A nomogram predicting the need for bleeding interventions after high-grade renal trauma: Results from the American Association for the Surgery of Trauma Multi-institutional Genito-Urinary Trauma Study (MiGUTS)

Sorena Keihani, MD, Douglas M. Rogers, MD, Bryn E. Putbrese, MD, Rachel A. Moses, MD, MPH, Chong Zhang, MS, Angela P. Presson, PhD, James M. Hotaling, MD, MS, Raminder Nirula, MD, MPH, Xian Luo-Owen, PhD, Kaushik Mukherjee, MD, MSCI, Bradley J. Morris, RN, CFRN, PA-C, Sarah Majercik, MD, MBA, Joshua Piotrowski, MD, PhD, Christopher M. Dodgion, MD, MSPH, MBA, Ian Schwartz, MD, Sean P. Elliott, MD, MS, Erik S. DeSoucy, DO, Scott Zakaluzny, MD, Brenton G. Sherwood, MD, Bradley A. Erickson, MD, MS, Nima Baradaran, MD, Benjamin N. Breyer, MD, MAS, Brian P. Smith, MD, Barbara U. Okafor, MBA, Reza Askari, MD, Brandi Miller, DO, Richard A. Santucci, MD, Matthew M. Carrick, MD, Jurek F. Kocik, MD, Timothy Hewitt, MD, Frank N. Burks, MD, Marta E. Heilbrun, MD, Jeremy B. Myers, MD, *and* **in conjunction with the Trauma and Urologic Reconstruction Network of Surgeons***, Salt Lake City, Utah*

AAST Continuing Medical Education Article

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint providership of the American College of Surgeons and the American Association for the Surgery of Trauma. The American College Surgeons is accredited by the ACCME to provide continuing medical education for physicians.

AMA PRA Category 1 Credits™

The American College of Surgeons designates this journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Of the *AMA PRA Category 1 Credit*™ listed above, a maximum of 1 credit meets the requirements for self-assessment.

Credits can only be claimed online

AMERICAN COLLEGE OF SURGEONS

Inspiring Quality: Highest Standards, Better Outcomes

100+years

Objectives

After reading the featured articles published in the *Journal of Trauma and Acute Care Surgery*, participants should be able to demonstrate increased understanding of the material specific to the article. Objectives for each article are featured at the beginning of each article and online. Test questions are at the end of the article, with a critique and specific location in the article referencing the question topic.

Claiming Credit

To claim credit, please visit the AAST website at http://www.aast.org/ and click on the "e-Learning/MOC" tab. You must read the article, successfully complete the post-test and evaluation. Your CME certificate will be available immediately upon receiving a passing score of 75% or higher on the post-test. Post-tests receiving a score of below 75% will require a retake of the test to receive credit.

Disclosure Information

In accordance with the ACCME Accreditation Criteria, the American College of Surgeons, as the accredited provider of this journal activity, must ensure that anyone in a position to control the content of *J Trauma Acute Care Surg* articles selected for CME credit has disclosed all relevant financial relationships with any commercial interest. Disclosure forms are completed by the editorial staff, associate editors, reviewers, and all authors. The ACCME defines a `commercial interest' as "any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients." "Relevant" financial relationships are those (in any amount) that may create a conflict of interest and occur within the 12'months preceding and during the time that the individual is engaged in writing the article. All reported conflicts are thoroughly managed in order to ensure any potential bias within the content is eliminated. However, if you'perceive a bias within the article, please report the circumstances on the evaluation form.

Please note we have advised the authors that it is their responsibility to disclose within the article if they are describing the use of a device, product, or drug that is not FDA approved or the off-label use of an approved device, product, or drug or unapproved usage.

Disclosures of Significant Relationships with Relevant Commercial Companies/Organizations by the Editorial Staff

Ernest E. Moore, Editor: PI, research support and shared U.S. patents Haemonetics; PI, research support, Instrumentation Laboratory, Inc.; Co-founder, Thrombo Therapeutics. Associate Editors David Hoyt, Ronald V. Maier and Steven Shackford have nothing to disclose. Editorial staff and Angela Sauaia have nothing to disclose.

Author Disclosures

Sean Elliott Utronic, Percuvision, Boston Scientific. Money/Grant Investigator.

Reviewer Disclosures

The reviewers have nothing to disclose.

Cost

For AAST members and *Journal of Trauma and Acute Care Surgery* subscribers there is no charge to participate in this activity. For those who are not a member or subscriber, the cost for each credit is $25.

System Requirements

The system requirements are as follows: Adobe® Reader 7.0 or above installed; Internet Explorer® 7 and above; Firefox® 3.0 and above, Chrome® 8.0 and above, or Safari™ 4.0 and above.

Questions

If you have any questions, please contact AAST at 800-789-4006. Paper test and evaluations will not be accepted.

BACKGROUND: The management of high-grade renal trauma (HGRT) and the indications for intervention are not well defined. The American Association for the Surgery of Trauma (AAST) renal grading does not incorporate some important clinical and radiologic variables associated with increased risk of interventions. We aimed to use data from a multi-institutional contemporary cohort to develop a nomogram predicting risk of interventions for bleeding after HGRT.

METHODS: From 2014 to 2017, data on adult HGRT (AAST grades III–V) were collected from 14 level 1 trauma centers. Patients with both clinical and radiologic data were included. Data were gathered on demographics, injury characteristics, management, and outcomes. Clinical and radiologic parameters, obtained after trauma evaluation, were used to predict renal bleeding interventions. We developed a prediction model by applying backward model selection to a logistic regression model and built a nomogram using the selected model.

RESULTS: A total of 326 patients met the inclusion criteria. Mechanism of injury was blunt in 81%. Median age and injury severity score were 28 years and 22, respectively. Injuries were reported as AAST grades III (60%), IV (33%), and V (7%). Overall, 47 (14%) underwent interventions for bleeding control including 19 renal angioembolizations, 16 nephrectomies, and 12 other procedures. Of the variables included in the nomogram, a hematoma size of 12 cm contributed the most points, followed by penetrating trauma mechanism, vascular contrast extravasation, pararenal hematoma extension, concomitant injuries, and shock. The area under the receiver operating characteristic curve was 0.83 (95% confidence interval, 0.81–0.85).

CONCLUSION: We developed a nomogram that integrates multiple clinical and radiologic factors readily available upon assessment of patients with HGRT and can provide predicted probability for bleeding interventions. This nomogram may help in guiding appropriate management of HGRT and decreasing unnecessary interventions. (*J Trauma Acute Care Surg.* 2019;86: 774–782. Copyright © 2019 American Association for the Surgery of Trauma.)

