Screening for alcohol and drug use in pediatric trauma

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Background: Level 1 pediatric trauma centres should screen all trauma patients aged 12 years and older for alcohol use and provide substance use interventions as a means to minimize relapse. We aimed to approximate the rate of alcohol and drug use screening in Canadian pediatric patients admitted for trauma in our centre, determine the prevalence of intoxication on admission and compare the injury characteristics and morbidity of patients with and without concomitant substance use.

Methods: We conducted a single-centre retrospective review of the Stollery Children’s Hospital’s medical records abstracted from the Alberta Trauma Registry database of patients aged 12–17 years who were admitted for trauma (Injury Severity Score ≥ 12) between Jan. 1, 2012, and Dec. 31, 2021.

Results: Of the 543 patients included in the analysis, 380 (70.0%) received screening for alcohol as a part of their trauma panel; meanwhile, only 5 (0.9%) patients were screened for drug use. Among the patients who were screened for alcohol, 47 (12.4%) had a positive blood alcohol level (BAC). Nine (7%) of 129 screened patients aged 12–14 years were found to have positive BACs compared with 38 (15.1%) of 251 screened patients aged 15–17 years. Patient age and mechanism of injury significantly affected rates of screening. Among patients with positive BACs on admission, the 3 most prevalent mechanisms of injury were motor vehicle accident (26 [55.3%]), assault (13 [27.7%]) and recreational vehicle accidents (4 [8.5%]). Patients with a positive BAC sustained significantly more severe injuries ($p = 0.003$).

Conclusion: These results provide evidence of the importance of standardized screening to identify pediatric patients admitted for trauma who are in need of treatment for alcohol and drug use. The Screening, Brief Intervention and Referral to Treatment model is the primary approach used to fulfill substance use identification and intervention recommendations. The Alcohol Use Disorders Identification Test and the Car, Relax, Alone, Forget, Friends, Trouble questionnaire are most suitable for adolescent populations.

Contexte : Les centres de traumatologie pédiatrique de niveau 1 devraient effectuer un test d’alcoolémie et offrir des interventions en toxicomanie à tous les jeunes poly-traumatisés de 12 ans et plus qu’ils reçoivent afin de prévenir les rechutes. Nous avons voulu mesurer approximativement les taux de consommation d’alcool et de drogues chez la population pédiatrique canadienne hospitalisée en traumatologie dans notre établissement, déterminer la prévalence des intoxications à l’arrivée et comparer les caractéristiques des blessures et la morbidité chez les jeunes ayant ou non consommé.

Méthodes : Nous avons procédé à une revue rétrospective monocentrique des dossiers médicaux de l’Hôpital pour enfants Stollery, à partir de la base de données du Registre de traumatologie de l’Alberta pour les jeunes de 12–17 ans hospitalisés en traumatologie (indice de gravité des blessures ≥ 12) entre le 1er janvier 2012 et le 31 décembre 2021.

Résultats : Parmi les 543 jeunes inclus dans notre analyse, 380 (70,0 %) ont été soumis à un test d’alcoolémie dans le cadre des analyses de routine en traumatologie, tandis que seulement 5 (0,9 %) ont subi un dépistage de drogues. Parmi les jeunes soumis au test d’alcoolémie, 47 (12,4 %) ont eu des résultats positifs. Neuf des 129 (7 %) jeunes de 12–14 ans soumis au dépistage avaient de l’alcool dans le sang, contre 38 des 251 (15,1 %) jeunes de 15–17 ans. L’âge et le mécanisme des blessures ont significativement affecté les taux de dépistage. Chez les jeunes qui avaient un test d’alcoolémie positif à l’admission, les 3 mécanismes des blessures les plus fréquents étaient accident de la route (26 [55,3 %]), voies de fait (13 [27,7 %]) et accident avec un véhicule récréatif (4 [8,5 %]). Les blessures étaient nettement plus graves chez les jeunes dont le test d’alcoolémie était positif ($p = 0,003$).
adolescent alcohol and drug use are strongly associated with increased incidence of traumatic injury,1 the leading cause of death in the pediatric population.2,3 Concomitantly, alcohol and drug use significantly contribute to the burden of trauma in Canada — a trend that is reflected globally.4 A 2016 Public Health Agency of Canada publication reports that one-half of all Canadian youth report first consuming alcohol between the ages of 12 and 14 years, a hazard that only increases with age as 46% report engaging in binge drinking during high school.5 Acute episodes of intoxication as well as chronic substance misuse substantially increase the risk of both accidental and intentional causes of injury in the adolescent population.6,7 A strong link has been established between adolescent substance use and increased morbidity and mortality from traumatic injury.

