  - Oxygen by nasal cannula
  - Avoid oversedation/narcotics
- Rescue Therapies
  - Emergent CSF drain if not already in place – drain to effect or headache (20-30 mL)
  - MAP > 100 mmHg – pressors if necessary
  - Mannitol/Naloxone/Steroids/Hyperbaric oxygen

Background

- Statins widely prescribed to all vascular surgery patients: protective effects on cardiovascular outcomes
- Statins have both neuroprotective and neurodegenerative effects
  - Black box warning for possible adverse effects on cognitive performance
  - But may decrease inflammation and risk of dementia
- Most studies centered around brain function – unknown influence on spinal cord function

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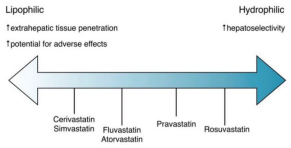

- Lipophilic vs hydrophilic
  - Lipophilic statins cross the blood-brain barrier
  - Lipophilic statins associated with increased risk of myopathy/myositis
  - Mitochondrial dysfunction
- Question: Is statin lipophilicity associated with risk of spinal cord ischemia after BEVAR?

Figure from Singla and Jacobson; Pulmonary Circulation 2012; 2(4):397-406

Study Design

Single-center prospective clinical trial of BEVAR for TAAA began in 2005 at UCSF

Current study: **2012-2022** (standardized SCI protection protocol)

- Preoperative lumbar drain – 10cc/h intraop and 24h postoperatively
- Maintenance of collateral pathways
- Avoidance of hypotension and anemia
- Removal of groin sheath after main body deployment (2010)
- Low profile stent graft (2011)
- Insulin infusion protocol for BG < 120 x48h (2016)

***Elective cases with branched endovascular repair and >10 cm supraceliac coverage**

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Study Design

Statins:

Lipophilic	Hydrophilic
• **Atorvastatin** (Lipitor)	• **Pravastatin** (Pravachol)
• **Simvastatin** (Zocor)	• **Rosuvastatin** (Crestor)
• **Lovastatin** (Mevacor)	

Primary Endpoint: Postoperative lower extremity weakness (LEW)

- Permanent LEW (p-LEW)
- Temporary LEW (t-LEW) – resolved by time of first follow-up visit

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Cohort Characteristics: Stratified by p-LEW

	Total Cohort (n=101)	Univariate Correlations with p-LEW After BEVAR		
		p-LEW (n=9; 8.9%)	No p-LEW (n=92; 91%)	p-value
Demographics, Comorbidities, Statin Use				
Age (years)	72.9 ± 8.3	72.4 ± 7.5	72.9 ± 8.4	0.86
Male	77 (76%)	9 (100%)	68 (74%)	0.11
Hyperlipidemia	82 (81%)	9 (100%)	73 (79%)	0.20
Diabetes mellitus	18 (18%)	2 (22%)	16 (17%)	0.66
Lipophilic Statin (vs. hydrophilic or no statin)	**69 (68%)**	**9 (100%)**	**60 (65%)**	**0.05**
Anatomic, Procedural, Post-Procedural Characteristics				
Aneurysm Extent Type 4/PVAA vs. other	52 (51%)	4 (44%)	48 (52%)	0.74
Contrast Volume (mL)	119 ± 49	116 ± 41	120 ± 50	0.96
Fluoroscopy Time (minutes)	118 ± 42	148 ± 54	115 ± 40	0.06
Insulin Infusion Protocol	46 (45%)	5 (56%)	41 (44%)	0.73

Cohort Characteristics: Stratified by t-LEW

	Total Cohort (n=92/101) *excl p-LEW	Univariate Correlations with t-LEW After b-EVAR		
		t-LEW (n=12/101; 12%)	No LEW (n=80/101; 80%)	p-value
Demographics, Comorbidities, Statin Use				
Age (years)	**72.9 ± 8.4**	**77.3 ± 6.5**	**72.3 ± 8.5**	**0.02**
Male	68 (74%)	9 (75%)	59 (74%)	1
Hyperlipidemia	82 (81%)	10 (83%)	63 (79%)	1
Diabetes mellitus	16 (17%)	3 (25%)	13 (16%)	0.43
Lipophilic Statin (vs. hydrophilic or no statin)	60 (65%)	8 (67%)	52 (65%)	1
Anatomic, Procedural, Post-Procedural Characteristics				
Aneurysm Extent Type 4/PVAA vs. other	52 (51%)	4 (33%)	44 (55%)	0.22
Contrast Volume (mL)	120 ± 50	139 ± 49	117 ± 50	0.11
Fluoroscopy Time (minutes)	115 ± 40	128 ± 39	113 ± 40	0.19
Insulin Infusion Protocol	**41 (44%)**	**2 (17%)**	**39 (49%)**	**0.06**

Conclusions & Limitations

Conclusions: Lipophilic statins significantly associated with **p-LEW but not t-LEW** after BEVAR for TAAA/PVAA

- ***Potential modifiable risk factor for reducing risk of p-LEW***

Limitations:

- Small sample size/low event rate limit multiple regression analysis

Future Directions

- Analysis in larger datasets – specific statin medications and dose dependency
- Analysis of blood and CSF for markers of mitochondrial dysfunction and recovery response

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