LEVEL OF EVIDENCE: Prognostic and epidemiological study, level III.

KEY WORDS: Renal trauma; nephrectomy; nomograms; conservative treatment; computed tomography; wounds and injuries; trauma centers; multicenter study.

The organ injury scoring scale, developed by the American Association for the Surgery of Trauma (AAST), is the most widely used tool to grade traumatic renal injuries.[1] The AAST grading for renal trauma encompasses a spectrum of severity within each injury grade, especially for higher-grade injuries. Despite being highly associated with outcomes such as nephrectomy,[2–5] the AAST grading system does not incorporate some key clinical and radiologic findings pertinent to bleeding interventions.[6] For example, it does not account for hemodynamic instability and mechanism of trauma, which are important factors to consider in renal trauma management. Similarly, the original AAST grading does not account for some radiologic findings such as the presence of active renal vascular bleeding, size of the perirenal hematoma, and laceration characteristics, which have been shown to be highly associated with nephrectomy and other bleeding control interventions.[7–9] Revisions to the AAST grading have been proposed to address some ambiguities within grade IV and V injuries[10] and to incorporate radiologic factors aimed at improving the discriminating power for higher-risk injuries.[8] However, these studies are limited by retrospective design and the rarity of renal trauma and related interventions in single-center studies.[8,11,12]

The majority of patients with high-grade renal trauma (HGRT) can be successfully managed without open surgery, as most renal injuries can heal with expectant management or use of more conservative endovascular interventions (i.e., selective angioembolization of bleeding vessels).[13] Despite this, the management of HGRT is variable between centers, and nephrectomy remains the most common intervention, performed in as many as 28% of patients with grades IV and V injuries.[5,14,15] Timely and accurate identification of patients with renal trauma who would benefit from intervention, as well as those that are at low risk for bleeding is paramount to guiding appropriate management. Recognizing factors that predict bleeding risk from renal injury and using a data-driven tool to predict interventions is the first step in achieving this goal. Such a tool could help clinicians rapidly obtain an estimated probability that a renal trauma patient would benefit from interventions to control bleeding or if the patient can be safely managed nonoperatively. To create such a tool, we used our multi-institutional prospective data to build an HGRT bleeding intervention nomogram using

From the Division of Urology, Department of Surgery (S.K., R.A.M., J.M.H., J.B.M.), Department of Radiology (D.M.R., B.E.P.), Division of Epidemiology, Department of Internal Medicine (C.Z., A.P.P.), and Department of Surgery (R.N.), University of Utah, Salt Lake City, Utah; Division of Acute Care Surgery (X.L-O., K.M.), Loma Linda University Medical Center, Loma Linda, California; Division of Trauma and Surgical Critical Care (B.J.M., S.M.), Intermountain Medical Center, Murray, Utah; Department of Urology (J.P.), and Department of Surgery (C.M.D.), University of Wisconsin, Milwaukee, Wisconsin; Department of Urology (I.S., S.P.E.), Hennepin County Medical Center, University of Minnesota, Minneapolis, Minnesota; Department of Surgery (E.S.D.), and Division of Trauma, Acute Care Surgery, and Surgical Critical Care, Department of Surgery (S.Z.), University of California Davis Medical Center, Sacramento, California; Department of Urology (B.G.S., B.A.E.), University of Iowa, Iowa City, Iowa; Department of Urology (N.B., B.N.B.), University of California—San Francisco, San Francisco, California; Division of Trauma and Surgical Critical Care (B.P.S.), Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania; Division of Trauma, Department of Surgery (B.U.O., R.A.), Brigham and Women's Hospital, Boston, Massachusetts; Department of Urology (B.M., R.A.S.), Detroit Medical Center, Detroit, Michigan; Medical City Plano (M.M.C.), Plano; Department of Surgery (J.F.K.), East Texas Medical Center, Tyler, Texas; Department of Urology (T.H., F.N.B.), Oakland University William Beaumont School of Medicine, Royal Oak, Michigan; Department of Radiology and Imaging Sciences (M.E.H.), Emory University Hospital, Atlanta, Georgia.

This study was presented at the 77th Annual Meeting of the American Association for the Surgery of Trauma and Clinical Congress of Acute Care Surgery and 4th World Trauma Congress, September 26–29, 2018, in San Diego, California.

Address for reprints: Sorena Keihani, MD, Division of Urology, Department of Surgery, University of Utah School of Medicine, 30 North 1900 East, Salt Lake City, UT 84132; email: sorena.keihani@hsc.utah.edu.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.jtrauma.com).

DOI: 10.1097/TA.0000000000002222

clinical and radiologic factors readily available at the time of trauma assessment.

PATIENTS AND METHODS

The data used for this study were collected as part of the Multi-institutional Genito-Urinary Trauma Study (MiGUTS - full study sites and collaborators' information is available at http://www.turnsresearch.org/page/aast-gu-trauma-study-group-author-list-renal-trauma). Details on the renal trauma study protocol and data collection have been previously published.[5] In brief, the study was a multi-institutional prospective collaborative effort of the AAST, in conjunction with the Trauma and Urologic Reconstruction Network of Surgeons (TURNS) that involved 14 level 1 trauma centers across the United States. From 2014 to 2017, clinical and radiologic data were collected from patients with HGRT (defined as AAST grades III–V) who were treated at the participating trauma centers. For this study, patients who underwent immediate surgery without imaging or those who died before undergoing diagnostic studies were excluded from the analysis. Thus, only patients who were stable enough to undergo diagnostic trauma computer tomography (CT) scan after renal trauma were included.

Clinical variables included age, sex, trauma mechanism (blunt vs. penetrating), side of renal injury (right, left, bilateral), injury severity score (ISS), hypotension/shock (defined as systolic blood pressure <90 mm Hg anytime during the first 4 hours from admission), Glasgow Coma Scale, number and type of blood products received in the first 24 hours, admission laboratory values (hematocrit/hemoglobin, lactate), and presence of any concomitant injury (including solid organ, gastrointestinal, spinal cord, major vascular, and pelvic fracture).