This association arises from 3 primary drivers: chronic substance addiction,8 risk-taking behaviour9 and trauma recidivism,10 which is defined as the need for medical intervention for traumatic injury on more than 1 occasion.11 Despite the paucity of data pertaining to alcohol-related trauma recidivism in pediatric populations, current evidence shows that adult patients admitted for trauma who have positive blood alcohol concentration (BAC) at the time of their admission are significantly more likely to be admitted to hospital in the future for a separate incident of traumatic injury.4,10 A recent systematic review found that 13% of all adult patients admitted for trauma had been admitted previously for trauma and that 41% of them had a positive BAC on at least 1 of their admissions.4 Identifying and addressing substance use disorders in patients admitted for trauma is therefore a vital step in reducing both the rate of trauma recidivism as well as general rates of trauma.12

Although the causality and immediate effects of traumatic injuries remain the focus of most admissions, the effects of trauma can take a long and protracted course in a pediatric patient’s life. As many as 19% of pediatric patients experience significant posttraumatic stress after traumatic injury, further exacerbating rates of substance use and dependence.13 Similar long-term effects are reflected in the prognosis of pediatric substance use. Adolescents who begin to consume alcohol before the age of 16 years are 4 times more likely to become addicted to alcohol than those who start drinking at the age of 21 years.8

In adult populations, the American College of Surgeons Committee on Trauma mandates that level 1 trauma centres universally screen for, and document, alcohol misuse as well as briefly intervene when problematic use is identified.14 Further, the Trauma Association of Canada Accreditation Guidelines suggest that level 1 trauma centres should screen all trauma patients aged 12 years and older for alcohol use and provide evidence-based substance use interventions as a means to minimize relapse.15 Even with established evidence and recommendations that screening should be universally administered, several studies in American trauma centres have shown that rates of screening in pediatric patients remain low.12,16 The consequences of insufficient and selective screening are missed potential insights into the patient’s immediate condition and broader clinical picture, as well as a forfeiture of the opportunity to attenuate long-term morbidity from future substance misuse and trauma recidivism.4

Currently, there is limited research describing screening rates for alcohol and drug use in pediatric patients admitted for trauma and a scarcity of data on the prevalence of substance use in this patient population in the Canadian context.17 Further, research regarding the association between inebriation on admission for pediatric trauma and injury characteristics, such as mechanism of injury, injury severity, outcomes and length of hospital stay, remains a gap in the literature. We aimed to approximate the rate of screening for alcohol and drug use in Canadian pediatric patients admitted for trauma in our centre, determine the prevalence of intoxication on admission and compare the injury characteristics and morbidity of patients with and without concomitant substance use.

**Methods**

**Study design**

We conducted a single-centre retrospective review of the Stollery Children’s Hospital’s medical records abstracted from the Alberta Trauma Registry (ATR) database. The Stollery Children’s Hospital is a level 1 pediatric trauma centre for the Edmonton zone and has a catchment that includes northern Alberta, substantial proportions of central Alberta and the northern territories. This study was approved by the University of Alberta Research Ethics Board (HREB no. Pro000117768).
To be included in our analysis, patients had to be 12–17 years old, have an Injury Severity Score (ISS) of 12 or more and be admitted to the Stollery Children’s Hospital for treatment of a traumatic injury between Jan. 1, 2012, and Dec. 31, 2021. Patients were excluded from analysis if they had incomplete medical records. De-identified medical records of eligible patients were extracted and analyzed.

**Chosen variables and demographic variables**

Two key dichotomous outcome variables were extracted from the ATR database: the proportion of patients who were administered alcohol and toxicology screening as a part of the standard trauma panel and the frequency with which those screens were determined to be positive. In addition, BAC (g/dL) were extracted for positive alcohol screens. Toxicology screens were determined to be positive if amphetamines, benzodiazepines, barbiturates, cocaine, methamphetamine, opioids or tetrahydrocannabinol were detected in any quantity.

