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Reading the Signs in Penetrating Cervical Vascular Injuries: Analysis of Hard/Soft Signs and Initial Management from a Nationwide Vascular Trauma Database.

--Manuscript Draft--

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Corresponding Author:	Matthew J. Martin, MD Los Angeles County University of Southern California Medical Center Los Angeles, CA UNITED STATES
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	Los Angeles County University of Southern California Medical Center
Corresponding Author's Secondary Institution:	
First Author:	Alexander Marrotte, MD
First Author Secondary Information:	
Order of Authors:	Alexander Marrotte, MD
	Richard Y Calvo, PhD
	Jayraan Badiee, MPH
	Alexandra S Rooney, MPH
	Andrea Krzyzaniak, MA
	Michael J Sise, MD
	Vishal Bansal, MD
	Joseph DuBose, MD
	Matthew J. Martin, MD
Order of Authors Secondary Information:	
Manuscript Region of Origin:	UNITED STATES
Abstract:	Background: Algorithms for management of penetrating cervical vascular injuries (PCVI) commonly call for immediate surgery with “hard signs” (HS) and imaging before intervention with “soft signs” (SS). We sought to analyze the association between initial exam and subsequent evaluation and management approaches. Methods: Analysis of PCVI from the AAST PROOVIT vascular injury registry from 25 US trauma centers. Patients were categorized by initial exam findings of HS or SS and subsequent imaging and surgical exploration/repair rates were compared. Results: Of 232 PCVI patients, 110 (47%) had HS (hemorrhage, expanding hematoma, or ischemia) and 122 (53%) had SS. With HS, 61 (56%) had immediate operative exploration and 44% underwent CT imaging (Figure). After CT, 20 (18%) required open surgical repair and 7% had endovascular intervention. Of note, 21 (19%) required no operative intervention. 122 (53%) patients had SS on initial exam; 37 (30%) had immediate surgery and 85 (70%) underwent CT imaging. After CT, 9% had endovascular repair, 7% had open surgery, and 65 (53%) were observed (Figure). No difference in mortality was observed for HS patients undergoing operative management vs observation alone (23% vs. 17%, p=0.6). Those with hemorrhage as the primary HS most often required surgery (76%), but no interventions were required

	in 19% of hemorrhage, 20% of ischemia, and 24% of expanding hematoma. Conclusion: Although HS in PCVI are associated with the need for operative intervention, initial CT imaging can facilitate endovascular options or nonoperative management in a significant subgroup. HS should not be considered an absolute indication for immediate surgical exploration. Level of Evidence: Level III, Prognostic and epidemiological.

Keck Medicine of USC

MATTHEW J. MARTIN, MD, FACS, FASMBS
Division of Acute Care Surgery
Professor of Surgery
Chief, Emergency General Surgery
Director of Acute Care Surgery Research

March 10, 2022

Raul Coimbra, MD, PhD
Editor in Chief, Journal of Trauma and Acute Care Surgery

Dear Dr. Coimbra,

Thank you for your consideration of our revised manuscript "**Reading the Signs in Penetrating Cervical Vascular Injuries: Analysis of Hard/Soft Signs and Initial Management from a Nationwide Vascular Trauma Database"** for consideration for publication in conjunction with an oral presentation at the 2022 Annual Meeting of the Western Trauma Association.

We have received the reviewer's comments and have addressed them in the responses below. Please pass on our gratitude for the reviewer's comments and suggestions. We hope that we have provided satisfactory responses and clarifications, and we believe that their input has greatly improved the manuscript. We greatly appreciate their positive comments, and hope that this algorithm will be useful for the trauma community.

Attached is a revised manuscript (with all changes highlighted in yellow) and a clean version of the manuscript with no highlighting enclosed for your review. Please do not hesitate to contact me if you have further questions or concerns. We would be happy to address any further questions or need for further revisions if deemed necessary by your reviewers.

Sincerely,

Matthew J. Martin, MD, FACS, FASMBS
Director of Acute Care Surgery Research
matthew.martin@med.usc.edu

Keck Medicine of USC

MATTHEW J. MARTIN, MD, FACS, FASMBS
Division of Acute Care Surgery
Professor of Surgery
Chief, Emergency General Surgery
Director of Acute Care Surgery Research

April 13, 2022

Raul Coimbra, MD, PhD
Editor in Chief, Journal of Trauma and Acute Care Surgery

Dear Dr. Coimbra,

Thank you for your consideration of our revised manuscript "**Reading the Signs in Penetrating Cervical Vascular Injuries: Analysis of Hard/Soft Signs and Initial Management from a Nationwide Vascular Trauma Database"** for publication in conjunction with an oral presentation at the 2022 Annual Meeting of the Western Trauma Association.

We apologize for the incomplete STROBE statement in our original submission. We have now used the MS Word version for cross-sectional studies instead of the pdf version which did not include a placeholder to indicate page numbers. This version of the STROBE statement has corresponding page number of the manuscript for each specific criteria. Our sincerest apologies for the oversight and all inconvenience.

Please do not hesitate to contact me if you have further questions or concerns. We would be happy to address any further questions or need for further revisions if deemed necessary by your reviewers.

Sincerely,

Matthew J. Martin, MD, FACS, FASMBS
Director of Acute Care Surgery Research
matthew.martin@med.usc.edu

University of Southern California
LAC+USC Medical Center, 2051 Marengo Street, IPT, C5L100, Los Angeles, CA 90033-1352 • Tel: 323 409 8604 • Fax: 323 441 9907

Background: Algorithms for management of penetrating cervical vascular injuries (PCVI) commonly call for immediate surgery with “hard signs” (HS) and imaging before intervention with “soft signs” (SS). We sought to analyze the association between initial exam and subsequent evaluation and management approaches.

Methods: Analysis of PCVI from the AAST PROOVIT vascular injury registry from 25 US trauma centers. Patients were categorized by initial exam findings of HS or SS and subsequent imaging and surgical exploration/repair rates were compared.

Results: Of 232 PCVI patients, 110 (47%) had HS (hemorrhage, expanding hematoma, or ischemia) and 122 (53%) had SS. With HS, 61 (56%) had immediate operative exploration and 44% underwent CT imaging (Figure). After CT, 20 (18%) required open surgical repair and 7% had endovascular intervention. Of note, 21 (19%) required no operative intervention. 122 (53%) patients had SS on initial exam; 37 (30%) had immediate surgery and 85 (70%) underwent CT imaging. After CT, 9% had endovascular repair, 7% had open surgery, and 65 (53%) were observed (Figure). No difference in mortality was observed for HS patients undergoing operative management vs observation alone (23% vs. 17%, p=0.6). Those with hemorrhage as the primary HS most often required surgery (76%), but no interventions were required in 19% of hemorrhage, 20% of ischemia, and 24% of expanding hematoma.

Conclusion: Although HS in PCVI are associated with the need for operative intervention, initial CT imaging can facilitate endovascular options or nonoperative management in a significant subgroup. HS should not be considered an absolute indication for immediate surgical exploration.

Level of Evidence: Level III, Prognostic and epidemiological.