Radiologic variables included vascular contrast extravasation (VCE), hematoma rim distance (HRD; i.e., the largest measure from the edge of the kidney to the hematoma rim), hematoma extension (none/subcapsular, perirenal, pararenal), and laceration location (lateral, medial, complex [both types]). Vascular contrast extravasation was defined as the presence of contrast accumulation outside of the renal parenchyma demonstrated on arterial or venous phase CT scan (Supplemental Digital Content 1, Supplemental Fig. 1, http://links.lww.com/TA/B295).[7] Hematoma rim distance was measured at the axial CT planes and was defined as the longest perpendicular distance from the renal parenchymal border to the hematoma border within the boundaries of upper and lower margins of the kidney (Supplemental Fig. 2, Supplemental Digital Content 1, http://links.lww.com/TA/B295). Laceration location was defined similar to Dugi et al.[8] using a perpendicular line to a plane through the renal hilum to define the medial and lateral halves of the kidney (Supplemental Fig. 3, Supplemental Digital Content 1, http://links.lww.com/TA/B295).

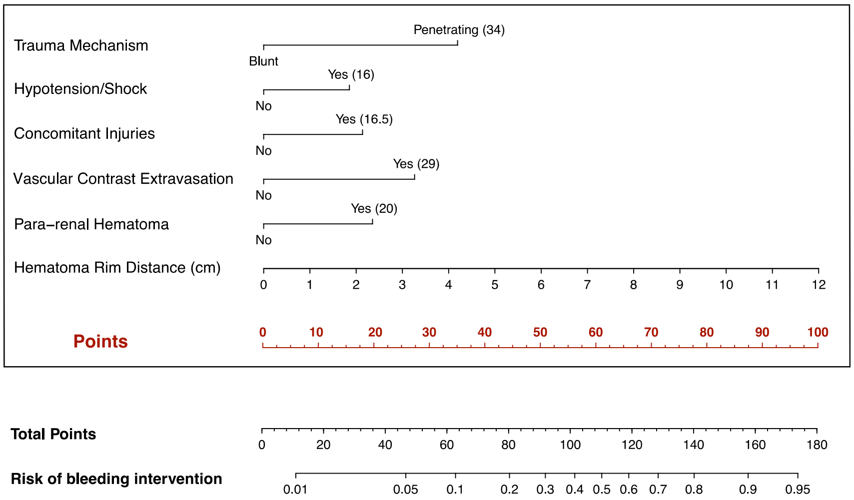

Figure 1. Nomogram for the regression model predicting bleeding interventions after HGRT.
How to read the nomogram: For HRD, take the size of hematoma in centimeters and draw a vertical line to the red bar labeled *Points* in the box to get the points. Then, sum the points of the HRD with the other five variables using the point values in the parentheses for each variable. Take the sum of the points and make a dot on the *Total Points* bar below the box on the nomogram. Connect this dot from the *Total Points* bar to the bottommost bar to obtain the predicted probability of undergoing bleeding interventions. Example 1: A patient is presented to the emergency department with a normal and stable blood pressure (i.e., no hypotension/shock during the first 4 hours of admission; 0 points) and with isolated high-grade renal injury (i.e., no concomitant injuries; 0 points) after a knife injury (penetrating injury; 34 points) to the left kidney; in the initial trauma CT scan, there is a 3-cm (HRD, 3 cm; 25 points) hematoma confined to the perirenal space (no pararenal; 0 points) without active VCE (no VCE, 0 points). Total points are 59 (0 + 0 + 34 + 25 + 0 + 0) corresponding to an intervention probability of less than 10%. (Supplemental Digital Content 1, Figure 6A, http://links.lww.com/TA/B295). Example 2: A patient is transferred to the emergency department in shock (16 points) after high-speed motor vehicle accident (blunt injury; 0 points). After initial fluid resuscitation and hemodynamic stabilization, the patient undergoes trauma CT scan, which shows liver and splenic lacerations without active bleeding (concomitant injuries; 16.5 points) and multiple deep lacerations in the right kidney with VCE from renal vessels (VCE; 29 points) and a 9-cm hematoma (HRD, 9 cm; 75 points) extending inferiorly into the pelvis (pararenal extension; 20 points). Total points are 156.5 (16 + 0 + 16.5 + 29 + 75 + 20) corresponding to an intervention probability of approximately 90%, suggesting that it is highly likely that the patient would need early angiography with or without angioembolization or an open intervention (Supplemental Digital Content 1, Figure 6B, http://links.lww.com/TA/B295).

Pararenal hematoma was defined as hematoma extending beyond aorta on the left or inferior vena cava on the right, or extending inferior to the aortic bifurcation into the pelvis (Supplemental Fig. 4, Supplemental Digital Content 1, http://links.lww.com/TA/B295). Definition of bleeding interventions included nephrectomy, partial nephrectomy, renorrhaphy, renal packing, and renal angioembolization. All deidentified radiologic studies were uploaded to a secure Web-based Orthanc[16] server for central review. Two radiologists, blinded to the intervention data and patient outcomes, reviewed the CT scans to extract injury specifics.

Descriptive statistics were used to summarize baseline patient characteristics as well as clinical and radiologic variables. Data are presented as mean (SD) or median (25th–75th interquartile range [IQR]) when appropriate. Comparisons were made between those who underwent interventions for renal bleeding control and those who did not. Independent samples *t* test (or Wilcoxon rank-sum test) and χ^2 test (or Fisher's exact test when appropriate) were used to compare continuous and categorical variables between groups, respectively. Mixed effect univariable and multivariable logistic regression models, with clustering by facility, were developed to predict bleeding interventions using selected clinical and radiographic variables. Variables were selected based on clinical relevance and availability at the time of initial trauma evaluation. Candidate predictors included the following: hypotension/shock, concomitant injuries, trauma mechanism, hemoglobin at admission, VCE, HRD, hematoma extension, and laceration location. Factors

TABLE 1. Demographics and Clinical and Radiologic Variables in a Cohort of Patients With HGRT (AAST III–V) Split by Bleeding Intervention

