

Evaluation and management of abdominal gunshot wounds: A Western Trauma Association critical decisions algorithm

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This is a recommended evaluation and management algorithm from the Western Trauma Association (WTA) Algorithms Committee addressing the management of adult patients with abdominal gunshot wounds (GSW). Because there is a paucity of published prospective randomized clinical trials that have generated class I data, these recommendations are based primarily on published prospective and retrospective cohort studies identified via structured literature search, and expert opinion of the WTA members. In addition to published clinical series, this algorithm attempts to incorporate and remain consistent (whenever possible) with the relevant evidence-based Eastern Association for the Surgery of Trauma Practice Management Guidelines.^{1,2} The final algorithm is the result of an iterative process including an initial internal review and revision by the WTA Algorithm Committee members, and then final revisions based on input during and after presentation of the algorithm to the full WTA membership (March 2018). We believe the algorithm (Fig. 1) and accompanying comments represent a safe and well-reasoned approach to the evaluation and management of the patient with an abdominal GSW in any location (including thoracoabdominal).

The algorithm was designed to be as widely applicable as possible across the spectrum of existing medical systems and centers but assumes that the patient is being cared for in a designated trauma center and under the direction of a staff trauma surgeon. We recognize that there will be multiple factors that may warrant or require deviation from any single recommended algorithm, and that no algorithm can completely replace expert bedside clinical judgment. We encourage institutions to use this

as a general framework in the approach to these patients, and to customize and adapt the algorithm to better suit the specifics of that program, personnel, or location. We also recognize that the majority of civilian experience and published literature comes from injuries due to standard low-velocity weapons and projectiles, and that there may be significant differences encountered when dealing with high-velocity projectiles or nonstandard types of GSW, such as shotgun blasts.³⁻⁶ However, the essential core elements and principles outlined in this algorithm should apply to nearly all patients regardless of the exact weapon or projectile type.

The overall incidence of penetrating truncal trauma in the civilian setting has sharply declined over recent decades. Penetrating mechanisms now account for less than 10% of all trauma evaluations at most modern trauma centers in the United States, with only a select few urban centers continuing to see rates of 20% or higher.⁷⁻⁹ Among these penetrating trauma cases, approximately half (50%) are due to GSWs, with the majority being from intentional assaults.¹⁰ Analysis of approximately 300,000 patients in the Spring 2019 Trauma Quality Improvement Program report found that gunshot injuries represented only 3.2% of all trauma incidents, with an associated case fatality rate of 10%.¹¹ This low incidence has resulted in a decreased experience with the evaluation and management of abdominal GSWs among physicians and other staff at many trauma centers. Thus, we believe there is an increased need for standardized protocols and an algorithmic approach supported by the best available evidence and expert opinion to optimize outcomes in this challenging patient population.

The following lettered sections correspond to the letters identifying specific sections of the algorithm shown in Figure 1. Following the in-depth review of the algorithm, we present a brief discussion of any major areas within the algorithm where there was controversy or lack of consensus and a listing of existing major knowledge gaps on this topic.

ABDOMINAL GUNSHOT WOUND ALGORITHM

(A) Initial Evaluation and Indications for Immediate Operation

The role of abdominal exploration for penetrating trauma has evolved significantly over the past several decades. The historical general policy of mandatory laparotomy for all penetrating abdominal trauma has gradually become replaced with a more selective policy based on the clinical evaluation and initial

