Study Title: Prospective, Observational Trial of Blunt Cerebrovascular Injury Management and Stroke Formation

PI: Dr. Margaret Lauerman

Email of PI: mlauerman@umm.edu

Co-Primary Investigator:

Dr. Deborah Stein

Background/Significance:

Scant research exists examining optimal therapy for patients with blunt cerebrovascular injury (BCVI). While medical therapy for BCVI is standard as it is associated with decreased rate of stroke, the optimal medical therapy overall and for each grade of injury is unknown. Patients with BCVI are often followed with serial radiographic imaging with unclear durations necessary between scans. Indications for and results with endovascular intervention (EI) in BCVI are similarly unclear. Complicating matters is the fact that BCVI is not a stagnant lesion, and injury grade can change over time. BCVI are comprised of both carotid and vertebral artery injuries, and practices may differ by vessel injured. Finally, risk factors associated with stroke development are unknown.

Given the large amount of unknowns in ideal management of BCVI, a multicenter trial is a critical need. The long-term goal of this prospective, multicenter, observational trial is to define rates of stroke development and risk factors for stroke formation. A secondary goal is to define the current practices in use for management of patients with BCVI; this would include medical therapy, radiologic imaging, use of diagnostic angiography and use of EI. Achieving these specific goals of this proposed trial will further our understanding for optimal treatment in patients with BCVI.

Primary Aim:

The primary aim of this study is to determine rates of stroke for BCVI overall and by grade of injury and predictors of BCVI related stroke formation.

Secondary Aims:

A secondary aim of this study is to determine rates of endovascular interventions for BCVI overall and by grade of injury.

A second aim of this study is to determine rates of diagnostic angiography for BCVI overall and by grade of injury.

A secondary aim of this study is to determine timing of follow-up radiographic imaging for BCVI overall and by grade of injury.

A secondary aim of this study is to determine rates of utilization of medical therapies for BCVI overall and by grade of injury.

Inclusion Criteria:

1. Age 18 years and greater
2. Traumatic injury
3. Blunt injury mechanism
4. Presence of BCVI (either internal carotid or vertebral artery injury)

Exclusion Criteria:

1. Age less than 18 years
2. Non-traumatic internal carotid or vertebral artery pathology
3. Penetrating injury mechanism

Therapeutic Interventions:

This is a prospective observational trial only. Patients will be managed according to the discretion of the treatment team at each individual institution. No alterations in patient care will occur because of this trial.

Primary Outcome:

BCVI related stroke

Secondary Outcomes:

Rates of diagnostic angiography

Rates of endovascular interventions

Timing of follow-up radiographic imaging

Rates of medical therapies

Variables:

1. Hospital geographic location
2. Hospital trauma yearly volume (patients/year)
3. Hospital urban environment
4. Hospital academic affiliation
5. Institution BCVI screening guidelines used.
6. Who is the team managing carotid injuries at your institution?

7. Who is the team managing vertebral injuries at your institution?
8. Do you have an institutional protocol for carotid injury management?
9. Do you have an institutional protocol for vertebral injury management?
10. Age
11. Race
12. Gender
13. Mechanism of Injury
14. Injury Severity Score
15. AIS Head
16. AIS Face
17. AIS Neck
18. AIS Spine
19. AIS Thorax
20. AIS Abdomen
21. AIS Lower Extremity
22. AIS Upper Extremity
23. Admission Systolic Blood Pressure
24. Admission Diastolic Blood Pressure
25. Admission Heart Rate
26. Admission Respiratory Rate
27. Admission oxygen saturation
28. Admission Eye GCS
29. Admission Voice GCS
30. Admission Motor GCS
31. Admission hemoglobin
32. Admission WBC
33. Admission lactate
34. Admission platelets
35. Admission INR
36. Admission Creatinine
37. First medical therapy for the BCVI
38. Time to first medical therapy for the BCVI (hours)
39. Repeat 28-29 for all medical therapy given
40. If the first medical therapy for the BCVI was not started within 1 day after diagnosis of the BCVI, what was the reason why?
41. Complication occurring with medical therapy for the BCVI.
42. Was a diagnostic angiography performed?
43. Time to diagnostic angiography (hours)
44. Indication for diagnostic angiography.
45. Grade of injury at the time of diagnostic angiography.
46. Was an endovascular intervention performed?
47. What type of endovascular intervention was performed?
48. Indication for endovascular intervention.
49. BCVI related stroke