	Total (N = 326)	No Intervention* (n = 279)	Intervention* (n = 47)	*p*†
Demographics				
Age, median (IQR), y	28 (22–46)	28 (22–44)	32 (23–47)	0.33
Body mass index, mean (SD), kg/m^2	27.4 (6.5)	27.4 (6.7)	27.1 (4.7)	0.74
Male sex, n (%)	248 (76)	206 (75)	42 (89)	**0.02**
Injury specifics				
ISS, median (IQR)	22 (16–33)	22 (16–33)	25 (18–35)	0.06
Trauma mechanism, n (%)				**0.01**
Blunt	263 (81)	232 (83)	31 (66)	
Penetrating	63 (19)	47 (17)	16 (34)	
HR on admission, mean (SD), beats/min	93.7 (22.5)	93.4 (22.6)	95.1 (22.4)	0.64
Tachycardia on admission, n (%)	123 (39)	99 (35)	24 (51)	0.11
SBP on admission, mean (SD), mm Hg	125.0 (25.3)	125.6 (25.1)	121.3 (26.4)	0.28
Hypotension/shock, n (%)	75 (23)	59 (21)	16 (34)	0.12
Hemoglobin on admission, mean (SD), mg/dL	12.7 (1.9)	12.8 (2.0)	12.1 (1.7)	**0.04**
PRBC transfusion in the first 24 h, n (%)	116 (35)	81 (29)	35 (74)	**<0.001**
Lactate, median (IQR), mmol/L	2.7 (1.6–4.4)	1.5 (1.0–4.3)	2.5 (2.0–5.7)	0.17
GCS score, median (IQR)	15 (14–15)	15 (14–15)	15 (14–15)	0.92
Concomitant injuries, n (%)‡	217 (66)	184 (66)	33 (70)	0.57
Length of hospital stay, median (IQR), d	6 (3–12)	6 (3–11)	10 (6–17)	**<0.001**
Mortality, n (%)	13 (4)	10 (4)	3 (6)	0.36
Radiologic variables				
AAST grade, n (%)				**0.01**
III	195 (60)	180 (64)	15 (32)	
IV	108 (33)	88 (32)	20 (43)	
V	23 (7)	11 (4)	12 (25)	
VCE, n (%)	73 (23)	44 (16)	29 (63)	**<0.001**
Hematoma rim diameter, mean (SD), cm	2.1 (2.0)	1.7 (1.5)	4.3 (2.8)	**<0.001**
Hematoma extent, n (%)				**<0.001**
None/subcapsular	43 (13)	42 (15)	1 (2)	
Perirenal	160 (49)	146 (52)	14 (30)	
Pararenal	123 (38)	91 (33)	32 (68)	
Laceration location, n (%)§				**<0.001**
Lateral	100 (31)	89 (33)	11 (24)	
Medial	67 (21)	65 (24)	2 (4)	
Both/complex	151 (48)	117 (43)	34 (72)	

*Bleeding interventions including nephrectomy, partial nephrectomy, renorrhaphy, renal packing, and renal-related angioembolization.
†Comparisons made between patients who underwent bleeding interventions and those who did not; bold numbers indicate statistically significant at $p < 0.05$ level.
‡Defined as presence of any concomitant injury, including: solid organ, gastrointestinal, spinal cord, major vascular, and pelvic fracture.
§Eight patients did not have parenchymal laceration.
HR, heart rate; SBP, systolic blood pressure; PRBC, packed red blood cells; GCS, Glasgow Coma Scale; VCE, vascular contrast extravasation.

TABLE 2. Univariable and Multivariable Mixed Effect Logistic Regression Models for Predicting Bleeding Interventions After HGRT

	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
Age (per year)	1.01 (0.9–1.03)	0.43	—	
Sex (male vs. female)	3.05 (1.25–9.17)	0.03	—	
Mechanism of injury (penetrating vs. blunt)	2.63 (1.28–5.33)	0.008	4.70 (1.76–13.06)	0.002
Hypotension/shock (yes vs. no)	1.93 (0.95–3.84)	0.06	1.82 (0.74–4.41)	0.19
HGB at admission (per mg/dL)	0.86 (0.73–1.00)	0.05	—	
Concomitant injuries (yes vs. no)	1.25 (0.64–2.56)	0.52	2.50 (0.98–7.02)	0.07
VCE (yes vs. no)	10.74 (5.23–23.22)	<0.001	3.88 (1.57–9.73)	0.003
HRD (per cm)	1.85 (1.54–2.29)	<0.001	1.54 (1.20–2.04)	0.001
Pararenal hematoma (yes vs. no)	4.57 (2.35–9.34)	<0.001	2.34 (0.83–6.73)	0.11
Laceration location (complex vs. lateral/medial)	3.38 (1.68–6.79)	<0.001	—	

HGB, hemoglobin; VCE, vascular contrast extravasation; HRD, hematoma rim distance.

such as ISS and number of blood products transfused were not included as they are not typically available at the initial assessment. Lactate levels were not included because of considerable amount of missing data (~39%) and also concerns about selection bias toward patients presenting with lactic acidosis and more severe injuries. The AAST grade was also not included because there is significant variability and some ambiguity about grading of high-grade injuries.[8,10] Some injury patterns are also not addressed in the current AAST grading system,[17] which decreases its accuracy in predicting urgent bleeding interventions.[6] In addition, since the radiographic appearance of the injuries was characterized in detail and included in the model and the intent of this study was to further characterize these risk factors separate from the AAST grade, inclusion of the AAST grade would not be appropriate.

Odds ratios (ORs) and *p* values from univariable mixed effect logistic models predicting bleeding interventions were reported for each candidate predictor. Stepwise regression evaluating Akaike information criterion with backward elimination was used to develop our prediction model using the candidate variables. Odds ratios and *p* values for the selected model were reported, and a nomogram was created to describe the relative contributions of risk for renal bleeding interventions of each predictor. For internal validation, model fit was assessed using the Hosmer-Lemeshow goodness of fit test and a calibration plot. To protect against overoptimism, prediction accuracy was estimated using 100 random iterations of 10-fold cross validation for the area under the receiver operating characteristic curve (AUC).[18] Statistical analyses were conducted in R version 3.4.0 (The R Foundation, Vienna, Austria).

The point values for each variable in the nomogram were assigned using the methodology outlined by Yang[19] for building prognostic nomograms. Briefly, the range for each predictor was calculated and multiplied by its beta coefficient to assess its predictive utility relative to the other predictors in the model. The predictor with the highest predictive strength, MaxX, was assigned 100 points, and then the point values for each other predictor, X_i, were calculated as 100*(predictive utility X_i)/(predictive utility MaxX). The nomogram can be read for a particular combination of patient characteristics by obtaining the corresponding points for each patient characteristic from the *Points* bar in the box and summing them. The sum of the points is then found on the *Total Points* bar below the box on the nomogram, and a straight line from the total points to the bottommost bar will provide the predicted probability of undergoing bleeding interventions. To assist with this process, we have provided the point values for categorical variables in parentheses. Point values for the continuous variable (i.e., HRD) must be obtained manually by comparing the variable's value to the points bar at the bottom (Fig. 1).