We also extracted patient demographic variables (age, sex) and variables describing injury characteristics (ISS, length of hospital stay, mechanism of injury, month of injury, discharge state). The mechanism of injury was determined by inspecting the individual trauma cases included in the study and subsequently allocating each case into 1 of 9 categories: motor vehicle accidents (MVAs; driver, passenger, pedestrian), recreational vehicle accidents, assault, drowning, fall, suicide attempt or self-harm, burn, sports and miscellaneous.

**Statistical analysis**

We performed all statistical analyses using SAS (version 9.4). Categorical variables are reported as percentages, and continuous variables are reported as means with standard deviations (SD; normal distribution) or medians and interquartile ranges (IQR; non-normal distribution). We conducted statistical tests to investigate potential associations between patient demographic or injury characteristics and group (screened v. not screened and intoxicated v. sober). For these comparisons, Mann–Whitney U tests were used for non-parametric continuous variables, while Welch t tests were used for parametric continuous variables. Continuous variables were assessed for suitability for parametric testing through inspection of Q–Q plots as well as through Shapiro–Wilk tests for normality. For comparisons of categorical variables, we used χ² tests of independence and Fisher exact tests. Further, for statistically significant associations between dichotomous variables, relative risks (RRs) were reported with 95% confidence intervals (CIs). We considered results to be significant at a p value of less than 0.05.

**Results**

**Population demographics**

A cohort of 543 patients met the inclusion criteria and were included in the analysis (Table 1). Patients had a median age of 15.9 (IQR 14.1–16.8) years, with 37.6% and 62.4% of patients aged 12–14 and 15–17 years, respectively. More than two-thirds of patients were male (71.6%). The median length of hospital stay was 5 days (IQR 3–12), and the median ISS was 20 (IQR 16–26). The top 5 mechanisms of traumatic injury in this population were MVAs (39.4%), recreational vehicle accidents (21.7%), falls (13.1%), assault (8.5%) and sports-related injuries (7.7%) (Table 2). Nearly one-half of all traumas occurred during the summer months of June–September (47%).

**Alcohol and drug screening**

Of the 543 patients included in the analysis, 380 (70.0%) received screening for alcohol intoxication as a part of their trauma panel (Table 3); meanwhile, only 5 (0.9%) patients were screened for drug use. Of the 380 patients who were screened for alcohol, 47 (12.4%) had a positive BAC (mean BAC on positive tests 0.098 g/dL ± 0.065).

Nine (7.0%) of 129 screened patients aged 12–14 years were found to have positive BACs compared with 38 (15.1%) of 251 screened patients aged 15–17 years. Stratified by sex, BACs were positive in 25 of 267 (9.4%) males

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**Table 1. Demographic and clinical characteristics of the study population (n = 543)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (IQR)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, no. (%)</td>
<td>389 (71.6)</td>
</tr>
<tr>
<td>Female, no. (%)</td>
<td>154 (28.4)</td>
</tr>
<tr>
<td>Age, yr</td>
<td>15.9 (14.1–16.8)</td>
</tr>
<tr>
<td>Injury Severity Score</td>
<td>20 (16–26)</td>
</tr>
<tr>
<td>Length of hospital stay, d</td>
<td>5 (3–12)</td>
</tr>
</tbody>
</table>

*IQR = interquartile range.
*Unless indicated otherwise.

**Table 2. Mechanism of injury in total patient population**

<table>
<thead>
<tr>
<th>Mechanism of injury</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor vehicle accident</td>
<td>214 (39.4)</td>
</tr>
<tr>
<td>Recreational vehicle accident</td>
<td>118 (21.7)</td>
</tr>
<tr>
<td>Fall</td>
<td>71 (13.1)</td>
</tr>
<tr>
<td>Assault</td>
<td>46 (8.5)</td>
</tr>
<tr>
<td>Sports</td>
<td>42 (7.7)</td>
</tr>
<tr>
<td>Suicide attempt or self-harm</td>
<td>34 (6.3)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>8 (1.5)</td>
</tr>
<tr>
<td>Burn</td>
<td>7 (1.3)</td>
</tr>
<tr>
<td>Drowning</td>
<td>3 (0.6)</td>
</tr>
</tbody>
</table>
and 22 of 113 (19.5%) females aged 12–17 years, 4 of 94 (4.3%) males and 5 of 35 (14.3%) females aged 12–14 years, and 21 of 173 (12.1%) of males and 17 of 78 (21.8%) of females aged 15–17 years.