50. Time until diagnosis of BCVI related stroke (hours)
51. Mortality during initial hospitalization
52. Cause of mortality during hospitalization
53. Hospital length of stay (days)
54. Glascow Outcomes Scale score
55. BCVI vessel injured
56. What was the radiologic modality used at BCVI imaging occurrence #1?
57. Time to BCVI imaging occurrence #1 (hours)
58. BCVI grade at imaging occurrence #1.
59. Presence of luminal stenosis at the time of imaging occurrence #1.
60. Estimated percentage luminal stenosis (0-100%) at the time of imaging occurrence #1.
61. Presence of intimal flap at the time of imaging occurrence #1.
62. Presence of intraluminal thrombus at the time of imaging occurrence #1.
63. Presence of pseudoaneurysm at the time of imaging occurrence #1.
64. Size of pseudoaneurysm (largest mm diameter) at the time of imaging occurrence #1.
65. Repeat 49-57 for each imaging occurrence

Data Collection and Statistical Analysis:

This is a prospective, observational trial. Collected variables will include those listed in the data dictionary, and the data points will be entered into the data collection form on the central data collection tool. The coordinating center team at the University of Maryland will maintain the database and evaluate the data for quality. The University of Maryland team will also be responsible for communication with participating centers. The University of Maryland team will also provide the statistician for data analysis.

For the statistical analysis we are proposing to perform univariate analysis for rates of the collected variables, focusing on the primary and secondary aims of medical therapy, diagnostic angiography, endovascular interventions, radiographic follow-up, and stroke formation. We will also examine radiographic lesion characteristics. Stratification may be performed by injury grade and by vessel injured (vertebral or carotid). We are then proposing examining risk factors for stroke development with bivariate analysis for the association of collected variables with stroke formation and subsequent binary logistic regression to determine factors influencing stroke development; the analysis for stroke formation may also undergo stratification by grade of injury and vessel injured. Other secondary outcome measures include radiographic lesion evolution and functional outcome.

Consent Procedures:

Informed consent will not be obtained as this is a prospective observational trial and there will be no alteration in patient care.

Risk/Benefit Analysis:

The optimal treatments for specific grades of BCVI are unknown, as are the benefits and risks of each specific treatment for individual grades of BCVI. Better delineating the optimal management of BCVI may be beneficial to future patients with BCVI by improving our treatment efficacy. The risk to patients in this trial is minimal as this is a prospective observational trial without alteration in patient care. The major risk to patients is loss of confidentiality, which we will guard against.

References:

Stein DM, Boswell S, Sliker CW, et al. Blunt cerebrovascular injuries: Does treatment always matter? *J Trauma*. 2009;66(1):132-43; discussion 143-4.

Edwards NM, Fabian TC, Claridge JA, et al. Antithrombotic therapy and endovascular stents are effective treatment for blunt carotid injuries: results from longterm followup. JACS. 2007;204(5):1007-13.

Burlew CC, Biffl WL, Moore EE, et al. Endovascular stenting is rarely necessary for the management of blunt cerebrovascular injuries. JACS. 2014;218(5):1012-7.

Miller PR, Fabian TC, Bee TK, et al. Blunt cerebrovascular injuries: Diagnosis and treatment. *J Trauma*. 2001;51(2):279-85; discussion 285-6.

Laser A, Bruns BR, Kufera JA, et al. Long-term follow-up of blunt cerebrovascular injuries: Does time heal all wounds? *J Trauma.* 2016;81(6):1063-1069.