RESULTS

From a cohort of 431 patients, 326 had initial CT scans available for review and were included in this study. Median age was 28.0 years (IQR, 22–46 years), and median ISS was 25 (IQR, 16–33). Mechanism of trauma was blunt in 263 patients (81%) and included motor vehicle collisions (140, 53%), pedestrian versus automobile (26, 10%), bicycle (11, 4%), falls (31, 12%), and other (e.g., sport related, assault, not specified; 55, 21%). Patient characteristics, as well as clinical and radiologic findings at the time of admission, separated by need for bleeding interventions, are presented in Table 1.

Overall, 47 patients (14%) underwent bleeding interventions including 19 renal angioembolizations, 16 nephrectomies, 3 partial nephrectomies, 7 renorrhaphies, and 6 renal packing for bleeding control; some patients underwent more than one intervention (e.g., both angioembolization and renorrhaphy). Patients who underwent bleeding interventions had higher rates of penetrating injuries and lower hemoglobin on admission; they also had higher-grade renal injuries, higher rate of VCE, more complex lacerations, and larger hematomas around the injured kidney (Table 1).

Table 2 presents the results from the univariable and multivariable regression models for the selected clinical and radiologic factors to predict undergoing bleeding interventions. In the multivariable model, a penetrating mechanism of injury and presence of VCE were associated with 4.7-fold and 3.9-fold increases in odds of undergoing bleeding interventions; each 1 cm increase in HRD was also associated with 54% increase in odds of undergoing bleeding interventions.

The nomogram for our bleeding intervention prediction model is presented in Figure 1. Risk of bleeding interventions was calculated using the logistic regression model as predicted probability = exp(*Y*)/(1 + exp(*Y*)), where *Y* was estimated as follows:

Y = − 5.109 + 1.586*(trauma mechanism) + 0.749*(hypotension/shock) + 0.768*(concomitant injuries) + 1.355*(VCE) + 0.927*(pararenal hematoma) + 0.389*(HRD in cm).

Both the calibration plot and Hosmer-Lemeshow goodness of fit test ($\chi^2 = 3.6$, $p = 0.31$) indicated that the data fit the model reasonably well (Supplemental Fig. 5, Supplemental Digital Content 1, http://links.lww.com/TA/B295). Of the clinical and radiologic variables entered in the model, only hemoglobin and laceration location were not included in the final model. Having an HRD of 12 cm contributed the most points to the nomogram, followed by penetrating trauma mechanism, presence of VCE, pararenal hematoma extension, presence of concomitant injuries, and hypotension/shock. The AUC was 0.83 (95% confidence interval [CI], 0.81–0.85). Examples for reading the nomogram using hypothetical patient scenarios are provided in Supplemental Figure 6 (Supplemental Digital Content 1, http://links.lww.com/TA/B295).

To determine if the nomogram predicted interventions better than the AAST grade alone, a separate univariable analysis was performed. The AAST grade was associated with a 3.4-fold increase in odds of bleeding interventions (OR, 3.41; 95% CI, 2.13–5.48), and the AUC for the univariable model was 0.69 (95% CI, 0.61–0.77). In addition, adding the AAST grade to the multivariable model did not significantly increase the AUC of the nomogram (data not shown).

DISCUSSION

We developed a nomogram to predict the risk of bleeding interventions after HGRT, which includes a combination of important clinical and radiologic factors, which are readily available during a trauma evaluation. This nomogram provides an evidence-based predictive tool that may help guide management decisions, especially in lower-volume centers with limited experience with management of HGRT.

There is well-established evidence that conservative management of renal trauma is safe and effective and that most stable patients with high-grade injuries can be managed nonoperatively.[13,20] Nephrectomy is avoidable in most patients, except those in extremis or with renal bleeding that fails to respond to alternate less invasive approaches, such as angioembolization and renorrhaphy. According to the National Trauma Data Bank, about 1 in every 3 patients with a grade IV renal injury and more than half of patients with grade V injuries undergo nephrectomy during their acute management.[14] Similarly, in our recent multi-institutional study, 15% of grade IV and 62% of grade V renal injuries underwent nephrectomy in level 1 trauma centers.[5] It has been shown that nephrectomy rates can be significantly lowered by implementing nonoperative management protocols.[21] Nonoperative strategies benefit from predictive tools, such as the proposed nomogram, to identify those patients at higher risk for failure of nonoperative management so that interventions can be performed early, encouraging a systematic approach to management.

Evidence-based nomograms have higher predictive values when compared with conventional grading systems and can provide highly accurate risk estimates to facilitate management-related decisions in different areas of medicine.[20,22] In addition, multiple variables can be combined in a nomogram that can increase the predictive accuracy when applied to individual patients. Previous efforts have suggested that a nomogram can be highly accurate in the setting of renal trauma;[23,24] however, these previous nomograms were limited by coming from single institutions, small sample size with very few bleeding interventions, and being based primarily upon the AAST grading rather than a combination of clinical and radiologic parameters.

The AAST grading system was initially designed to summarize the anatomy of the renal injury and does not provide specific information about factors directly related to higher risk of bleeding, and for some injuries, it may not be necessarily accurate in the initial trauma evaluation or for predicting bleeding interventions. Using the AAST grading in a predictive nomogram is associated with several problems.[6] For example, subtleties in grading such as deep lacerations with segmental vascular injuries but without urinary extravasation can be interpreted as grade III instead of grade IV, dramatically changing the prediction of risk. On the other hand, a parenchymal injury with minimal bleeding risk but a minor urinary extravasation will be categorized as a grade IV injury, overestimating the risk of needing acute interventions. In addition, many patients do not undergo excretory imaging during their initial trauma CT and an AAST grade cannot be determined in many cases without information about urinary extravasation from the kidney.[25] These situations will potentially obviate the power of a nomogram in predicting the bleeding risk if the nomogram is primarily dependent upon AAST grade. In addition, the incorporation of low-grade injuries (grades I and II), which are seldom associated with significant bleeding, will artificially increase the predictive accuracy of a nomogram. This undermines the purpose of a predictive tool, as the tool needs to be accurate for predicting bleeding interventions in relevant patients. In our study, using the AAST grades in a univariable model to predict bleeding interventions resulted in an AUC of 0.69 in comparison with an AUC of 0.83 for our nomogram. This indicates that, using the nomogram, which is based upon the combination of clinical and radiologic factors, is more predictive for bleeding interventions compared with the AAST grades alone.