Keywords: Penetrating neck, trauma, vascular trauma, hard signs

Reading the Signs in Penetrating Cervical Vascular Injuries: Analysis of Hard/Soft Signs and Initial Management from a Nationwide Vascular Trauma Database

Short Title: Reading the Signs in Penetrating Cervical Vascular Injury

Alexander Marrotte MD*, Richard Y Calvo PhD*, Jayraan Badiee MPH*, Alexandra S Rooney MPH*, Andrea Krzyzaniak MA*, Michael Sise, MD*, Vishal Bansal MD*, Joseph DuBose MD**, Matthew J Martin MD***, and the AAST PROOVIT Study Group

*Trauma Service, Department of Surgery, Scripps Mercy Hospital, San Diego, California

**Department of Surgery and Perioperative Care, University of Texas-Austin, Dell Medical School, Austin, TX

***Division of Trauma and Acute Care Surgery, Department of Surgery, Los Angeles County + USC Medical Center, Los Angeles, CA

Address correspondence to:

Matthew J Martin, MD
Division of Trauma and Acute Care Surgery
2051 Marengo Street, IPT, Room C5L100
Los Angeles, CA 90033
Phone: (323) 409-8604
Email: matthew.martin@med.usc.edu

Author's email addresses:

Alexander Marrotte MD: Alexander.marrotte@gmail.com; Jayraan Badiee: badiee.jayraan@scrippshealth.org; Alexandra S Rooney MPH: rooney.alexandra@scrippshealth.org; Richard Y. Calvo PhD: calvo.richard@scrippshealth.org; Andrea Krzyzaniak MA: krzyzaniak.andrea@scrippshealth.org; Michael J. Sise MD: sise.mike@scrippshealth.org; Vishal Bansal MD: bansal.vishal@scrippshealth.org; Joseph DuBose MD: JJD3C@yahoo.com; Matthew J Martin MD: matthew.martin@med.usc.edu

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PROOVIT Study Group Collaborators: Tiffany Bee MD; Emily Lenart, MD; Suzanne Moyer CRNP, University of Tennessee Health Sciences Center – Memphis; Jonny Morrison, MD, PhD; David Feliciano, MD; Thomas M. Scalea, MD, University of Maryland R Adams Cowley Shock Trauma Center Baltimore, MD, USA; David Skarupa, MD; Jennifer A. Mull, RN, CCRC; Yohan Diaz Zuniga, MD, University of Florida – Jacksonville Jacksonville, FL, USA; Jeanette M Podbielski, RN, CCRP; Garrett Jost, University of Texas Health Sciences Center– Houston Houston, TX, USA; Richard D. Catalano, MD; Ahmed M. Abou-Zamzam Jr, MD; Xian Luo-Owen, PhD, Loma Linda University Medical Center Loma Linda, CA, USA; Jennie Kim, MD; Kenji Inaba, MD Los Angeles County + University of Southern California Hospital Los Angeles, CA, USA; Nathaniel Poulin, MD; East Carolina Medical Center; John Myers, MD; Michael Johnson, MD; Kristin Rocchi, RN, The University of Texas Health Sciences Center at San Antonio San Antonio, TX, USA; John K. Bini, MD; Joshua Pringle, MD; Karen Herzing, BSN, RN; Kailey Nolan, BS Wright State Research Institute - Miami Valley Hospital Dayton, OH, USA; Ramyar Gilani, MD; Tikesha Smith; Reginva Knight, Ben Taub General Hospital / Baylor College of Medicine Houston, TX, USA JBSA Fort Sam Houston, TX, USA; Peter Hammer, MD Indiana University School of Medicine Indianapolis, IN, USA; Scott T. Trexler, MD San Antonio Military Medical Center / US Army Institute of Surgical Research; Nicholas Namias, MD, MBA; Jonathan P Meizoso, MD Ryder Trauma Center, University of Miami / Jackson

Memorial Miami, FL, USA; Juan Asensio, MD FACS Creighton University School of Medicine Omaha, Nebraska, USA; Joseph M. Galante, MD; Misty Humphries, MD University of California – Davis Sacramento, CA, USA; Ravi R. Rajani, MD; Jaime Benarroch-Gampel, MD; Christopher Ramos, MD Emory University School of Medicine – Grady Memorial Hospital Atlanta, GA, USA; George Dulabon, MD; Riyad Karmy-Jones Peace Health Southwest Washington Medical Center Vancouver, Washington, USA; Andreas Larentzakis MD, George Velmahos, MD Massachusetts General Hospital Boston, Massachusetts, USA; Suresh Agarwal, MD University of Wisconsin Madison, WI, USA; Jayraan Badiee MPH; Michael Sise, MD; Matthew Martin, MD Scripps Mercy Hospital San Diego, CA, USA; Daniel Cucher, MD; Annette Taylor, RN, BSN, CCRC; Charlotte Tanner, RN, BSN, CRC Chandler Regional Medical Center Chandler, AZ, USA; Fausto Y. Vinces, DO; Salvatore Docimo, DO Lutheran Medical Center Brooklyn, New York, USA; Matthew M. Carrick, MD; Kathy Rodkey, RCIS, CCRC Medical City Plano Plano, TX, USA; Sameer Hirji, MD; Reza Askari, MD Brigham and Women's Hospital Boston, MA, USA; Forrest O. Moore, MD; Richard Butler, MD John Peter Smith Hospital Fort Worth, TX, USA; James Haan, MD; Kelly Lightwine, MPH Ascension Via Christi Hospitals Wichita, Kansas

Responses to Reviewer Comments

Are the criteria for inclusion and exclusion of study subjects explicitly stated? Does the manuscript include a flow diagram that identifies both excluded patients and those who were ultimately included in the analysis?

Reviewer #1: Yes

Reviewer #2: No: Inclusion/exclusion criteria are outlined in the Methods section, but there is no flow diagram included

Response: A Flow diagram of inclusion criteria is now included as Figure 1.

Additional Comments to Author(s):

In the abstract under results, the third line refers to "Figure". I believe this should read "Figure #1"

Response: Figure renamed to Figure 2 in abstract.

In the Background section of the paper, it refers to the "Western Association for Trauma algorithm". I believe that should read "Western Trauma Association algorithm".

Response: Thank you for catching this! Edit changed in manuscript, it now reads as:

The current Western Trauma Association algorithm follows this pattern.

Although not statistically significant, should there be some discussion regarding patients that present with soft signs and imaged first having a 10.3% mortality vs. 0% in those with immediate operative intervention?

Response: Yes, this is a great point and bears further discussion. These patients were overall older, had higher ISS and lower GCS upon presentation indicating that they were more severely injured likely via non neck injuries and had high risk factors for in hospital mortality. Whether or not their initial presentation or the state of their other injuries played a role in the management of their cervical vascular injury is not capture by the database.

The paragraph now reads:

Patients who were first imaged were more likely to die compared to patients who received immediate operative intervention, although the difference was not statistically significant (10.3% vs. 0.0%, $p = 0.143$). This cohort of patients when compared to the rest of the patients who presented with soft signs were older, had a higher overall Injury Severity Score and lower GCS making them at a higher overall risk for in hospital mortality. They also had significantly shorter hospital stays indicating they died within a short interval of injury. What factor these patient’s overall prognosis had on decision making in regards to their penetrating cervical vascular injury is not captured in this database.