Hospital Characteristics:

1. Hospital geographic location
    a. Northeast
    b. Southeast
    c. Midwest
    d. West
2. Hospital trauma yearly volume (patients/year)
3. Hospital urban environment
    a. Urban
    b. Non-urban
4. Hospital academic affiliation
    a. Teaching
    b. Non-teaching
5. Institution BCVI screening guidelines used.
    a. Hospital protocol
    b. East
    c. Denver criteria
    d. Other (specify)
    e. No guidelines are used
6. Who is the team managing carotid injuries at your institution?
    a. Trauma Team
    b. Neurosurgery
    c. Medicine Team
    d. Vascular Team
    e. Interventional Radiology Service
    f. Other (specify)
7. Who is the team managing vertebral injuries at your institution?
    a. Trauma Team
    b. Neurosurgery
    c. Medicine Team
    d. Vascular Team
    e. Interventional Radiology Service
    f. Other (specify)
8. Do you have an institutional protocol for carotid injury management?
    a. Yes
    b. No
9. Do you have an institutional protocol for vertebral injury management?
    a. Yes
    b. No

BCVI Specific Characteristics:

1. Age

2. Race
    a. Caucasian
    b. African American
    c. Hispanic
    d. Asian
    e. Other
3. Gender
    a. Male
    b. Female
4. Mechanism of Injury
    a. MVC
    b. MCC
    c. Pedestrian struck
    d. ATV crash
    e. Bicycle crash
    f. Fall
    g. Crush injury
    h. Other (specify)
5. Injury Severity Score
6. AIS Head
7. AIS Face
8. AIS Neck
9. AIS Spine
10. AIS Thorax
11. AIS Abdomen
12. AIS Lower Extremity
13. AIS Upper Extremity
14. Admission Systolic Blood Pressure
15. Admission Diastolic Blood Pressure
16. Admission Heart Rate
17. Admission Respiratory Rate
18. Admission oxygen saturation
19. Admission Eye GCS
20. Admission Voice GCS
21. Admission Motor GCS
22. Admission hemoglobin
23. Admission WBC
24. Admission lactate
25. Admission platelets
26. Admission INR
27. Admission Creatinine
28. First medical therapy for the BCVI
    a. No medical therapy
    b. Aspirin only

    c. Plavix only
    d. Aspirin/Plavix combination
    e. Heparin infusion
    f. Therapeutic Lovenox
    g. Coumadin
    h. Novel oral anticoagulant
    i. Other (specify)
29. Time to first medical therapy for the BCVI (hours)
30. Repeat 28-29 for all medical therapy given
31. If the first medical therapy for the BCVI was not started within 1 day after diagnosis of the BCVI, what was the reason why?
    a. Traumatic brain injury
    b. Spine injury
    c. Extremity injury
    d. Thoracic injury
    e. Abdominal injury
    f. Unclear
    g. Other (specify)
    h. Medical therapy started within 1 day
    i. No medical therapy for the BCVI
32. Complication occurring with medical therapy for the BCVI.
    a. GI bleed
    b. Hemoptysis
    c. Worsening TBI
    d. Other (specify)
    e. No complication
    f. No medical therapy for the BCVI
33. Was a diagnostic angiography performed?
    a. Yes
    b. No
34. Time to diagnostic angiography (hours)
35. Indication for diagnostic angiography.
    a. Determine presence of injury
    b. Determine grade of injury
    c. Concerning imaging characteristics on CT/MRI/US
    d. Other (specify)
36. Grade of injury at the time of diagnostic angiography.
    a. 1
    b. 2
    c. 3
    d. 4
    e. 5
37. Was an endovascular intervention performed?
    a. Yes