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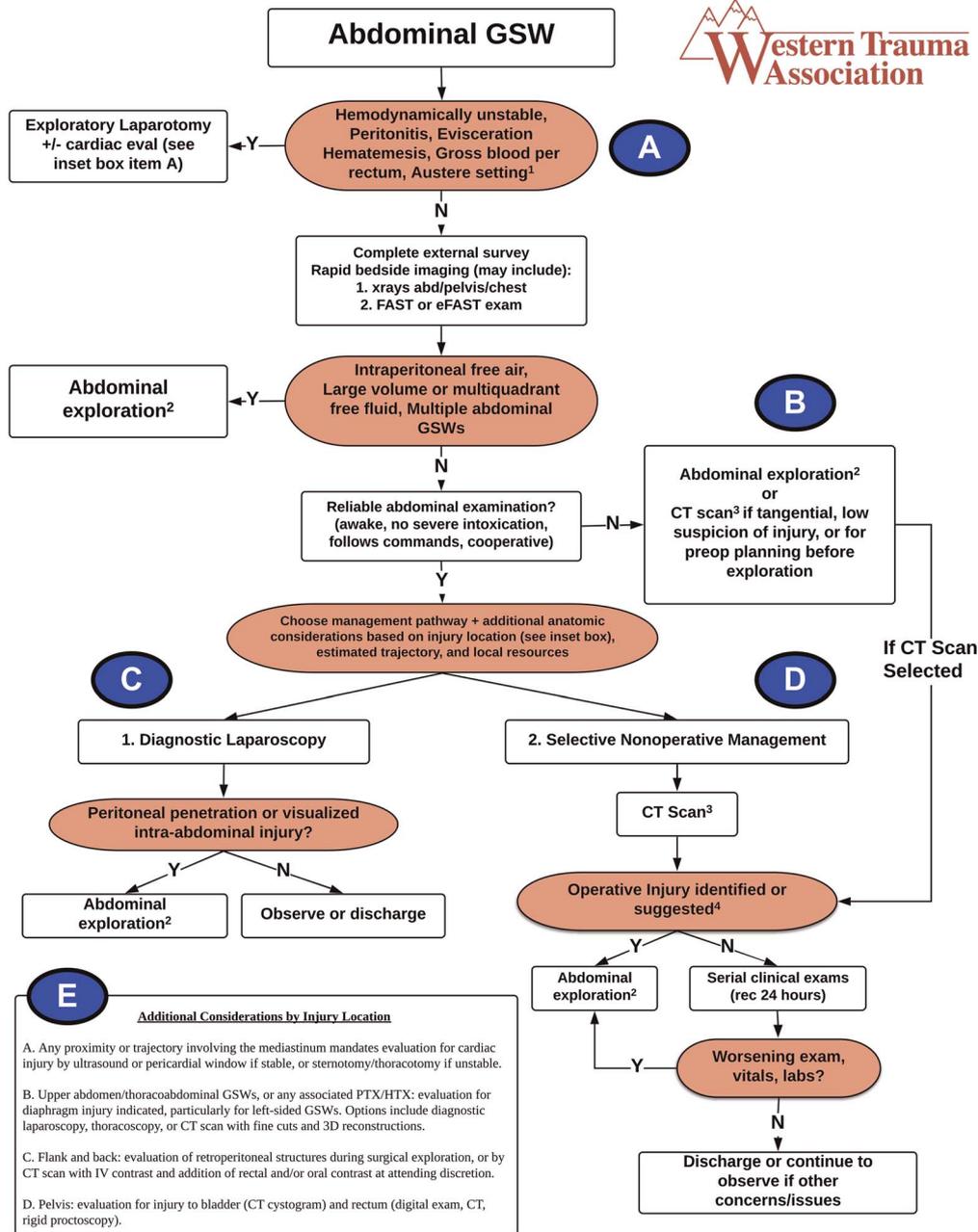


Figure 1. Western Trauma Association algorithm for the evaluation and management of patients with abdominal gunshot wounds. Circled letters correspond to sections in the associated article. Superscript numbers refer to the following footnotes:¹ Austere or low resourced environments may include military or remote rural settings, lack of key personnel (surgeon, anesthesia support), lack of radiologic capabilities or immediate imaging interpretation (CT scan, ultrasound), or the lack of blood bank or other resources for resuscitation and management (nursing, ICU, etc.). In this environment, mandatory exploratory laparotomy or immediate transfer to a trauma center are warranted.² Abdominal exploration should be performed for either clinical signs of abdominal injury or for positive findings on a diagnostic laparoscopy. This may be performed via open laparotomy or a complete laparoscopic exploration and repair of injuries depending on the patient clinical status, nature of injuries, and skillset of the managing surgeon.³ Modern multidetector CT scan technology has greatly improved the ability to identify most abdominal injuries, and to reconstruct the missile tract and proximity to key structures. Initial CT scan is usually performed with IV contrast only. External wounds should be marked with radiolucent markers, and fine cuts with multiplanar reconstructions should be performed through the area of the missile tract. Rectal and/or oral contrast may be added to the initial CT or to a repeat CT to fully evaluate the key retroperitoneal structures for flank and back GSWs, or any trajectory involving the retroperitoneum.⁴ Operative injuries identified on CT scan typically include proven or suspected hollow viscus injury, major vascular injury, diaphragm injury, or operative solid organ injury. Note that isolated solid organ injuries (liver, spleen, kidneys) without clinical or radiologic evidence of an associated operative injury may be managed per standard blunt solid organ injury nonoperative management guidelines.