Among all patients with positive BACs on admission, the top 3 most prevalent mechanisms of injury were MVA (26 [55.3%]), assault (13 [27.7%]) and recreational vehicle accidents (4 [8.5%]) (Table 4).

**Differences in screening between groups**

Patients aged 15–17 years were found to have significantly higher rates of screening for alcohol than patients aged 12–14 years (74.0% v. 63.2%, p = 0.008), indicating that patients aged 12–14 years were 1.42 times less likely (RR 1.42, 95% CI 1.10–1.83) to be screened for alcohol on admission than patients aged 15–17 years. No significant difference was found in screening rates between male and female patients (69% v. 73%, p = 0.28). Clinicians were 1.35 times more likely (RR 1.35, 95% CI 1.22–1.50) to screen for alcohol intoxication if injuries were sustained from an MVA compared with all other injuries (83% v. 61%, p ≤ 0.0001).

Female patients admitted for trauma were fewer in total number than male patients admitted for trauma, but were 2.07 times more likely (RR 2.07, 95% CI 1.23–3.53) to have positive BACs than male patients (test positivity 19.5% v. 9.4%, p = 0.003). Patients who tested positive for alcohol were found to be significantly older than patients who tested negative (16.1 yr v. 15.4 yr, p = 0.02). We found that patients with positive BACs had significantly higher ISS than patients with negative BACs (25.0 v. 21.9, p = 0.003). Further, it was determined that patients were 4.13 times more likely (RR 4.13, 95% CI 2.33–7.32) to have positive BACs when sustaining trauma from assault than trauma from all other causes (test positivity 28.3% v. 6.8%, p ≤ 0.0001). It was also determined that patients were 1.90 times more likely (RR 1.90, 95% CI 1.10–3.29) to have positive BACs when sustaining trauma from an MVA than from all other causes (test positivity 12.1% v. 6.4%, p = 0.02). We were unable to perform statistical tests on drug screening and drug use positivity rates owing to small sample size.

**Discussion**

We found that only 70% of pediatric patients aged 12–17 years received screening for alcohol intoxication on admission for trauma. Although this screening rate represents a significant departure from the universal alcohol screening standards recommended by the American College of Surgeons and the Trauma Association of Canada, it is still a markedly higher rate of alcohol screening than those recorded in previous single-centre studies. These rates range from 26% to 61%, with the average rate for pediatric trauma being less than 50%. In comparison, recent adult Trauma Quality Improvement Program data, with more than 2 million entries in the United States, show that 52.9% of adult patients admitted for trauma were screened for alcohol and 36.5% were screened for drugs, of whom, 22.1% patients tested positive for alcohol and 44.3% tested positive for drugs. The alcohol screening rates of Canadian adults admitted for trauma can be appreciated in a study from Halifax that reported a 61% screening rate (range 34%–90%).
depending on the year), with a positive uptick around and after trauma accreditation. A possible explanation for our above-average alcohol screening rates is that a substantial number of trauma patients in our study cohort were admitted by way of the Stollery Children’s Hospital’s emergency department, and we are the only port of entry, thus reducing variability. Over the last several years, the department has made a concerted effort to increase rates of alcohol screening in pediatric patients by including BAC screening in the prepopulated laboratory order set for pediatric patients aged 12 years and older admitted for trauma — this imitates standard practice in adult patients admitted for trauma. This is in contrast to other emergency departments around the country, where BAC screens are usually ordered on a case-by-case basis. We also recently underwent trauma accreditation, and that process has focused our emergency department team efforts for screening.