    b. No
38. What type of endovascular intervention was performed?
    a. Stent
    b. Embolization
    c. Stent/embolization combination
    d. Other (specify)
39. Indication for endovascular intervention.
    a. Injury grade
    b. Size of pseudoaneurysm
    c. Presence of pseudoaneurysm
    d. Worsening pseudoaneurysm
    e. Presence of luminal stenosis
    f. Percentage of luminal stenosis
    g. Worsening luminal stenosis
    h. Active extravasation
    i. Arteriovenous fistula
    j. Recanalization prevention
    k. Symptomatic BCVI
    l. Other (specify)
40. BCVI related stroke
    a. Yes
    b. No
41. Time until diagnosis of BCVI related stroke (hours)
42. Mortality during initial hospitalization
    a. Yes
    b. No
43. Cause of mortality during hospitalization
    a. BCVI
    b. Other (Specify)
    c. No mortality
44. Hospital length of stay (days)
45. Glascow Outcomes Scale score
    a. 1
    b. 2
    c. 3
    d. 4
    e. 5
46. BCVI vessel injured
    a. Internal carotid artery
    b. Vertebral artery
47. What was the radiologic modality used at BCVI imaging occurrence #1?
    a. CT arterial phase
    b. CT angiography
    c. MRI

    d. US
    e. Diagnostic angiography
48. Time to BCVI imaging occurrence #1 (hours)
49. BCVI grade at imaging occurrence #1.
    a. 1
    b. 2
    c. 3
    d. 4
    e. 5
50. Presence of luminal stenosis at the time of imaging occurrence #1.
    a. Yes
    b. No
51. Estimated percentage luminal stenosis (0-100%) at the time of imaging occurrence #1.
52. Presence of intimal flap at the time of imaging occurrence #1.
    a. Yes
    b. No
53. Presence of intraluminal thrombus at the time of imaging occurrence #1.
    a. Yes
    b. No
54. Presence of pseudoaneurysm at the time of imaging occurrence #1.
    a. Yes
    b. No
55. Size of pseudoaneurysm (largest mm diameter) at the time of imaging occurrence #1.
56. Repeat 49-57 for each imaging occurrence

Hospital Characteristics:

Hospital geographic location	Location of the hospital enrolling patients
Hospital trauma yearly volume	Trauma patient visits per year in the enrolling hospital
Hospital urban environment	Urban: ≥50,000 people in city of the enrolling hospital Non-urban: <50,000 people in city of the enrolling hospital
Hospital academic affiliation	Teaching: has residents on the trauma service at the enrolling hospital Non-teaching: does not have residents on the trauma service at the enrolling hospital
Institution BCVI screening guidelines	Hospital protocol: A protocol for screening that was developed at that specific institution and is in use at the enrolling hospital. EAST guidelines: Guidelines from EAST that are available at: https://www.east.org/education/practice-management-guidelines/blunt-cerebrovascular-injury#h3. Denver criteria: Criteria from the Denver group that are available at: https://jamanetwork.com/journals/jamasurgery/fullarticle/405142. Using no guidelines: BCVI screening is per individual provider judgement at the enrolling hospital
Team managing carotid injuries	Team dictating the care of patients with carotid injuries at the enrolling hospital
Team managing vertebral injuries	Team dictating the care of patients with vertebral injuries at the enrolling hospital
Institutional protocol for carotid injury management	Use of an institution specific protocol for carotid BCVI management

Institutional protocol for vertebral injury management	Use of an institution specific protocol for vertebral BCVI management

BCVI Specific Characteristics:

Age	Age of patient enrolled
Race	Race of patient enrolled
Gender	Gender of patient enrolled
Mechanism of Injury	Single choice for mechanism of injury of patient enrolled MVC: motor vehicle crash MCC: motor cycle crash ATV: all-terrain vehicle
Injury Severity Score	Numerical value for injury severity score (ISS)
AIS Head	Numerical value for abbreviated injury score (AIS) head
AIS Face	Numerical value for abbreviated injury score (AIS) face
AIS Neck	Numerical value for abbreviated injury score (AIS) neck
AIS Spine	Numerical value for abbreviated injury score (AIS) spine
AIS Thorax	Numerical value for abbreviated injury score (AIS) thorax
AIS Abdomen	Numerical value for abbreviated injury score (AIS) abdomen