Reviewer #2:

Accepting the status quo prevents advancement in medical therapy, and with advancements in the quality of CT imaging, the wider-spread presence of hybrid operating rooms, and improving endovascular techniques, this paper provides evidence to at least partially debunk the dogma of hard signs of vascular injuries requiring immediate operative repair.

PROOVIT is a well-known large, multi-institutional database of vascular injuries, from which the authors drew the 232 patients included in the study. As noted in the limitations, drawing conclusions from information contained in databases can be risky, and in this study, none of the clinical decision making leading to operative intervention is known, which could significantly alter the data, though likely in favor of observational management. Additionally, the definition of nonoperative management in the Results section, where endovascular intervention was included in the operative group (p 11, lines 7-14), does not match that in the Discussion section, with endovascular repairs being considered nonoperative (p 14, line 59). Can the authors clarify?

Response: In the results section, the word "operative" was removed. It now reads:

The remaining 21 (42.8%) of imaged patients required no intervention and were observed.

This should allow clarity that these patients underwent neither operative nor endovascular intervention. We also concur with the comments about the lack of granular clinical data on decision making and have added this to the limitations paragraph.

In the discussion, the authors refer to the 'WTA-defined hard signs" but do not list those signs. For the purposes of the paper, they should be included in the manuscript and the reader should not be expected to have access to the referenced manuscript. (The reference is also not labelled with a number).

Response: In regards to the WTA hard signs, they are previously listed out and the WTA guidelines is referenced in the background, as written:

"Many algorithms continue to center on the presence of these "hard signs" which include active hemorrhage, expanding/ pulsatile hematoma, neurological deficits for vascular injuries and airway compromise, subcutaneous emphysema, and hematemesis for aerodigestive injuries in addition to hemodynamic stability. The current Western Trauma Association algorithm follows this pattern10."

To clarify and further reference the hard signs, a table of hard signs has been created and annotated as Table 1. See below:

Hard signs in penetrating neck injuries	
Vascular	Active hemorrhage, Expanding hematoma, ischemia/neurological deficits
Airway	Airway compromise, subcutaneous emphysema, air bubbling through wound
Digestive	Hematemesis

In regard to the missing reference in the discussion, the information being cited is from the Schroll et al. paper and is now referenced in the paper as reference number 23.

The authors do a good job of showing that zones of injury mean less than clinical findings and CT imaging and provide good evidence that imaging can result in decreased unnecessary operative intervention in "select" patients. They should, however, be a bit more specific in defining "select".

Response: Select patients further defined as hemodynamically stable, with a secure airway, and manageable hard signs. It now reads:

In conclusion, although hard signs in penetrating cervical vascular injury are associated with the frequent need for operative intervention, initial CT imaging in select patients (hemodynamically stable, with a secure airway, and manageable hard signs) appears safe and can facilitate endovascular options or nonoperative management in a significant subgroup.

Further clarifying edits were made that were not indicated by the reviewers:

1. In the evaluation of patients who presented with soft signs of vascular trauma, 14 patients were excluded due to missing/incomplete data. A statement indicating this was not included in the initial submission. A sentence stating this was included and reads: Of the 122 patients who presented with soft signs, 14 patients were excluded due to missing diagnostic and management data.
2. In the soft signs group, percentages were reflected out of all patients who presented with soft signs versus out of the subgroup of patients imaged. This was inconsistent with how the hard signs cohort was presented. The percentages have been updated to reflect this change.
3. The demographics table (Table 2) had a typo where "internal jugular vein" and "carotid artery" were switched. This typographical error has been corrected.
4. Further analysis was performed regarding patients who presented with hypotension on admission, defined as systolic blood pressure < 90. This further analysis was added to the results portion of the manuscript. It reads
    a. Patients presenting with an admission SBP < 90 were defined as hypotension on admission. Hypotension was present in 19% of patients with hard signs, compared to 9% for patients without hard signs (p = 0.026). Among those with soft signs, zero hypotensive patients had surgery first compared with 7 who had been scanned first (p = 0.206). Among patients with hard signs, 21 patients were hypotensive and had surgery or imaging. 26% had surgery and 10% had been imaged first (p = 0.034).
5. Table 3. Hard Signs by Repair methodology was reanalyzed to include multiple signs and has been adjusted
6. A visual Abstract has been created and attached separately.
7. A separate figure legend has been added after the references

We again would like to express our gratitude to the reviewers for their careful review and time spent reviewing the manuscript.

BACKGROUND

Penetrating neck trauma is a relatively common injury in both military and civilian trauma which can present with significant vascular, airway, and/or digestive tract involvement (1-3). Historically, penetrating neck injuries were managed using an anatomically-based "zone approach" with injuries to Zone 1 (below the cricoid cartilage) and Zone 3 (above the angle of the mandible) in stable patients requiring employment of bronchoscopy, endoscopy and invasive angiography due to surgical inaccessibility or morbidity of access to these regions. Penetrating injuries in Zone 2, the area in between, were recommended to undergo operative neck exploration as opposed to pursuing a complex and timely diagnostic evaluation. This led to an unnecessarily high amount of non-operative neck explorations with retrospective studies showing surgical exploration to be therapeutic in 70% of patients with hard signs but only 40% of patients with soft signs(4-9). With improvements in the quality and accessibility of computed tomography angiography (CTA), the standard for evaluating most penetrating neck injuries has recently shifted to a "no zone" approach utilizing screening CTA in stable patients and immediate operative exploration in unstable patients or those with hard signs of vascular or aerodigestive injuries(4, 8, 10). Many algorithms continue to center on the presence of these "hard signs" which include active hemorrhage, expanding/ pulsatile hematoma, neurological deficits for vascular injuries and airway compromise, subcutaneous emphysema, and hematemesis for aerodigestive injuries in addition to hemodynamic stability (Table 1). The current Western Trauma Association algorithm follows this pattern(10). However, recent literature has begun to question the validity of these hard signs for directing mandatory and immediate operative exploration, particularly for vascular injury. There exists a significant gap in the literature due to the relative infrequency of these injuries in most centers resulting in the majority of published reports having small sample sizes and being underpowered.

The American Association for the Surgery of Trauma began the PROspective Observational Vascular Injury Treatment (PROOVIT) registry in 2013, a multicenter database regarding the diagnosis, management, and outcomes for patients with vascular injury in trauma(11). This database allows for analysis of modern diagnosis, management, and subsequent outcomes of patients with penetrating cervical vascular injuries (PCVI). We sought to analyze a large modern sample of patients with PCVI from the PROOVIT database and to specifically examine the association between hard signs and outcomes including need for operative interventions and mortality.

METHODS

The PROspective Observational Vascular Injury Treatment (PROOVIT) registry is a 31-center vascular injury registry sponsored by the American Association for the Surgery of Trauma (AAST). After obtaining institutional review board approval, enrolled trauma centers submit data directly to the PROOVIT study via an internet-based portal. Approval for this analysis was granted by the PROOVIT study review panel. Deidentified data for admissions occurring between January 29, 2012 and September 30, 2020 were used as this was when accrued data were last reported. STROBE guidelines for cross-sectional studies were followed(12).