Clinical factors need to be readily available if they are to be helpful in a nomogram. For instance, 24-hour blood and platelet transfusions have been previously suggested to predict intervention;[23,24] however, these are not helpful in predicting critical interventions, as most interventions will occur in the first few hours after patient arrival. All of the clinical factors in our nomogram can be obtained at the time of initial assessment or shortly thereafter, and the radiologic factors are based upon the initial CT scans. The radiologic parameters also are easily obtained and do not rely upon extensive knowledge about the subtleties of the AAST grading system. These considerations would clarify communication between the radiology, trauma, and urology teams about the renal injury severity. The high AUC from this proposed nomogram suggests that high predictive accuracy is obtainable without incorporating the AAST grades.

Several studies have assessed important radiologic factors that are associated with bleeding interventions and nephrectomy after renal trauma.[7–9,11,12] For example, Dugi et al.[8] found that VCE, HRD, and laceration location are all important factors that should be incorporated into predictive tools. Although renal vascular bleeding can be self-limiting because of the tamponade effect of the retroperitoneal space, presence of VCE signals active bleeding that may benefit from early interventions, such as selective angioembolization. In our study, 16 (84%) of 19 patients who underwent renal angioembolization had VCE in their initial scans; however, it is unknown if the other 3 patients underwent prophylactic angioembolization or had signs of active bleeding at the time of angiography that was not evident in the initial scan. A large hematoma (as measured in the axial [transverse] plane of a CT scan) and a hematoma crossing the midline or extending beyond the aortic bifurcation into the pelvis may also suggest an active and expanding hematoma or lack of tamponade effect, which merit close monitoring and or earlier intervention. The predictive power for laceration location has been less consistent. Medial and complex (both medial and lateral) lacerations were suggested as significant factors predicting interventions by Dugi et al.,[8] but the results were not reproduced in other studies.[9,11,12] In our models, only complex lacerations were significantly associated with bleeding interventions, and this did not improve the overall predictive accuracy of the nomogram. However, HRD and VCE were strong predictors in our model. Pararenal extension of the hematoma (i.e., bleeding extending laterally beyond the abdominal aorta or inferior vena cava, or bleeding extending inferiorly to the aortic bifurcation) was also an important factor. Although highly correlated with HRD, pararenal extension of hematoma also independently increased the nomogram's accuracy. It provides additional information particularly in cases where there is massive lower pole bleeding that may not cause a hematoma extending in the axial plane (measured by HRD).

A major limitation of our study is the exclusion of 105 patients (24%) of the initial HGRT cohort from the Genito-Urinary Trauma Study because of lack of initial imaging data. These patients had higher rates of shock and penetrating and concomitant injuries, leading directly to surgical exploration. As expected, most of these patients underwent immediate surgery without imaging studies; furthermore, the rates of bleeding interventions were significantly higher for these patients compared with those who were included in the study (54% vs. 14%, $p < 0.001$), and nephrectomy rates were also higher for these patients (39 nephrectomies [37%] vs. 16 nephrectomies [5%], $p < 0.001$). The inability to include these patients limits our nomogram findings to patients who were hemodynamically stable enough to get an initial CT scan. However, these may be the patients for whom a predictive nomogram is most helpful, rather than those that are in extremis from hemorrhage when a nephrectomy may be lifesaving. Another limitation, inherent to all studies on renal trauma management, is a lack of criterion standard measure for patients who need intervention for bleeding. We can only state that our nomogram will predict with a certain accuracy when trauma surgeons *felt intervention was needed* and not whether an intervention truly was needed or what the consequence would have been had the intervention not taken place. Also, management was not standardized in our multicenter study setting, and there are likely significant differences among these centers and providers in management of HGRT. However, our data reflect the real-world management from level 1 trauma centers across the country, which by default have more experience in management of high-grade traumas. Lack of long-term renal function data and consistent follow-up after patient discharge is another weakness of the study, which limits discussion of our findings to the acute trauma period. The final limitation is lack of validation of the nomogram with external data. We are currently collecting these data from several high-volume centers, not involved in the initial phase of the study, to complete external validation of the nomogram. Despite these limitations, this is the first renal trauma nomogram, predicting bleeding risk and interventions for bleeding, which was developed using contemporary data in a multi-institutional setting, using clinical and imaging data targeted at renal injury management.

CONCLUSIONS

We developed a nomogram that integrates multiple clinical and radiologic factors readily available upon assessment of the trauma victim, which can provide predicted probability for risk of undergoing bleeding interventions after HGRT. This nomogram can be used to identify important factors for bleeding interventions and may help decrease unnecessary interventions, especially at lower-volume trauma centers with limited experience with high-grade renal injuries.

AUTHORSHIP

J.B.M. and S.K. designed the study. B.E.P., D.M.R., M.E.H., and S.K. reviewed the imaging data and interpreted the results. C.Z., A.P.P., R.A.M., S.K., and J.B.M. participated in data analysis and interpretation. J.B.M., R.A.M., and S.K. drafted the article. X.L.-O., K.M., B.J.M., S.M., J.P., C.M.D., I.S., S.P.E., E.S.D., S.Z., B.G.S., B.A.E., N.B., B.N.B., B.P.S., B.U.O., R.A., B.M., R.A.S., M.M.C., J.F.K., T.H., F.N.B., S.K., and J.B.M. participated in the data collection and revisions for this article. J.B.M., J.M.H., and R.N. provided critical revisions for this article. All the authors read and approved the final submission.

ACKNOWLEDGMENT

We thank the staff and contributors from the Trauma and Urologic Reconstruction Network of Surgeons (http://www.turnsresearch.org/page/aast-gu-trauma-study-group-author-list-renal-trauma) and all the participating centers for sharing their data and supporting the study, as well as the AAST and the Multi-institutional Trials Committee for providing continuous support for the project.

DISCLOSURE

This study was not directly supported by any industrial or federal funds. The investigation was in part supported by the University of Utah Study Design and Biostatistics Center, with funding in part from the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through grant 5UL1TR001067-05 (formerly 8UL1TR000105 and UL1RR025764).

REFERENCES

1. Moore EE, Shackford SR, Pachter HL, McAninch JW, Browner BD, Champion HR, Flint LM, Gennarelli TA, Malangoni MA, Ramenofsky ML, et al. Organ injury scaling: spleen, liver, and kidney. *J Trauma*. 1989;29(12):1664–1666.
2. Santucci RA, McAninch JW, Safir M, Mario LA, Service S, Segal MR. Validation of the American Association for the Surgery of Trauma organ injury severity scale for the kidney. *J Trauma*. 2001;50(2):195–200.