diagnostic studies. Although widely adopted and accepted for abdominal stab wounds, selective nonoperative management (SNOM) of abdominal GSWs has been more controversial and slower to gain acceptance.¹² This is most likely due to the significantly higher overall incidence of hollow viscus and other operative injuries from missile wounds compared with knife/stabbing trauma, and the attendant higher associated morbidity and mortality.^{7,8,12}

Similar to any other trauma evaluation, the initial evaluation of patients with abdominal GSWs should focus on identifying those with immediately life-threatening pathologies or injuries that require prompt surgical control and repair. This will most often include large volume hemorrhage or hollow viscus perforation with intra-abdominal spillage. Hemodynamic instability with signs of shock (evidence of inadequate end-organ perfusion) is a clear warning sign for ongoing massive hemorrhage and should prompt immediate exploratory laparotomy along with blood product resuscitation. Other “hard signs” that should prompt immediate abdominal exploration include peritonitis, evisceration, hematemesis, and blood per rectum. Patients meeting one or more of these criteria have been shown to have an 80% or greater incidence of operative injuries on exploration.^{1,13–17} The primary focus in the hypotensive patient with penetrating abdominal trauma should be in minimizing delays to laparotomy and operative hemorrhage control, as even short delays have been shown to be associated with increased mortality.^{18,19} A recent multicenter study demonstrated not only the high mortality among hypotensive patients requiring emergent laparotomy (46%), but that these rates have not significantly improved over the past two decades.^{8,20}

Although mandatory laparotomy for stable patients with abdominal GSWs is no longer practiced at most trauma centers, there is still a role for immediate exploration in austere settings where further evaluation and potential nonoperative management is not safe or practical. This would include some battlefield or other limited resource settings where most imaging modalities are not available and close observation is not possible, or where the resources and available expertise are inadequate for safe nonoperative management (see Footnote 1 of algorithm).^{21,22} Alternatively, if rapid transfer to an adequately resourced trauma center is available then this should be accomplished without delay.

For patients that meet none of the above criteria, a focused bedside clinical evaluation and additional tailored imaging studies should be performed, again with the purpose of identifying injuries that require surgical exploration or that have a high likelihood of operative injury. This will typically involve one or more x-rays and potentially a sonographic assessment (FAST or eFAST examination). The utilization and indications for these will vary by center and by provider, and also by the specifics of the GSW (location, number, etc.). We recommend a chest x-ray at a minimum, particularly for any upper abdominal or thoracoabdominal GSWs. This will identify any free air (which should usually prompt surgical exploration), the presence of an associated hemothorax or pneumothorax, and the location of any retained missiles/fragments if visualized. Additional abdominal and pelvic x-rays have little utility in identifying hard signs of injuries but can provide valuable data on the location of any retained missiles (and thus the estimated trajectory).

The role of the FAST examination in penetrating abdominal trauma continues to be hotly debated and varies widely between centers. Proponents for FAST examination in penetrating trauma argue that it can provide clinically relevant evidence of peritoneal penetration, the volume and location of any free abdominal fluid, and most importantly the presence of any pericardial fluid or tamponade.²³ However, a major limitation of the FAST examination that must be appreciated is the reliability of a negative examination for ruling out major hemorrhage or other operative injuries. Multiple series have described the high rates of false negative examinations, even among the cohort of patients requiring emergent laparotomy for noncompressible truncal hemorrhage.^{23–25} Although there may be a role for additional imaging or tests such as a diagnostic peritoneal aspirate following a negative or equivocal FAST examination in the presence of concerning hemodynamics or examination findings, this is primarily for blunt trauma patients.²⁶ We recommend proceeding immediately to operative exploration in this scenario (hypotension, concerning examination) for abdominal GSW regardless of the results of the FAST examination. Additional results of the initial bedside evaluation including intraperitoneal free air on x-ray or large volume or multiquadrant free fluid on FAST examination should prompt abdominal exploration. Similarly, the presence of multiple abdominal GSWs carries an extremely high incidence of operative injury, and should usually prompt immediate surgical exploration (see Footnote 2 of algorithm).