Patients who sustained any penetrating injury to the external carotid artery (ECA), internal carotid artery (ICA), common carotid artery (CCA), vertebral artery, or jugular vein were included (Figure 1). Penetrating mechanisms were categorized as gunshot wounds (GSW), stabbings, or other. Patients with other penetrating injuries were specified as having a penetrating type of injury but with a specified mechanism of industrial accident, motor vehicle crash, or unspecified. Patients were categorized based on presence of hard signs for any of the above-named vessels. Hard signs were defined as presence of hemorrhage, expanding hematoma, or ischemia, as outlined by the PROOVIT data collection methodology. Patients with multiple hard signs vs. singular hard signs were identified and classified accordingly. Soft signs captured by the PROOVIT registry included wound proximity, reduced pulses, and fracture/dislocation pattern. Patients who had multiple cervical vascular injuries were similarly categorized separately to those with a singular vascular injury. Patients were excluded if they had missing data pertaining to diagnostic methods or course of care.

The primary risk factors of interest were preoperative imaging with CTA. For each injured vessel, usage of pre-operative CTA or operative exploration were assessed. The primary outcomes were operative management of the vascular injury or observation without surgery. Operative management categories were open operative intervention, endovascular intervention, or observation. Timing of the first intervention utilized the following categories based on the PROOVIT methodology: < 1 hour from admission, within 1–3 hours from admission, within 3–6 hours from admission, or >6 hours from admission.

Additional risk factors of interest include patient age at admission, sex, presence of concomitant non-cervical injuries, Injury Severity Score, Glasgow Coma Scale score, admission systolic blood pressure, adjunctive medical therapy, hospital length of stay, ventilator days, and in-hospital death. Hemodynamic instability was defined as a systolic blood pressure < 90 mmHg. Severe traumatic injury was defined as an ISS > 15. Presence of concomitant non-head injuries was identified using presence of AIS body region scores for non-head locations.

Data were managed and analyzed using Stata MP v17.0 (StataCorp LLC, College Station, TX). Descriptive statistics were calculated and displayed as means with standard deviation (SD), medians with interquartile ranges (IQR), or proportions, as appropriate. Descriptive analyses included the t-test, chi-square test, and rank-sum test to evaluate patient and clinical characteristics by presence of hard signs. Chi-square tests were used to evaluate differences in the presence of specific hard signs by course of care. Statistical significance was attributable to comparisons with resultant p-values < 0.050.

RESULTS

The PROOVIT registry contained 4,618 patients, of which 232 experienced PCVI with injury to a named cervical vessel. Singular ICA injuries were the most frequent (23.7%), followed by jugular injuries (23.3%), vertebral artery injuries (18.5%), CCA injuries (12.5%), and ECA injuries (6.0%). Multiple vessel injuries were seen in 16.0% of the sample. The most prevalent mechanism of injury was gunshot wounds (59.9%), followed by stabbings (34.9%) and other (5.2%). Overall, 110 (47.4%) presented with hard signs and 122 (52.6%) had soft signs. Between patients with hard signs and soft signs, there were no statistical differences detected regarding patient age, reported sex, ISS, ICU length of stay, or Glasgow Coma Scale score (Table 2). However, the median hospital length of stay was shorter for patients who had hard signs compared to those with soft signs. Similarly, patients with hard signs were more likely to have presented with a systolic blood pressure < 90 mmHg, have a stabbing-type mechanism of injury, and to have died during their hospital stay.

Of those with hard signs, 61 (55.5%) underwent immediate operative exploration and 49 (44.5%) underwent diagnostic CT imaging. Of those imaged first, 14 (28.5%) had open surgical repair, 11 (22.4%) had endovascular intervention, and 3 (6.1%) had operative exploration without a subsequent repair. The remaining 21 (42.8%) of imaged patients required no intervention and were observed. Ultimately, 19% of all patients who presented with hard signs were managed with observation alone (Figure 2). There was no statistical difference in mortality between patients with hard signs who underwent operative management versus observation alone (12.5% vs. 26.3%, p = 0.248).

The proportion of hard signs at presentation in the sample were 48.2% hemorrhage, 21.8% hematoma, 0.9% ischemia, and 29.1% with multiple. Regarding specific vessels, hard signs comprised 58.7% of CCA injuries, 36.1% of ICA injuries, 40.0% of ECA injuries, 66.2% of jugular injuries, and 33.3% of vertebral artery injuries. Those with a singular hard sign of hemorrhage were more likely to have open repair and endovascular repair of their injury compared to patients who experienced a singular hematoma or ischemia; However, these differences were not statistically significant (Table 3). No interventions were required in 19.4% of hemorrhage or 21.1% of patients with singular expanding hematoma. Among 32 patients with multiple hard signs, 23 (71.9%) received open repair, 1 (3.1%) received open and endovascular repair, and 8 (25.0%) received no intervention.

Of the 122 injured patients who presented with soft signs, 27.1% were ICA, 23.0% were vertebral, 16.4% were jugular, 12.3% were CCA, and 7.4% were ECA. Seventeen (13.9%) of soft sign patients had multiple vascular injuries. Nineteen patients (15.6%) had immediate surgery compared to 89 (73.0%) that underwent CT imaging. Of the 122 patients who presented with soft signs, 14 patients were excluded due to missing diagnostic and management data. After imaging, 10 (11.2%) had open surgery, 12 (13.4%) had endovascular repair, and 66 (74.1%) were observed. Patients who were first imaged were more likely to die compared to patients who received immediate operative intervention, although the difference was not statistically significant (10.3% vs. 0.0%, p = 0.143). This cohort of patients when compared to the rest of the patients who presented with soft signs were older, had a higher overall Injury Severity Score and lower GCS making them at a higher overall risk for in hospital mortality. They also had significantly shorter hospital stays indicating they died within a short interval of injury. What factor these patient's overall prognosis had on decision making in regards to their penetrating cervical vascular injury is not captured in this database.

Among all patients in our sample, those who had hard signs were more likely to receive their first operative intervention within one hour of injury compared to those with only soft signs (45.9% vs. 25.6%, p = 0.032). Earlier timing of the first intervention was not directly attributable to a specific vessel injury before or after stratification by presence of hard signs. Similarly, timing of the first intervention was not associated with mortality. Patients who experienced a stabbing-type mechanism of injury were statistically significantly more likely to have had a surgical intervention within 1 hour of injury (50.0% vs. 42.8% for other vs. 28.8% for gunshot, p = 0.030). However, after stratification by presence of hard signs, the strength of the associations diminished.

Patients presenting with an admission SBP < 90 were defined as hypotension on admission. Hypotension was present in 19% of patients with hard signs, compared to 9% for patients without hard signs (p = 0.026). Among those with soft signs, zero hypotensive patients had surgery first compared with 7 who had been scanned first (p = 0.206). Among patients with hard signs, 21 patients were hypotensive and had surgery or imaging. 26% had surgery and 10% had been imaged first ($p = 0.034$).