3. Shariat SF, Roehrborn CG, Karakiewicz PI, Dhami G, Stage KH. Evidence-based validation of the predictive value of the American Association for the Surgery of Trauma kidney injury scale. *J Trauma*. 2007;62(4):933–939.
4. Kuan JK, Wright JL, Nathens AB, Rivara FP, Wessells H, American Association for the Surgery of T. American Association for the Surgery of Trauma Organ Injury Scale for kidney injuries predicts nephrectomy, dialysis, and death in patients with blunt injury and nephrectomy for penetrating injuries. *J Trauma*. 2006;60(2):351–356.
5. Keihani S, Xu Y, Presson AP, Hotaling JM, Nirula R, Piotrowski J, Dodgion CM, Black CM, Mukherjee K, Morris BJ, et al. Contemporary management of high-grade renal trauma: results from the American Association for the Surgery of Trauma Genitourinary Trauma study. *J Trauma Acute Care Surg*. 2018;84(3):418–425.
6. Chiron P, Hornez E, Boddaert G, Dusaud M, Bayoud Y, Molimard B, Desfemmes FR, Durand X. Grade IV renal trauma management. A revision of the AAST renal injury grading scale is mandatory. *Eur J Trauma Emerg Surg*. 2016;42(2):237–241.
7. Nuss GR, Morey AF, Jenkins AC, Pruitt JH, Dugi DD 3rd, Morse B, Shariat SF. Radiographic predictors of need for angiographic embolization after traumatic renal injury. *J Trauma*. 2009;67(3):578–582. discussion 582.
8. Dugi DD 3rd, Morey AF, Gupta A, Nuss GR, Sheu GL, Pruitt JH. American Association for the Surgery of Trauma grade 4 renal injury substratification into grades 4a (low risk) and 4b (high risk). *J Urol*. 2010;183(2):592–597.
9. Zemp L, Mann U, Rourke KF. Perinephric hematoma size is independently associated with the need for urological intervention in multisystem blunt renal trauma. *J Urol*. 2018;199(5):1283–1288.
10. Buckley JC, McAninch JW. Revision of current American Association for the Surgery of Trauma Renal Injury grading system. *J Trauma*. 2011;70(1):35–37.
11. Figler BD, Malaeb BS, Voelzke B, Smith T, Wessells H. External validation of a substratification of the American Association for the Surgery of Trauma renal injury scale for grade 4 injuries. *J Am Coll Surg*. 2013;217(5):924–928.
12. Hardee MJ, Lowrance W, Brant WO, Presson AP, Stevens MH, Myers JB. High grade renal injuries: application of Parkland Hospital predictors of intervention for renal hemorrhage. *J Urol*. 2013;189(5):1771–1776.
13. Chouhan JD, Winer AG, Johnson C, Weiss JP, Hyacinthe LM. Contemporary evaluation and management of renal trauma. *Can J Urol*. 2016;23(2):8191–8197.
14. McClung CD, Hotaling JM, Wang J, Wessells H, Voelzke BB. Contemporary trends in the immediate surgical management of renal trauma using a national database. *J Trauma Acute Care Surg*. 2013;75(4):602–606.
15. van der Wilden GM, Velmahos GC, Joseph DK, Jacobs L, Debusk MG, Adams CA, Gross R, Burkott B, Agarwal S, Maung AA, et al. Successful nonoperative management of the most severe blunt renal injuries: a multicenter study of the research consortium of New England Centers for Trauma. *JAMA Surg*. 2013;148(10):924–931.
16. Jodogne S. The Orthanc ecosystem for medical imaging. *J Digit Imaging*. 2018; 31(3): 341–352.
17. Chong ST, Cherry-Bukowiec JR, Willatt JM, Kielar AZ. Renal trauma: imaging evaluation and implications for clinical management. *Abdom Radiol (NY)*. 2016;41(8):1565–1579.
18. Kohavi R, ed. A study of cross-validation and bootstrap for accuracy estimation and model selection. International Joint Conference on Artificial Intelligence (IJCAI). Montreal, Canada: Morgan Kaufmann Publishers Inc. San Francisco, CA, USA; 1995.
19. Yang D, ed. Build prognostic nomograms for risk assessment using SAS. Proceedings of SAS Global Forum. SAS Institute Inc., North Carolina, USA; 2013.
20. Dagenais J, Leow JJ, Haider AH, Wang Y, Chung BI, Chang SL, Eswara JR. Contemporary trends in the management of renal trauma in the United States: a national community hospital population-based analysis. *Urology*. 2016;97:98–104.
21. Hammer CC, Santucci RA. Effect of an institutional policy of nonoperative treatment of grades I to IV renal injuries. *J Urol*. 2003;169(5):1751–1753.
22. Shariat SF, Capitanio U, Jeldres C, Karakiewicz PI. Can nomograms be superior to other prediction tools? *BJU Int*. 2009;103(4):492–495. discussion 495–7.
23. Shariat SF, Trinh QD, Morey AF, Stage KH, Roehrborn CG, Valiquette L, Karakiewicz PI. Development of a highly accurate nomogram for prediction of the need for exploration in patients with renal trauma. *J Trauma*. 2008; 64(6):1451–1458.
24. Shoobridge JJ, Bultitude MF, Koukounaras J, Royce PL, Corcoran NM. Predicting surgical exploration in renal trauma: assessment and modification of an established nomogram. *J Trauma Acute Care Surg*. 2013;75(5):819–823.
25. Hardee MJ, Lowrance W, Stevens MH, Nirula R, Brant WO, Morris SE, Myers JB. Process improvement in trauma: compliance with recommended imaging evaluation in the diagnosis of high-grade renal injuries. *J Trauma Acute Care Surg*. 2013;74(2):558–562.

DISCUSSION

NEIL PARRY, M.D. (London, Ontario, Canada): Good afternoon. Drs. Davis and Campbell. I would first like to thank the AAST and Dr. Reilly for inviting me to critique this paper and for Dr. Keihani for providing me with a well-written paper early-on and for his excellent presentation today.

The vast majority of renal injuries can be managed nonoperatively, as we know. High-grade renal injuries, however, are not terribly common.

Recent data suggests there still is a high nephrectomy rate certainly with Grade IV and V injuries. And apart from hemodynamic instability, what is or are the trigger points to intervene?

As discussed, the authors used a retrospective, multi-institutional data base for high-grade renal injuries to develop a nomogram to accurately predict the need for hemorrhage control. Only early clinical and radiographic data from hemodynamically-stable patients were used.