(B) The “Unexaminable” Patient

The next step in the algorithm centers on differentiating the examinable versus unexaminable patient, although the definition of “unexaminable” has not been standardized and has varied widely in the literature.^{27,28} Common reasons for a compromised level of alertness in this patient population include alcohol and/or drug intoxication, major psychiatric illness, analgesic/sedating medications, spinal cord injury with loss of abdominal pain sensation, or co-existing traumatic brain injury. A frequently stated criteria for potential nonoperative management is a normal mental status and reliable examination, and in general most patients who do not meet this strict criteria should undergo abdominal exploration.^{28–30} However, there are several exceptions to this principle that we outline in the algorithm. The first is if there is a strong suspicion based on the initial examination and bedside imaging that the GSW is superficial/tangential and likely did not enter the abdominal cavity. The second is if the altered mental status is mild and expected to be of short duration, as may be seen among patients who are intoxicated but able to focus appropriately on the abdominal examination and can be reliably observed. Of note, several trials of SNOM in penetrating abdominal trauma have included intoxicated patients, with no reported increase in adverse outcomes or false negative physical examinations.^{1,16,31}

We recommend that these stable patients undergo immediate high-quality abdominal/pelvic computed tomography (CT), with further management based on consideration of the imaging findings and the bedside clinical evaluation (see section D below). The CT scan is typically performed with intravenous contrast only and should not be delayed for prolonged efforts at administering oral contrast. The addition of oral and/or rectal contrast appears to add little diagnostic value for intraperitoneal

structures, although it may be useful in evaluating retroperitoneal structures (most commonly for back or flank GSWs). This issue is discussed further in the section below on areas of controversy and debate. This is also a patient population where laparoscopy has been suggested as an alternative or adjunct to laparotomy and is becoming more widely utilized for both blunt and penetrating trauma. As noted in the algorithm and Footnote 2, “abdominal exploration” may include either open or laparoscopic approaches. See section C for additional details on this area.

For patients not meeting any of the above criteria for immediate abdominal exploration and who have a reliable abdominal examination, the algorithm then splits into two distinct management pathways (section C or D) that can be selected based on surgeon preference, experience, and local resources/expertise.

(C) Diagnostic Laparoscopy

Diagnostic laparoscopy for the purpose of identifying peritoneal penetration is relatively simple and has been shown to be highly accurate and reliable.¹ Several series have reported significant reductions in the rate of nontherapeutic laparotomy using diagnostic laparoscopy as a screening procedure, although they include relatively small numbers of GSW patients.^{32–36} However, if peritoneal violation is identified then the safety and accuracy of laparoscopy for identifying all significant injuries remains an area of study and significant debate, and can be expected to vary based on the experience and expertise of the surgeon.^{32,35–38} Several series have reported excellent results with therapeutic laparoscopy for penetrating abdominal trauma when performed by skilled and experienced surgeons and using a systematic approach to complete abdominal exploration and injury repair.^{34–37} As noted in the algorithm and Footnote 2, “abdominal exploration” may include either an open or laparoscopic approach as determined by the managing surgeon. However, this should be reserved for hemodynamically stable patients with injuries that are amenable to minimally invasive repair. In addition, the procedure should be immediately converted to open surgery if there is clinical deterioration or in cases where there is failure to progress in a timely manner. Laparoscopy also is the procedure of choice for evaluating for an associated injury to the diaphragm, and any diagnostic laparoscopy for upper abdominal or thoracoabdominal wounds should include careful inspection of the diaphragm (see section E for more detailed discussion).