DISCUSSION

The evaluation and management of penetrating cervical trauma and particularly cervical vascular injuries has continued to evolve significantly over the past several decades. The historical approaches of extensive imaging and endoscopic workups for zone 1 and 3 neck injuries and mandatory neck exploration for zone 2 trauma has given way to management strategies based primarily on the bedside physical exam and assessment for hard or soft signs of injury, and with CTA as the primary imaging adjunct that can then guide the need for additional diagnostic evaluation or surgical exploration. Although the oft-cited "hard signs" of cervical vascular injury are typically used as an indication to proceed with immediate operative exploration, their actual reliability and predictive value has not been well validated in penetrating neck trauma. Here we report the first analysis of the nationwide PROOVIT database of traumatic vascular injuries examining these issues for penetrating neck injury. We specifically examined the outcomes and need for operative repair among cohorts with reported hard signs who underwent immediate operation versus those who underwent diagnostic imaging. Our results indicate a significant proportion of patients with hard signs who may benefit from CTA imaging to direct less invasive interventions or to avoid the need for surgery altogether.

The currently utilized hard signs of vascular injury were initially described in peripheral vascular trauma in the early 1960's and slowly refined and generalized to include cervical vascular injuries(13). However, few have challenged and verified these signs in the decades since. Recently, Romagnoli et. al, used the PROOVIT database to compare management of hemorrhagic versus ischemic hard signs in traumatic extremity injuries. They concluded that using clinical hard signs had significant limitations in characterizing extremity vascular injury and found that patients who underwent CTA imaging required less operative intervention and had similar outcomes(14). Our aim was to utilize this same multicenter database to explore the value of hard signs in penetrating cervical vascular trauma.

After analyzing the PROOVIT database, we found that a significant number of patients presenting with hard signs of vascular injury after penetrating cervical vascular injury did not require operative intervention and were able to be observed clinically before discharge. Most patients who presented with hard signs underwent immediate operative intervention, although it is unclear whether this was due to a clinical necessity for operative intervention or simply following current local management algorithms. However, of those who were imaged initially, 65.2% were managed without operative intervention (42.8% observation, 22.4% endovascular). 34.6% of imaged patients did undergo operative exploration but 17.6% of those patients had nontherapeutic operations. The choice to undertake operative exploration after imaging in these patients was likely due to equivocal imaging findings or the necessity to operate on hard signs despite imaging, although the true motivation for these decisions was not captured by the database. However, patients who underwent immediate operative repair did not have worse outcomes than those who were observed alone. Further, the data showed that although imaging delayed time to operation, there was no significant increase in mortality. Hemorrhage was the most commonly presenting hard sign, followed by multiple hard signs. Hemorrhage was also more likely to be intervened on than other hard signs. Unlike extremity vascular trauma where loss of distal pulses is a reliable hard sign, there is no distal pulse exam in cervical vascular trauma. The closest equivalent is the resultant neurologic sequelae that can occur from occlusion of the carotid and/or vertebral vessels, which would typically manifest as focal neurologic deficits similar to a stroke presentation. However, these can be highly variable depending on the location and type of injury, the presence of collateral vessels, and the neurologic exam can also be compromised by factors like shock, associated brain injury, intoxication, or the need for early intubation and sedation. In this series, neurological deficits or ischemia was the least commonly reported hard sign at less than 1 percent, and thus there is little that can be extrapolated about this small subset in terms of the utility of immediate operative intervention versus performing CTA or other imaging studies. The most injured vessels to present with hard signs were the jugular vein and the common carotid artery. Of note, 30% of patients presenting with hard signs had isolated jugular vein injuries. Current literature shows that non operative management of isolated internal jugular vein injury to be safe and effective with no increased morbidity or mortality (15, 16). Under current protocols, a significant number of patients with internal jugular injuries would undergo unnecessary neck explorations. Theoretically, hard signs are meant to represent arterial injury that necessitates operative repair. However, given the high preponderance of isolated jugular vein injuries presenting with hard signs, the validity of this interpretation comes into question.

Regarding soft signs, as expected, the majority of these patients underwent diagnostic imaging (54.1%) and most (75%) were treated with observation alone. A small proportion underwent immediate repair, although it is difficult to ascertain whether this was due to clinical gestalt or provider preference. However, as expected, only 18% of patients required any intervention after imaging. There was no statistically significant difference for patients with soft signs who were observed.

The movement away from a zone approach to penetrating neck injuries was spurred by two things, the advancement and accessibility of CTA but also the unreliability of external zones to correlate with internal injury(7, 8, 17-20). Further evaluation of CTA in penetrating neck injuries by Inaba et al. showed that CTA was a highly sensitive and specific screening modality for evaluating vascular trauma(21). A study by Woo et al. further demonstrated that CTA evaluation reduced the rates of nontherapeutic neck exploration, invasive angiography and endoscopy(22). However, these studies still utilized hard signs as absolute indications for operative intervention and these patients were excluded from evaluation. Schroll et al. performed a 4-year single center retrospective analysis of patients with penetrating neck trauma who presented with hard signs and underwent imaging first. Of 183 patients who have penetrating neck injuries, 23 clinically stable patients with WTA-defined hard signs were identified. Seventeen of these patients had negative CT findings and did not require neck exploration. The most specific hard signs in their review were hard signs for aerodigestive injury (air bubbling through wound and subcutaneous emphysema. Hard signs for vascular injury were found to be much less specific with patients only requiring neck exploration in 39% to 55%. Their analysis found that hard signs had a sensitivity of 84%, specificity of 84%, PPV of 47% and NPV of 97%. In comparison, they found that CTA in the presence of hard signs had 83% sensitivity, 100% specificity, PPV of 100% and NPV of 94%. Ultimately, CTA in this patient population was able to significantly reduce the rate of non-therapeutic neck exploration without increasing risk of missed injury(23). This study was limited by being a single center review with relatively low sample size. Another retrospective study done by Madsen et al., investigated 380 stable patients with penetrating neck injuries who underwent CTA imaging. Although only 13 (3%) of these patients had hard signs, CTA was able to detect arterial injury in 11 (84.6%) and 38.5%

were able to be managed non-operatively. They found no clinically significant delay or increased morbidity associated with imaging first management. They determined hard signs to be only 76.9% effective for predicting arterial injury compared to 93.9% sensitivity of CTA. Further, they demonstrated soft signs to be only 16.4% sensitive(18). Our study further supports the above findings as almost two thirds of patients with hard signs who were imaged were able to avoid a neck exploration despite being associated with a true vascular injury.

Our study does have significant limitations given that the exact indications for operative management are often multifactorial and guided by clinical picture, surgeon judgement, and hospital resources among other variables. These variables are often difficult to capture in a large database, and the exact reasoning behind any captured decision in the dataset is unknown. Additionally, inclusion in the PROOVIT database requires presence of a named vascular injury and thus analysis of this data cannot be used to determine sensitivity, specificity, or predictive value of hard signs due to the missing denominator data of all patients who presented with a penetrating neck injury but did not have a vascular injury identified. Further delineation of these variables would require larger prospective studies aimed at analyzing the positive and negative predictive values of hard signs based on CTA findings. However, our study does set the precedent that routine CTA imaging in stable patients is safe and effective.

In conclusion, although hard signs in penetrating cervical vascular injury are associated with the frequent need for operative intervention, initial CT imaging in select patients (hemodynamically stable, with a secure airway, and manageable hard signs) appears safe and can facilitate endovascular options or nonoperative management in a significant subgroup. There also appear to be variable patterns in the incidence of associated vascular injury, need for operative repair, and outcomes including mortality based on which hard sign is present alone or in combination. Further study with larger sample sizes will be required to achieve the required power to adequately examine these issues among subgroups of individual hard and soft signs following penetrating cervical trauma with associated vascular injuries. Based on the data from this analysis, hard signs should not be considered an absolute indication for immediate surgical exploration in all penetrating cervical trauma patients, and select use of CTA can identify a significant subgroup for alternative interventions or nonoperative management.