Although patient sex did not affect rates of screening, our study identified substantial variation in screening based on patient age and mechanism of injury. Patients aged 12–14 years were found to be 1.42 times more likely to have BAC screening omitted than patients aged 15–17 years. Among screened patients aged 12–14 years, 7% still registered a positive BAC on admission. This finding suggests that substance use may begin early in adolescence and that clinicians may wrongfully discount the possibility of concomitant substance use in trauma owing to the patient’s younger age. This is problematic because accurately identifying substance use in patients aged 12–14 years is of vital importance, as patients who begin using alcohol at this age are more than 10 times more likely to develop lifetime alcohol dependence than adults.8 Further, it was also found that adolescents injured in MVAs were 1.35 times more likely to be screened than those with other mechanisms of injury. It is likely that alcohol screens are completed with greater consistency in this population owing to ubiquitous awareness of the association between intoxication and MVAs. These associations suggest that toxicological screens continue to be completed inconsistently and that subjective clinical suspicion of intoxication substantially affects whether clinicians will elect to conduct alcohol screening in patients admitted for trauma. Omission of screening from the standard trauma panel results in the discharge of pediatric patients who would have benefitted from intervention for their alcohol use. This leads to a significant number of adolescents experiencing greater long-term morbidity and death from their substance use as well as from the increased likelihood that they will experience recurrent trauma.

Although our study found relatively high levels of alcohol screening (70%), it was concerning to find that almost no patients received drug screening. Among our patient cohort (n = 543), only 5 patients were tested for intoxication from drugs. Consequently, it was not possible to determine an accurate rate of drug use in our trauma population, and there was insufficient power to conduct meaningful analyses between groups of patients. However, we believe that the prevalence of drug use, and in particular marijuana use, was significant in our trauma population and went uncaptured owing to lack of drug testing. This conjecture is based on previous single-centre studies in the United States that found substantial rates of positive screens for marijuana in pediatric patients admitted for trauma. These studies identified minimum prevalence of marijuana intoxication in their pediatric patients admitted for trauma of at least 8.3%–10.2%.6,12,19 We hypothesize that the reason we observed substantially lower rates of drug screening than alcohol screening is because clinicians tend to view alcohol status as more important to understanding the acute clinical picture of patients admitted for trauma. For example, delineating alcohol intoxication from neurological injury is of high clinical utility, whereas knowledge of current use or history of using many types of drugs is less immediately imperative. Further, the majority of observations in our study occurred before the legalization of marijuana in Canada, before which physicians may have had lower suspicion of pediatric use of marijuana. However, rates of marijuana use reached 18% in adolescents in grades 7–12 in 2019,22 and recent studies report that youth presenting to the emergency department with cannabis-related problems are significantly younger in the post-legalization period.21 Thus, it is imperative that clinicians begin to increase the rate of routine screening for drug use in pediatric patients admitted for trauma to identify those who require interventions for drug use.

Whereas the prevalence of alcohol intoxication in adults admitted for trauma is well described, considerably less data describing the adolescent population are available. We found that 12.4% of screened pediatric patients admitted for trauma had a positive BAC test. This is consistent with positivity rates reported in previous studies, which varied from 9.5% to 14%.6,17,19 Among patients who tested positive, the average BAC was 0.098 g/dL, which suggests substantial intoxication associated with binge drinking, causing considerable impairment of decision-making and motor function.24

Previous studies12 show the likelihood of positive BAC increased with age as the positivity rate for BAC was twice as high in patients aged 15–17 years than in those aged 12–14 years. Although considerably more male than female patients were admitted to the Stollery for trauma, female patients were substantially more likely to test positive for BAC on screening: 19.5% compared with 9.4%, representing a test positivity rate 2.07 times higher in female than male patients. We believe that this somewhat counterintuitive finding may be explained by a combination of factors. Unlike in the adult population, where males exhibit higher rates of alcohol consumption, there is no difference between males and females in rates of drinking...
or heavy drinking in the adolescent age demographic (12–17 yr). Rates of problematic drinking behaviours, such as alcohol use disorder, are more than 1.6 times higher in females aged 12–17 years than males of the same age. In addition, males engage in more high-risk behaviour in a sober state than females, which may explain the reduced alcohol screen positivity rate in male patients admitted for trauma in relation to females.