(D) Selective Nonoperative Management

For patients who reach this point in the algorithm and thus do not have any identified or strongly suspected operative abdominal injuries, a trial of SNOM is typically appropriate. This is based on multiple series demonstrating that an approach based on mandatory laparotomy for abdominal GSW will result in approximately one-quarter of patients undergoing a negative or nontherapeutic laparotomy.^{1,12} Although the majority of patients with abdominal GSWs will have an operative abdominal injury, if only the cohort of awake and alert patients with a benign abdominal examination are analyzed, the vast majority (approximately 90%) will not have an injury that requires operative intervention.^{12,28,30,39} These findings have also been confirmed in the 2010 EAST PMG on SNOM for penetrating abdominal

trauma (included both knife and GSWs) and in a 2018 systematic review and meta-analysis specifically analyzing civilian abdominal GSWs.^{1,40} In addition to the associated pain, costs, and utilization of resources, several studies have demonstrated a significant rate of postoperative complications and long-term morbidity following negative or nontherapeutic laparotomies.^{41–43}

Patients selected for SNOM should be awake, alert, and have a reliable abdominal examination that can be followed with serial examinations. In addition, they should have no other injuries that require immediate operative intervention, and any required semielective operations (such as fracture fixation) should be delayed for at least 24 hours to facilitate close monitoring and serial abdominal examinations. We recommend that all patients selected for SNOM undergo a high-quality CT scan of the abdomen and pelvis (with addition of chest CT for upper abdominal/thoracoabdominal) that is immediately reviewed by both the trauma surgeon and trauma radiologist. This review should focus on identifying hard signs of any obvious injuries, assessing the trajectory and path of the projectile(s) to determine proximity to critical structures, and examining for any secondary signs of hollow viscus injury (bowel thickening, free fluid, mesenteric stranding/hematoma, etc.) or vascular injury.^{1,40,44} The importance and added value of routine CT scan in this cohort has been demonstrated in multiple systematic literature reviews, and includes higher sensitivity and specificity versus clinical examination alone and a decreased risk of failure of SNOM.^{1,40,44}

If an operative injury is identified or strongly suspected based on the initial CT scan, then prompt abdominal exploration should be performed (see Algorithm Footnote 4). For all others, the patient should be admitted to the hospital in an area where they can be closely monitored and undergo serial clinical examinations. There is no widespread agreement on the frequency and specifics of what these evaluations should include, but at a minimum there should be an assessment of vital signs and a focused abdominal examination performed frequently over the first 24 hours. A complete blood count repeated at intervals can allow for assessment of ongoing bleeding and trending of the white blood cell count, but there is little role for any additional routine laboratory testing. This initial observation period should focus on the early identification of signs of an injury requiring further intervention, and would include ongoing bleeding, the development of peritonitis on examination, and signs of a systemic inflammatory response including fever, tachycardia, rising white blood cell count, and hypotension. Patients developing these signs or other evidence of an operative abdominal injury should undergo immediate abdominal exploration. The two most common subgroups of patients who undergo SNOM will be those where the missile tract crosses a focal area of the abdominal cavity that does not contain any critical structures, or those with an isolated penetrating injury to a solid organ (liver, kidney, spleen). Among these, an injury to the liver is the most common given the size and amount of space it occupies compared to other abdominal solid organs. Multiple series have demonstrated that isolated penetrating solid organ injuries can be successfully and safely managed nonoperatively, and should be treated similar to a comparable blunt injury to that organ.^{29,45} A more recent analysis of National Trauma Data Bank (NTDB) data on penetrating injuries to the liver demonstrated that SNOM

was utilized in 39% of cases, and was associated with decreased morbidity and mortality versus operative intervention.⁴⁶

A recent meta-analysis demonstrated that the pooled risk of failure of SNOM is 7%, and the pooled mortality in this group is 0.4%. The risk of failure of SNOM will also vary by the injury location, with the lowest risk for back GSWs (3.1%) followed by right thoracoabdominal (3.4%), flank (7%), and the highest in anterior abdominal wounds (13.2%).⁴⁰ Finally, although there is no set standard for the optimal duration of observation, multiple series have shown that almost all failures of SNOM will occur within the first 12 hours to 24 hours.^{1,12,39,45} Several studies have also specifically examined the question of when it is safe to discharge these patients. In a retrospective study of 863 patients that was followed by a prospective study of 270 patients with abdominal GSWs, Inaba and colleagues found that all patients who failed SNOM did so within 24 hours of presentation. We therefore recommend at least 24 hours of initial close observation in this algorithm.