Author Contribution: A.M. conducted the literature search. A.M., J.B., A.S.R., R.Y.C., M.J.S., A.K., V.B., M.J.M, participated in the conception or design of the work. A.M., R.Y.C., M.J.M., acquired, analyzed, or interpreted the data for the work. A.M., J.B., A.S.R., R.Y.C., M.J.S., A.K., V.B., M.J.M, participated in drafting the work or revising it for important intellectual content. All authors approved the final version of the work to be published.

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Figure Legend

Figure 1. Inclusion criteria

Figure 2. Breakdown of management by hard and soft signs

BACKGROUND

Penetrating neck trauma is a relatively common injury in both military and civilian trauma which can present with significant vascular, airway, and/or digestive tract involvement (1-3). Historically, penetrating neck injuries were managed using an anatomically-based “zone approach” with injuries to Zone 1 (below the cricoid cartilage) and Zone 3 (above the angle of the mandible) in stable patients requiring employment of bronchoscopy, endoscopy and invasive angiography due to surgical inaccessibility or morbidity of access to these regions. Penetrating injuries in Zone 2, the area in between, were recommended to undergo operative neck exploration as opposed to pursuing a complex and timely diagnostic evaluation. This led to an unnecessarily high amount of non-operative neck explorations with retrospective studies showing surgical exploration to be therapeutic in 70% of patients with hard signs but only 40% of patients with soft signs(4-9). With improvements in the quality and accessibility of computed tomography angiography (CTA), the standard for evaluating most penetrating neck injuries has recently shifted to a “no zone” approach utilizing screening CTA in stable patients and immediate operative exploration in unstable patients or those with hard signs of vascular or aerodigestive injuries(4, 8, 10). Many algorithms continue to center on the presence of these “hard signs” which include active hemorrhage, expanding/ pulsatile hematoma, neurological deficits for vascular injuries and airway compromise, subcutaneous emphysema, and hematemesis for aerodigestive injuries in addition to hemodynamic stability (Table 1). The current Western Trauma Association algorithm follows this pattern(10). However, recent literature has begun to question the validity of these hard signs for directing mandatory and immediate operative exploration, particularly for vascular injury. There exists a significant gap in the literature due to the relative infrequency of these injuries in most centers resulting in the majority of published reports having small sample sizes and being underpowered.

The American Association for the Surgery of Trauma began the PROspective Observational Vascular Injury Treatment (PROOVIT) registry in 2013, a multicenter database regarding the diagnosis, management, and outcomes for patients with vascular injury in trauma(11). This database allows for analysis of modern diagnosis, management, and subsequent outcomes of patients with penetrating cervical vascular injuries (PCVI). We sought to analyze a large modern sample of patients with PCVI from the PROOVIT database and to specifically examine the association between hard signs and outcomes including need for operative interventions and mortality.

METHODS

The PROspective Observational Vascular Injury Treatment (PROOVIT) registry is a 31-center vascular injury registry sponsored by the American Association for the Surgery of Trauma (AAST). After obtaining institutional review board approval, enrolled trauma centers submit data directly to the PROOVIT study via an internet-based portal. Approval for this analysis was granted by the PROOVIT study review panel. Deidentified data for admissions occurring between January 29, 2012 and September 30, 2020 were used as this was when accrued data were last reported. STROBE guidelines for cross-sectional studies were followed(12).

Patients who sustained any penetrating injury to the external carotid artery (ECA), internal carotid artery (ICA), common carotid artery (CCA), vertebral artery, or jugular vein were included (Figure 1). Penetrating mechanisms were categorized as gunshot wounds (GSW), stabbings, or other. Patients with other penetrating injuries were specified as having a penetrating type of injury but with a specified mechanism of industrial accident, motor vehicle crash, or unspecified. Patients were categorized based on presence of hard signs for any of the above-named vessels. Hard signs were defined as presence of hemorrhage, expanding hematoma, or ischemia, as outlined by the PROOVIT data collection methodology. Patients with multiple hard signs vs. singular hard signs were identified and classified accordingly. Soft signs captured by the PROOVIT registry included wound proximity, reduced pulses, and fracture/dislocation pattern. Patients who had multiple cervical vascular injuries were similarly categorized separately to those with a singular vascular injury. Patients were excluded if they had missing data pertaining to diagnostic methods or course of care.

The primary risk factors of interest were preoperative imaging with CTA. For each injured vessel, usage of pre-operative CTA or operative exploration were assessed. The primary outcomes were operative management of the vascular injury or observation without surgery. Operative management categories were open operative intervention, endovascular intervention, or observation. Timing of the first intervention utilized the following categories based on the PROOVIT methodology: < 1 hour from admission, within 1–3 hours from admission, within 3–6 hours from admission, or >6 hours from admission.

Additional risk factors of interest include patient age at admission, sex, presence of concomitant non-cervical injuries, Injury Severity Score, Glasgow Coma Scale score, admission systolic blood pressure, adjunctive medical therapy, hospital length of stay, ventilator days, and in-hospital death. Hemodynamic instability was defined as a systolic blood pressure < 90 mmHg. Severe traumatic injury was defined as an ISS > 15. Presence of concomitant non-head injuries was identified using presence of AIS body region scores for non-head locations.

Data were managed and analyzed using Stata MP v17.0 (StataCorp LLC, College Station, TX). Descriptive statistics were calculated and displayed as means with standard deviation (SD), medians with interquartile ranges (IQR), or proportions, as appropriate. Descriptive analyses included the t-test, chi-square test, and rank-sum test to evaluate patient and clinical characteristics by presence of hard signs. Chi-square tests were used to evaluate differences in the presence of specific hard signs by course of care. Statistical significance was attributable to comparisons with resultant p-values < 0.050.

RESULTS

The PROOVIT registry contained 4,618 patients, of which 232 experienced PCVI with injury to a named cervical vessel. Singular ICA injuries were the most frequent (23.7%), followed by jugular injuries (23.3%), vertebral artery injuries (18.5%), CCA injuries (12.5%), and ECA injuries (6.0%). Multiple vessel injuries were seen in 16.0% of the sample. The most prevalent mechanism of injury was gunshot wounds (59.9%), followed by stabbings (34.9%) and other (5.2%). Overall, 110 (47.4%) presented with hard signs and 122 (52.6%) had soft signs. Between patients with hard signs and soft signs, there were no statistical differences detected regarding patient age, reported sex, ISS, ICU length of stay, or Glasgow Coma Scale score (Table 2). However, the median hospital length of stay was shorter for patients who had hard signs compared to those with soft signs. Similarly, patients with hard signs were more likely to have presented with a systolic blood pressure < 90 mmHg, have a stabbing-type mechanism of injury, and to have died during their hospital stay.