Nomograms have been used for some time in surgery, especially in surgical oncology. However, they are not too frequently used in trauma. We're a little more used to predictive tools that are more dichotomous with a yes/no answer or those that will guide us down the left side or the right side of an algorithm.

The first nomogram used to predict the need for renal exploration after renal trauma was published in 2008. As the authors point out in their paper, this was based on a single institution data and it failed to be externally validated. I commend the authors for developing this nomogram at a multi-institutional level.

I think the main strength of this paper is that the nomogram inherently pulls together these high-risk features for bleeding. So in a sense it formalizes the clinical acumen that we use when treating these patients every day.

In doing so it provides us with a statistic probability that the patient will require an intervention to control the bleeding rather than just our gut feeling. However, it does not provide the yes/no answer.

The main limitation, as the authors point out in their paper, is that the nomogram is only predictive of the probability of bleeding and the potential need for intervention, but not whether it was truly needed or if the intervention was ultimately helpful.

For instance, a patient who fell five meters, who is not hypotensive, has a hemo/pneumo, some rib fractures, a four centimeter hematoma with vascular contrast extravasation would have around a 55 percent risk of bleeding intervention as per the nomogram. Does that perform better than our gut feeling?

The nomogram is attempting to predict a moving target, which is difficult. The patient's condition and bleeding are dynamic.

I have a few questions.

Number 1. From your data do you have a sense of the timing to intervention? Who is involved with the treatment of these renal injuries in this patient population?

Number 2. I'm not a statistician but can you explain why the hematoma rim diameter of 12 centimeters contributed the most to the nomogram? And why was type of laceration location not included in the model?

Number 3. Do you expect that the use of this nomogram will ultimately result in decreased nephrectomy rates for the high Grade IV and V injuries?

Number 4. What do you suggest is the cut-off for intervention? Is there one? 50 percent? 75 percent?

Number 5. What are your next steps you are going to take with this nomogram?

Thanks again for the excellent presentation, the interesting paper and for the privilege to discuss.

PAL A. NAESS, M.D. (Oslo, Norway): The CT scan you showed us of the Grade V injury, isn't that strictly an arterial injury and should be coded as an injury of the renal artery, according to the AIS coding?

SORENA KEIHANI, M.D. (Salt Lake City, Utah): Thank you, Dr. Parry for the thoughtful comments and summary, and I'd also like to thank the audience and Dr. Naess for his question.

The first question was about timing and the reasons for intervention and also who was involved in the treatment process. We do have data on timing of interventions. In the initial data that we published last year, I think about 80 percent of nephrectomies were performed within the first four hours of patient admission. In the current study, for example, from the patients who had CT scans available, from 16 nephrectomies, only one was after four hours of admission. So most interventions are done within the first few hours of patient admission.

We don't have the details on the reasons and the course that led to interventions; however, most patients, I would say, were hemodynamically stable in this study. In fact, we expect that most patients who arrive in shock would be taken to the OR without imaging and would not be included in such a nomogram. So the majority of the patients included in this study were not in extremis.

However, the data is still observational and there is for sure some heterogeneity and variability in management and making the decisions. But we believe that it reflects the real-world scenario from Level I trauma centers.

About who was involved in making the decisions and doing the interventions, it was a combination of trauma surgeons, interventional radiologists, and also urologists who did the interventions. But, of course, the trauma surgeons are the first line stabilizing these patients and taking care of them so it is expected that most interventions are done by the trauma team. In most centers I would say urology would not be involved or would be less involved for bleeding interventions unless there are concerns about urine leakage or urinary extravasation.

The second question was about hematoma rim diameters and the factors that were not included in the nomogram. Hematoma rim diameter was treated as a continuous variable so the larger the hematoma the more likely that the patient underwent some kind of intervention. A hematoma of 12 centimeters contributed the most points simply because it was the largest value that we had in our data set.

About laceration location and why it was not included in the model, we selected a number of variables based on their relevance to the study and entered them into the backward model selection. The way it works is that each variable is tested to see if it will increase the area on the curve of the model. So laceration location was not included in the final model because it simply did not increase the area on the curve. And probably for laceration location it is likely that patients with complex lacerations also had larger hematomas and vascular contrast extravasation, which better predicted the bleeding interventions.

Another question was do we expect that the nomogram would ultimately result in decreased nephrectomy rates. It's hard to say. We don't expect that an experienced trauma surgeon would actually look at the nomogram and calculate the risk of bleeding and then make a decision. But we hope that considering these factors that are included in the nomogram would help in making a more systematic and more evidence-based decision. It is important to note that most nephrectomies are done for patients who are rushed to the operating room without undergoing any kind of imaging. But there are a group of patients who would actually benefit from considering these factors after undergoing imaging or damage control intervention.

Also, small trauma centers see very few patients with high-grade renal injuries so having some predictive tool beyond that of the AAST grading may actually help these centers to decrease their intervention rates.

What do we suggest as a cut-off for intervention, well, I wish I had a simple answer to this but it would definitely still depend on the clinical status of the patient. We recently conducted an online survey from trauma stakeholders, mostly trauma surgeons and trauma urologists, and specifically asked what would be cut-off that they would use for intervention. About 30 percent responded that they would only decide based on continued bleeding and also the hemodynamic status of the patient, not based on a cut-off. And among others there was not consensus on a specific cut-off for intervention. And, again, we don't believe that any predictive tool or a clear-cut cut-off would replace the clinical decision of the treating surgeon.

What are the next steps? The first step would be to validate our findings using external data so we can actually show that these are reproducible and reliable factors to use. We are in the process of collecting data from several high-volume centers who were not involved in the initial phase of the study.

However, I also believe that there is only so much you could do with observational data and retrospective studies so far are showing that we need to decrease the unnecessary intervention rates.

So I think the next step would definitely involve performing a multi-center study, a multi-center prospective study, to look at different management protocols. And we need data to study the immediate and long-term impacts of conservative approaches as well as operative management and nephrectomy.

And about the CT scan of grade V injury, it showed a completely devascularized kidney because of injury to the main renal artery. According to the proposed revisions to the AAST grading, it can be classified as grade IV or V based on presence or absence of active bleeding.

We envisioned this nomogram could potentially function as a key element in a prospective trial; however, it is a very challenging step because trauma studies are under-funded and they are difficult to perform. But hopefully with the support of the AAST and the Multi-Institutional Trials Committee it should be possible to do.

Thank you.