(E) Additional Considerations by Injury Location

One of the unique hallmarks of GSWs as compared with other types of penetrating trauma (such as stab wounds) is that the projectile can and will frequently cross multiple regions of the abdomen, or involve other body cavities such as the thoracic cavity or mediastinum. Although this algorithm primarily focuses on the evaluation and management of the abdominal component, there are multiple other considerations that come into play based on the location of the wounds or estimated trajectory. Although there is ongoing debate about the role of the FAST examination for abdominal GSWs, the pericardial window of the FAST should be performed immediately in all patients with upper abdominal or thoracoabdominal GSWs to evaluate for possible cardiac injury and/or tamponade. An additional consideration for all wounds in these locations is the relatively high incidence of occult traumatic diaphragmatic injury (TDI). These injuries are frequently clinically silent and not detected on the initial radiographic evaluations, and thus a high index of suspicion must be maintained. The gold standard for both identifying and treating TDI is laparoscopy, with thoracoscopy as a reasonable alternative particularly in the presence of coexisting pathology requiring intervention such as a retained hemothorax.^{33,47–50} However, we do recognize that there is an increasing body of literature on the improved sensitivity of modern CT scan imaging as an option for identifying signs of TDI.^{51–54}

For flank and back GSWs, the initial evaluation and criteria for immediate operation are no different than other locations. However, subsequent CT imaging or surgical exploration should include complete evaluation of the retroperitoneal structures that are typically at risk from these wounds. There should also be an appreciation that there can be significant operative injuries present despite a negative FAST examination, and that may not progress immediately to peritonitis on physical examination. There remains significant discussion and debate on the type of contrast CT scan that should be obtained, with some arguing for the addition of oral and rectal contrast (“triple contrast”) to increase the sensitivity for key structures such as the retroperitoneal duodenum or colon. Triple-contrast CT scan has been reported to have sensitivity of 100%, specificity of 96% to 100%, and accuracy of 98% for identifying operative injuries

after penetrating trauma.^{55–57} However, others have reported similar good results without the addition of enteral contrast.^{44,58–60} We recommend a high-quality CT scan with IV contrast as the usual study to be initially obtained, with the addition of oral/rectal contrast at the discretion of the attending surgeon and radiologist. For GSWs to the pelvis, and particularly for trans-pelvic wounds, the initial evaluation and imaging must pay particular attention to the bladder, rectum, and iliac vasculature.^{61,62} The addition of a dedicated CT cystogram for potential bladder injuries and rigid proctoscopy for potential rectal injuries has been shown to be highly accurate and reliable for identifying operative injuries to these structures.^{63–65}

AREAS OF CONTROVERSY AND EXISTING KNOWLEDGE/RESEARCH GAPS

It is also important to note that there are many areas of this algorithm that lack high quality evidentiary support, and where further focused research is required. Table 1 provides a list of the most important specific topics or existing research “gaps” related to this topic that were identified by the authors during the development of this algorithm. There were also several areas of the algorithm related to optimal evaluation and management strategies that generated significant debate and lower degrees of consensus among the committee members.

The role and type of x-rays to be obtained in the initial evaluation was an area of significant heterogeneity and debate, with some advocating for no x-rays and others advocating for multiple truncal x-rays to identify injuries and search for bullet/fragment locations, as well as identifying any associated spine or pelvic fractures. The final consensus was that at least a chest x-ray should usually be obtained shortly after arrival, and always for upper abdominal or thoracoabdominal wounds. Upright or reverse Trendelenburg positioning was advocated by some to increase the utility for identifying free intraperitoneal air, but with others raising concerns about the effect on hemodynamics if the patient is unstable. Additional x-rays would be at the discretion of the managing physician but have little utility if the patient is going to undergo truncal CT scan as the next step in evaluation. Similar to discussions for the previously published algorithm for abdominal stab wounds,⁵⁴ there was significant discussion and debate around the issue of occult traumatic diaphragm injury in this patient population. Although there was consensus that all GSWs involving the upper abdomen or thoracoabdominal regions require some evaluation for TDI, there was debate about whether this required routine versus selective laparoscopic or thoracoscopic examination of the diaphragm. As discussed above in section E, there is recent literature supporting a high sensitivity for modern CT scan imaging to detect TDI, and some authors support using this to select patients who require operative evaluation of the diaphragm.^{51–53} However, it is critical to carefully review the multiplanar reformats of the CT scan (including coronal, sagittal, and even off-plane) to reliably detect signs of TDI. There was also debate about whether routine diaphragm evaluation should be performed only in left-sided GSWs as there is felt to be a protective effect of the liver and lower risks of subsequent herniation for right sided injuries.^{48,66,67} The majority opinion after these discussions were generally concurrent with the EAST PMG recommendations, including the superiority of laparoscopy