Of those with hard signs, 61 (55.5%) underwent immediate operative exploration and 49 (44.5%) underwent diagnostic CT imaging. Of those imaged first, 14 (28.5%) had open surgical repair, 11 (22.4%) had endovascular intervention, and 3 (6.1%) had operative exploration without a subsequent repair. The remaining 21 (42.8%) of imaged patients required no intervention and were observed. Ultimately, 19% of all patients who presented with hard signs were managed with observation alone (Figure 2). There was no statistical difference in mortality between patients with hard signs who underwent operative management versus observation alone (12.5% vs. 26.3%, $p = 0.248$).

The proportion of hard signs at presentation in the sample were 48.2% hemorrhage, 21.8% hematoma, 0.9% ischemia, and 29.1% with multiple. Regarding specific vessels, hard signs comprised 58.7% of CCA injuries, 36.1% of ICA injuries, 40.0% of ECA injuries, 66.2% of jugular injuries, and 33.3% of vertebral artery injuries. Those with a singular hard sign of hemorrhage were more likely to have open repair and endovascular repair of their injury compared to patients who experienced a singular hematoma or ischemia; However, these differences were not statistically significant (Table 3). No interventions were required in 19.4% of hemorrhage or 21.1% of patients with singular expanding hematoma. Among 32 patients with multiple hard signs, 23 (71.9%) received open repair, 1 (3.1%) received open and endovascular repair, and 8 (25.0%) received no intervention.

Of the 122 injured patients who presented with soft signs, 27.1% were ICA, 23.0% were vertebral, 16.4% were jugular, 12.3% were CCA, and 7.4% were ECA. Seventeen (13.9%) of soft sign patients had multiple vascular injuries. Nineteen patients (15.6%) had immediate surgery compared to 89 (73.0%) that underwent CT imaging. Of the 122 patients who presented with soft signs, 14 patients were excluded due to missing diagnostic and management data. After imaging, 10 (11.2%) had open surgery, 12 (13.4%) had endovascular repair, and 66 (74.1%) were observed. Patients who were first imaged were more likely to die compared to patients who received immediate operative intervention, although the difference was not statistically significant (10.3% vs. 0.0%, p = 0.143). This cohort of patients when compared to the rest of the patients who presented with soft signs were older, had a higher overall Injury Severity Score and lower GCS making them at a higher overall risk for in hospital mortality. They also had significantly shorter hospital stays indicating they died within a short interval of injury. What factor these patient's overall prognosis had on decision making in regards to their penetrating cervical vascular injury is not captured in this database.

Among all patients in our sample, those who had hard signs were more likely to receive their first operative intervention within one hour of injury compared to those with only soft signs (45.9% vs. 25.6%, p = 0.032). Earlier timing of the first intervention was not directly attributable to a specific vessel injury before or after stratification by presence of hard signs. Similarly, timing of the first intervention was not associated with mortality. Patients who experienced a stabbing-type mechanism of injury were statistically significantly more likely to have had a surgical intervention within 1 hour of injury (50.0% vs. 42.8% for other vs. 28.8% for gunshot, p = 0.030). However, after stratification by presence of hard signs, the strength of the associations diminished.

Patients presenting with an admission SBP < 90 were defined as hypotension on admission. Hypotension was present in 19% of patients with hard signs, compared to 9% for patients without hard signs (p = 0.026). Among those with soft signs, zero hypotensive patients had surgery first compared with 7 who had been scanned first (p = 0.206). Among patients with hard signs, 21 patients were hypotensive and had surgery or imaging. 26% had surgery and 10% had been imaged first (p = 0.034).

DISCUSSION

The evaluation and management of penetrating cervical trauma and particularly cervical vascular injuries has continued to evolve significantly over the past several decades. The historical approaches of extensive imaging and endoscopic workups for zone 1 and 3 neck injuries and mandatory neck exploration for zone 2 trauma has given way to management strategies based primarily on the bedside physical exam and assessment for hard or soft signs of injury, and with CTA as the primary imaging adjunct that can then guide the need for additional diagnostic evaluation or surgical exploration. Although the oft-cited "hard signs" of cervical vascular injury are typically used as an indication to proceed with immediate operative exploration, their actual reliability and predictive value has not been well validated in penetrating neck trauma. Here we report the first analysis of the nationwide PROOVIT database of traumatic vascular injuries examining these issues for penetrating neck injury. We specifically examined the outcomes and need for operative repair among cohorts with reported hard signs who underwent immediate operation versus those who underwent diagnostic imaging. Our results indicate a significant proportion of patients with hard signs who may benefit from CTA imaging to direct less invasive interventions or to avoid the need for surgery altogether.

The currently utilized hard signs of vascular injury were initially described in peripheral vascular trauma in the early 1960's and slowly refined and generalized to include cervical vascular injuries(13). However, few have challenged and verified these signs in the decades since. Recently, Romagnoli et. al, used the PROOVIT database to compare management of hemorrhagic versus ischemic hard signs in traumatic extremity injuries. They concluded that using clinical hard signs had significant limitations in characterizing extremity vascular injury and found that patients who underwent CTA imaging required less operative intervention and had similar outcomes(14). Our aim was to utilize this same multicenter database to explore the value of hard signs in penetrating cervical vascular trauma.

After analyzing the PROOVIT database, we found that a significant number of patients presenting with hard signs of vascular injury after penetrating cervical vascular injury did not require operative intervention and were able to be observed clinically before discharge. Most patients who presented with hard signs underwent immediate operative intervention, although it is unclear whether this was due to a clinical necessity for operative intervention or simply following current local management algorithms. However, of those who were imaged initially, 65.2% were managed without operative intervention (42.8% observation, 22.4% endovascular). 34.6% of imaged patients did undergo operative exploration but 17.6% of those patients had nontherapeutic operations. The choice to undertake operative exploration after imaging in these patients was likely due to equivocal imaging findings or the necessity to operate on hard signs despite imaging, although the true motivation for these decisions was not captured by the database. However, patients who underwent immediate operative repair did not have worse outcomes than those who were observed alone. Further, the data showed that although imaging delayed time to operation, there was no significant increase in mortality. Hemorrhage was the most commonly presenting hard sign, followed by multiple hard signs. Hemorrhage was also more likely to be intervened on than other hard signs. Unlike extremity vascular trauma where loss of distal pulses is a reliable hard sign, there is no distal pulse exam in cervical vascular trauma. The closest equivalent is the resultant neurologic sequelae that can occur from occlusion of the carotid and/or vertebral vessels, which would typically manifest as focal neurologic deficits similar to a stroke presentation. However, these can be highly variable depending on the location and type of injury, the presence of collateral vessels, and the neurologic exam can also be compromised by factors like shock, associated brain injury, intoxication, or the need for early intubation and sedation. In this series, neurological deficits or ischemia was the least commonly reported hard sign at less than 1 percent, and thus there is little that can be extrapolated about this small subset in terms of the utility of immediate operative intervention versus performing CTA or other imaging studies. The most injured vessels to present with hard signs were the jugular vein and the common carotid artery. Of note, 30% of patients presenting with hard signs had isolated jugular vein injuries. Current literature shows that non operative management of isolated internal jugular vein injury to be safe and effective with no increased morbidity or mortality (15, 16). Under current protocols, a significant number of patients with internal jugular injuries would undergo unnecessary neck explorations. Theoretically, hard signs are meant to represent arterial injury that necessitates operative repair. However, given the high preponderance of isolated jugular vein injuries presenting with hard signs, the validity of this interpretation comes into question.