AIS Lower Extremity	Numerical value for abbreviated injury score (AIS) lower extremity
AIS Upper Extremity	Numerical value for abbreviated injury score (AIS) upper extremity
Admission Systolic Blood Pressure	Systolic blood pressure on admission in mmHg
Admission Diastolic Blood Pressure	Diastolic blood pressure on admission in mmHg
Admission Heart Rate	Heart rate on admission in beats per minute
Admission Respiratory rate	Respiratory rate on admission in breaths per minute
Admission oxygen saturation	Oxygen saturation on admission as a percentage
Admission Eye GCS	Numerical eye Glascow Coma Scale (GCS) score on admission
Admission Voice GCS	Numerical voice GCS score on admission
Admission Motor GCS	Numerical motor GCS score on admission
Admission hemoglobin	Hemoglobin value on admission in g/dL
Admission WBC	White blood cell count (WBC) in K/mcl on admission
Admission lactate	Lactate value on admission in mmol/L
Admission platelets	Platelet value on admission in K/mcL

Admission INR	International normalized ratio (INR) on admission
Admission Creatinine	Creatinine level on admission in mg/dL
First medical therapy for the BCVI	Initial pharmacologic therapy used to treat the BCVI during the admission.
Time to medical therapy for the BCVI	Time in hours to medical therapy for the BCVI after admission
Delay in medical therapy	Reason greater than 1 day passed until administration of the first medical therapy for the BCVI
Complication occurring with medical therapy for the BCVI.	Any worsening in patient condition attributed to the BCVI pharmacologic therapy
Diagnostic angiography	Diagnostic angiography is a catheter contrast study without an associated endovascular intervention.
Time to diagnostic angiography	Time in hours to diagnostic angiography from admission
Indication for diagnostic angiography	Rationale for obtaining a diagnostic angiography
Grade of injury at the time of diagnostic angiography.	Grade of the BCVI using the following scale: 1: < 25% luminal stenosis 2: ≥ 25% luminal stenosis and ≤ 99% luminal stenosis 3: pseudoaneurysm 4: 100% luminal stenosis 5: Active extravasation

Endovascular intervention	Endovascular intervention is an endovascular procedure performed, such as stent placement or coil placement.
Indication for endovascular Intervention	Stated reason for performing the endovascular intervention
BCVI related stroke.	This is a stroke in the distribution of the vessel with the BCVI. Strokes occurring outside that distribution are excluded.
Time until diagnosis of BCVI related stroke	Time in hours from admission to radiographic stroke diagnosis
Mortality during initial hospitalization	Whether patient expired during initial hospitalization
Cause of mortality	Stated cause of the patient's death
Hospital length of stay	Length of hospital stay from admission to discharge in days
Glascow Outcomes Scale	Numerical score for the Glascow outcomes scale 1: death 2: persistent vegetative state 3: severe disability 4: moderate disability 5: good recovery
BCVI vessel injured	Specific vessel injured (either internal carotid or vertebral)
Radiologic modality	Specific radiographic imaging technique used to image the BCVI

	CT: computerized tomography MRI: magnetic resonance imaging US: ultrasound Arterial phase: arterial contrast but not an angiographic study
Time to BCVI imaging occurrence	Time in hours to the imaging of the BCVI from admission
BCVI grade at imaging occurrence	Grade of the BCVI at each imaging occurrence using the above scale
Luminal stenosis	Luminal stenosis is defined as narrowing of the injured vessel lumen
Percentage luminal stenosis (0-100%)	Numerical percentage from 0-100% of the vessel narrowing at its most narrow
Intimal flap	Occurrence of an intimal flap within the vessel lumen
Intraluminal thrombus	Occurrence of a thrombus, or clot, seen within the vessel lumen
Pseudoaneurysm	Vessel outpouching
Size of pseudoaneurysm	Largest mm diameter of the pseudoaneurysm