TABLE 1. Top Identified Knowledge and Research Gaps Related to the Management of Abdominal GSWs

Topic or Research Gap	Algorithm Section
(1) Role of FAST and extended FAST in the initial management of abdominal GSWs	A
(2) Role of CT scan in the “unstable” penetrating trauma patient	A
(3) Safety and applicability of SNOM to patients with altered mental status or otherwise unreliable examinations	B
(4) Performance and reliability of diagnostic laparoscopy in patients with abdominal GSWs	C
(5) Safety and efficacy of open versus laparoscopic repair of injuries due to penetrating abdominal trauma	C
(6) Routine versus selective use of abdominal CT scan in SNOM of abdominal GSWs	B, D
(7) Optimal timing and routes of contrast administration for CT scan evaluation of abdominal GSWs	B, D
(8) Identification of abdominal GSW patients who can be discharged from the ED or after shorter periods of observation	D
(9) Optimal imaging techniques for retroperitoneal and pelvis GSWs	E
(10) CT scan versus routine laparoscopy or thoracoscopy for the evaluation of diaphragm injury in abdominal GSWs	E

versus CT scan for diagnosis of penetrating TDI and the use of routine exploration for TDI only in left sided injuries.² If CT scan is utilized as a decision-tool for TDI, then the majority felt that the patients should be followed closely for at least the first year, and that a repeat CT scan be performed at 6–12 months to evaluate for any delayed presentation of organ or visceral herniation.

There was significant debate about the use of “triple-contrast” (rectal, oral, and intravenous) versus single- or double-contrast CT scans for the evaluation of flank and back GSWs. The final consensus among the committee was that the details of the type of contrast to administer should be at the discretion of the attending surgeon and radiologist, and that close attention to the wound tract and adequate imaging of the structures at risk is paramount. It was the consensus opinion that a repeat CT scan with added oral or rectal contrast can be a valuable adjunct if the initial CT scan findings are equivocal or unclear in the area of interest.

Finally, there was significant debate about whether SNOM should now be considered the standard of care at all modern trauma centers, and whether the use of diagnostic and/or therapeutic laparoscopy was an acceptable option versus SNOM. As noted almost universally in the published literature on SNOM, this approach requires adequate resources, staffing, and expertise to be safely and successfully utilized. Although there was consensus that nontrauma centers would not be expected to have these qualifications, there was debate and disagreement about whether all designated trauma centers (particularly Level 2 or 3 centers) would be expected to meet these requirements. There was also debate about the role of diagnostic laparoscopy as a “compromise” option between mandatory laparotomy and SNOM, and about whether there was adequate experience to recommend therapeutic laparoscopy for the management of identified injuries. The majority opinion after discussion was that most designated trauma centers should be utilizing SNOM for eligible patients, but that diagnostic laparoscopy was an acceptable alternative if the local resources or expertise was not amenable to SNOM. There was broad consensus that there was no longer a role for mandatory laparotomy in all abdominal GSW patients (other than austere environments as discussed above), and that both SNOM and diagnostic laparoscopy have been shown to markedly reduce the rates of negative or nontherapeutic laparotomy.^{1,40,68} There was also broad consensus that the use of laparoscopy, and particularly therapeutic laparoscopy, should be limited to trauma surgeons and teams with significant

skill and experience in both advanced laparoscopy and open surgical management.

AUTHORSHIP

All authors meet authorship criteria for this article as described below. All authors have seen and approved the final article as submitted. The first author (M.J.M.) had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. M.J.M., D.V.S., C.V.R.B., K.I. participated in the conception and design. M.J.M., C.J.H., D.V.S. participated in the acquisition of data. M.J.M., D.V.S., H.A., K.B., C.J.H., M.dM., E.E.M., G.V. participated in the analysis and interpretation of data. M.J.M., C.V.R.B., D.V.S., E.E.M. participated in the drafting of the article. H.A., K.B., C.J.H., M.dM., E.E.M. G.V. participated in the critical revision of the article. M.J.M. have shared his statistical expertise. M.J.M., K.I., D.V.S. participated in the administrative, technical, or material support. M.J.M., K.B., E.E.M. K.I., D.V.S., C.J.H. participated in the supervision.

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