We have shown that injury characteristics and mechanisms differed between patients who tested positive than negative for BAC. A major finding was that patients who tested positive for BAC sustained significantly more severe injuries than those who tested negative for BAC, with average ISS of 25 and 21.9 (p = 0.003), respectively. We believe that severity of injury is associated with alcohol status because of the specific mechanisms of injury that had high incidence in patients who tested positive for BAC. The 3 mechanisms of injury with the greatest proportion of patients testing positive for alcohol intoxication were assault (28.3%), MVA (12.2%) and suicide or self-harm (8.8%). Patients sustaining trauma from an assault were more than 4 times more likely to screen positive for alcohol intoxication than from all other causes of injury, whereas patients sustaining trauma from an MVA were nearly twice as likely to screen positive. Most (83%) of the intoxicated patients sustained their injuries from either an MVA or assault, and these mechanisms are more associated with severe multisystem trauma than other causes of injury. Despite a relatively high positivity rate of alcohol screening in patients sustaining trauma from suicide attempts or self-harm, the positivity rate did not significantly differ from that associated with other causes of injury.

Motor vehicle accidents accounted for more than half of all traumatic injuries in patients who were intoxicated in our study and are still potentially under-represented owing to the lethality of MVAs, the leading cause of death among adolescents. This is unsurprising as studies have shown that driving with a BAC of 0.08% is associated with a relative risk of an accident of 2.69, whereas youth aged 16–20 years achieve a comparable level of risk with a BAC of only 0.02%–0.04%. Further, a BAC of 0.07%–0.10% is associated with risky road-crossing decisions and pedestrian fatalities. However, while a prevalence of alcohol intoxication of 12% is substantial, our study’s inability to capture rates of intoxication from marijuana may result in an underestimation of the true rate of intoxication associated with MVAs. This inference is based on Canadian rates of alcohol and marijuana use before operating a vehicle as well as their known associated relative risks of MVAs. The prevalence of driving under the influence of cannabis among youth has surpassed the prevalence of driving while intoxicated, with 7% of Canadian youth in grades 10–12 who have a driver’s licence reporting having used cannabis within 1 hour of operating a vehicle compared with only 4% reporting having consumed alcohol within 1 hour. Further, the relative risk of a crash associated with driving under the influence of cannabis is about double that of an unimpaired driver. Thus, based on the similarities between known prevalence of alcohol and cannabis use before operating a vehicle as well as similarities in their associated RRs of MVAs, we propose that it is possible that the true prevalence of combined cannabis and alcohol intoxication in MVAs in our study population may be more than double our reported rate.

These results provide further evidence of the importance of accurately identifying pediatric patients admitted for trauma who are in need of treatment for alcohol and drug use. The Screening, Brief Intervention and Referral to Treatment (SBIRT) model is the primary approach used to fulfill substance use identification and intervention recommendations. In executing SBIRT, it is best practice to administer a validated substance use disorder identification survey in addition to toxicological screening. This comprehensive approach is important as many patients test negative for acute intoxication on laboratory screening but are later confirmed positive for a substance use disorder when assessed with a validated survey. In addition to reducing false-negative screening results, the validated survey helps to contextualize positive toxicological screens and elicit information about substance use patterns. The Alcohol Use Disorders Identification Test and the Car, Relax, Alone, Forget, Friends, Trouble (CRAFFT) questionnaire are most suitable for adolescent populations; the CRAFFT questionnaire is preferred owing to its brevity and high sensitivity. Patients screening positive receive standardized, brief interventions in the form of motivational interviews regarding the consequences and dangers of substance use. This is followed by referral to appropriate child mental health or addiction treatment. Previous studies have shown that brief intervention in adolescent patients being treated for alcohol-related injuries decreases future alcohol consumption, frequency of driving while intoxicated and incidence of alcohol-related injuries. Consequently, SBIRT may represent a particularly economical aspect of treatment in pediatric patients admitted for trauma, as intervention at a young age to prevent future injury and morbidity from substance use has the potential to result in considerable improvements to life expectancy and quality-adjusted life years.

**Limitations**

Our study had several limitations. We did not capture patients who sustained minor trauma as our analysis was limited to patients with an ISS of 12 or more. The generalizability of our findings are inherently limited by the fact that our study was carried out in a single level 1


3. Committee on Pediatric Emergency Medicine, Council on Injury, Violence, and Poison Prevention, Section on Critical Care, Section on Orthopaedics, Section on Surgery, Section on Transport Medicine, Pediatric Trauma Society, Society of Trauma Nurses, Pediatric Committee. Management of pediatric trauma. Pediatrics 2016;138(2):e20161569.