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Author Contribution: A.M. conducted the literature search. A.M., J.B., A.S.R., R.Y.C., M.J.S., A.K., V.B., M.J.M, participated in the conception or design of the work. A.M., R.Y.C., M.J.M., acquired, analyzed, or interpreted the data for the work. A.M., J.B., A.S.R., R.Y.C., M.J.S., A.K., V.B., M.J.M, participated in drafting the work or revising it for important intellectual content. All authors approved the final version of the work to be published.

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Figure Legend

Figure 1. Inclusion criteria

Figure 2. Breakdown of management by hard and soft signs

Table 1. Hard signs as defined by the Western Trauma Association

Hard signs in penetrating neck injuries	
Vascular	Active hemorrhage, Expanding hematoma, ischemia/neurological deficits
Airway	Airway compromise, subcutaneous emphysema, air bubbling through wound
Digestive	Hematemesis

Table 3. Hard signs by repair methodology.

Hard Sign Category	N	Definitive Open	Definitive Endovascular	Observation	p-value
Hemorrhage Only	58	74.1%	13.8%	12.1%	0.048
Hematoma Only	29	75.9%	6.9%	17.2%	
Neurologic Symptoms Only	1	0%	100%	0%	
Multiple Signs	15	68.2%	0%	31.8%	

Table 2

Table 2. Demographics.

Characteristic	**Any Hard Signs (n = 110)**	**Only Soft Signs (n = 122)**	**p-value**
Age, mean (sd)	33.8 (14.8)	35.7 (15.7)	0.360
ISS, median (IQR)	16 (10 – 25)	16.5 (10 – 26)	0.840
Male sex, n (%)	95 (86.4)	99 (81.2)	0.284
Hospital LOS, median (IQR)	6 (3 – 16)	9 (4 – 18)	0.042
ICU LOS, median (IQR)	3 (1 – 7)	4 (1 – 9)	0.429
GCS score, median (IQR)	12.5 (3 – 15)	15 (3 – 15)	0.207
Hemodynamic instability, n (%)	21 (19.1)	11 (9.0)	0.026
Mechanism of injury, n (%)			0.026
Gunshot	58 (52.7)	81 (66.4)	
Stabbing	48 (43.6)	33 (27.1)	
Other	4 (3.6)	8 (6.6)	
Vessels injured, n (%)			0.060
Common carotid	14 (12.7)	15 (12.3)	
Internal carotid	22 (20.0)	33 (27.1)	
External carotid	5 (4.6)	9 (7.4)	
Internal jugular vein	34 (30.9)	20 (16.4)	
Carotid artery	15 (13.6)	28 (23.0)	
Multiple vessels	20 (18.2)	17 (13.9)	
In-hospital death, n (%)	23 (21.3)	11 (9.7)	0.016

Figure 1

Figure 1.

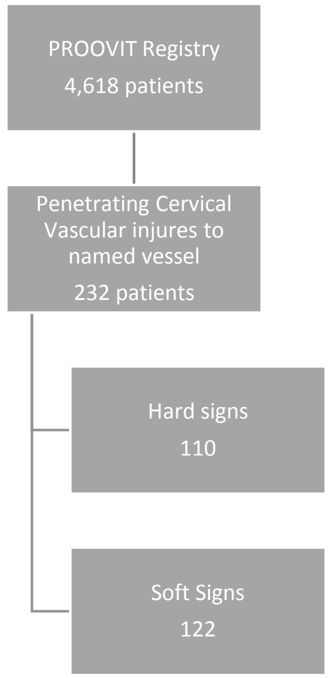
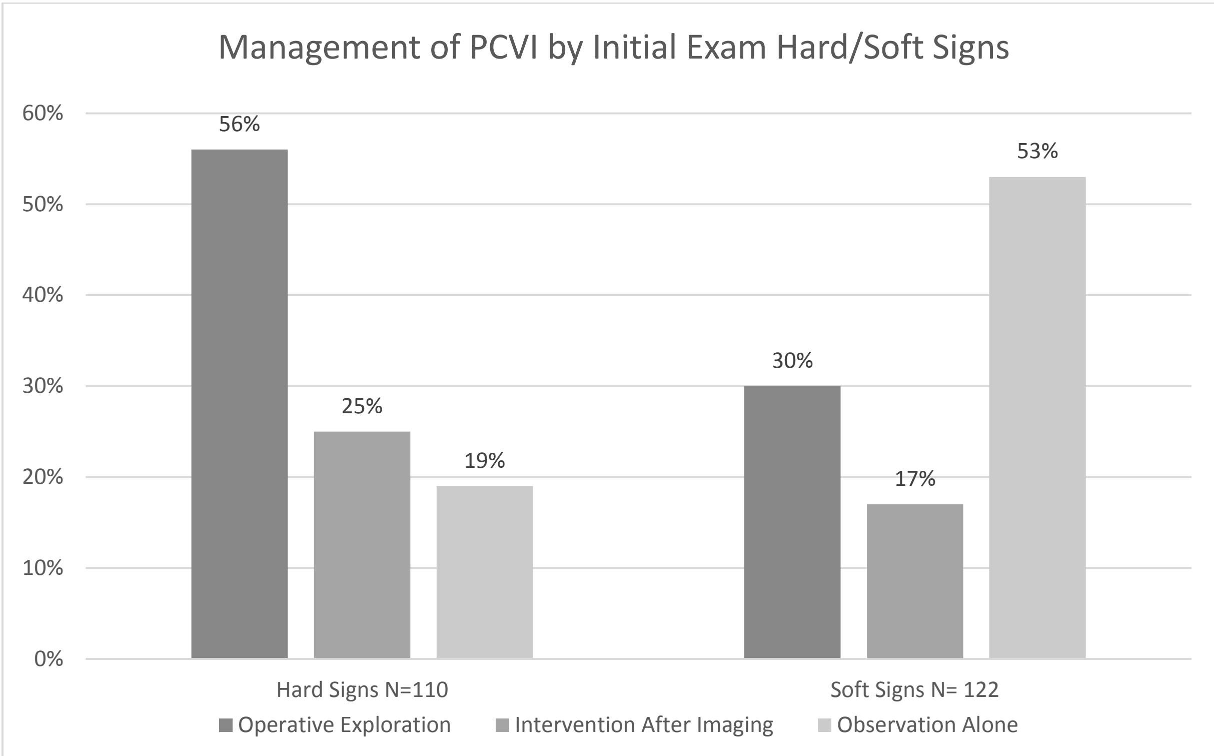


Figure 2

Figure 2.



PCVI, penetrating cervical vascular injuries.

Click here to access/download
Supplemental Data File (.doc, .tif, pdf, etc.)
PROOVIT.JOT.Response.STROBE.docx

Visual Abstract

Reading the Signs in Penetrating Cervical Vascular Injuries

Study Population

PROOVIT dataset

Penetrating neck injuries: 232 patients

Results

Hard Signs
n = 110

↓

Diagnostic Imaging
45%

↓

Observation
43%

20% Overall

Conclusions

Early CT imaging

=

Reduced operations

+

facilitated observational management

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