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ORIGINAL ARTICLE

Mild traumatic brain injury: not always a mild injury

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Abstract

Purpose In general, risk of mortality after trauma correlates with injury severity. Despite arriving in relatively stable clinical condition, however, some patients are at risk of death following mild traumatic brain injury (TBI). The study objective was delineation of patients who die in-hospital following mild isolated TBI in order to inform Emergency Department (ED) disposition and care discussions with patients and families.

Methods In this retrospective cohort study, patients from the National Trauma Data Bank (NTDB) (2007–2018) were included if they were injured by blunt trauma and sustained a mild TBI (defined as Head Abbreviated Injury Scale [AIS] score of 1 or 2 and arrival Glasgow Coma Scale [GCS] score of 13–15). Exclusions were severe associated injuries (extracranial AIS > 2); transfers; and missing data. Patients were defined by in-hospital mortality: Survivors vs. Mortalities. Demographics, clinical/injury data, and the outcomes were collected and compared with univariate analysis. Multivariate analysis established independent factors associated with in-hospital mortality following mild TBI.

Results In total, 932,107 patients (10% of NTDB population) met study criteria: 928,542 (99.6%) Survivors and 3,565 (0.4%) Mortalities. In general, comorbidities (including home anticoagulation, cardiac disease, and diabetes mellitus) were significantly more common among patients who died ($p < 0.001$), although drug and alcohol intoxication on arrival were more common among Survivors (16% vs. 7%, $p < 0.001$; 13% vs. 10%, $p < 0.001$). In terms of insurance status, Private/Commercial insurance was more common among Survivors (39% vs. 20%, $p < 0.001$) while Governmental Insurance was more common among Mortalities (55% vs. 36%, $p < 0.001$). On multivariate analysis, age ≥ 65 was most strongly associated with death (OR 26.43, $p < 0.001$), followed by ED intubation (OR 10.08, $p < 0.001$), admission hypotension (OR 4.55, $p < 0.001$), and comorbidities, particularly end-stage renal disease (ESRD) (OR 3.03, $p < 0.001$) and immunosuppression (OR 2.18, $p < 0.001$).

Conclusions Survivors differed substantially from Mortalities after mild TBI in terms of comorbidities, intoxicants, and insurance status. Independent variables most strongly associated with in-hospital death following mild head injury included age ≥ 65, intubation in the ED, admission hypotension, and comorbidities (particularly ESRD and immunosuppression). Increased clinical vigilance, including a mandatory period of clinical observation, for patients with these risk factors should be considered to optimize outcomes and potentially mitigate death after mild TBI.

Keywords Traumatic brain injury · Minor trauma · Trauma mortality

Background

Mortality after trauma tends to correlate with the severity of injuries, although this is not uniformly true. Minor injuries can lead to death, particularly among patients with lower physiologic reserve, such as the elderly [1–4] and the comorbid [5–8]. This may be especially relevant after traumatic brain injuries (TBI), whose clinical course can be unpredictable.

A better understanding of patients who are at risk of death from minor injuries would be helpful to inform clinical prognostication and care discussions with patients and families. The aim of this study was to define independent predictors of death following isolated mild TBI. Secondary objectives included delineation of the patient demographics and injury characteristics of patients who die in-hospital

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following isolated mild TBI. The overall goal of the study was to improve patient disposition to the appropriate level of care out of the Emergency Department (ED) and allow more realistic care expectation setting after mild head injuries. We hypothesized that elderly, comorbid patients would be at the highest risk for death following mild head injury.

Methods

All patients entered into the National Trauma Data Bank (NTDB) from January 1, 2007 and December 31, 2018 were screened for inclusion in this retrospective observational study. The NTDB is the world's largest trauma data repository with more than 7.5 million electronic records from trauma centers across the United States [9]. Patients injured by blunt trauma with a mild TBI, defined as Head Abbreviated Injury Scale (AIS) score of 1 or 2 (which was calculated retrospectively at the conclusion of hospital admission) and Glasgow Coma Scale (GCS) score of 13–15 on arrival to the ED, were included. Exclusions were penetrating or unspecified mechanism of injury; patients with severe associated injuries, defined as extracranial region AIS of > 2; transfers; and patients with missing discharge disposition. Institutional Review Board approval was sought and exemption was granted due to the retrospective and deidentified nature of the dataset.

Extracted variables included patient demographics (age, sex, comorbid conditions, insurance status, social history); clinical data (first ED vital signs); injury data (mechanism of injury, Injury Severity Score [ISS], and AIS by body region); interventions; and outcomes. The primary outcome was in-hospital mortality. Secondary outcomes included ED disposition, hospital discharge disposition, hospital complications, hospital length of stay [LOS] in days, intensive care unit [ICU] LOS, ventilator days, and time to death.

Patients were divided into two mutually exclusive study groups according to in-hospital mortality status: Survivors, defined by patients who survived to hospital discharge, vs. Mortalities. Continuous variables are presented as mean ± standard deviation; median [interquartile range]. Categorical variables are presented as number (percentage). Patient demographics, clinical and injury variables, interventions, and outcomes were compared between groups with the Fisher's exact test, Pearson chi-square, and Mann – Whitney *U* test, as appropriate. Binary logistic regression determined independent factors associated with in-hospital mortality. Variables were included in the regression model based on the clinical relevance as well as those that differed by $p < 0.2$ on univariate analysis. Statistical significance was defined as $p < 0.05$. All data were analyzed using SPSS version 28.0 (IBM Corporation, Armonk, NY).

Results

Of the nearly 10 million patients entered into the NTDB over the study period, 932,107 (10%) satisfied study criteria: 928,542 (99.6%) survived to hospital discharge and 3,565 (0.4%) died in hospital (Fig. 1). Among the Mortalities, 10% ($n = 368$) had a documented code status of Do Not Resuscitate (DNR). Survivors were younger than Mortalities (median age 39 [22–60] vs. 72 [50–82], $p < 0.001$) with a lower proportion of male patients ($n = 576{,}346$; 62% vs. $n = 2{,}090$; 59%, $p < 0.001$) (Table 1). In terms of insurance status, Private/Commercial insurance was more common among Survivors ($n = 360{,}063$; 39% vs. $n = 722$; 20%, $p < 0.001$) while Governmental Insurance was more common among Mortalities ($n = 1955$; 55% vs. $n = 332{,}061$; 36%, $p < 0.001$). Comorbidities varied between study groups and in general were more common among Mortalities ($p < 0.001$), especially cardiorespiratory diseases (Table 1). Alcohol and illicit drug intoxication on admission were

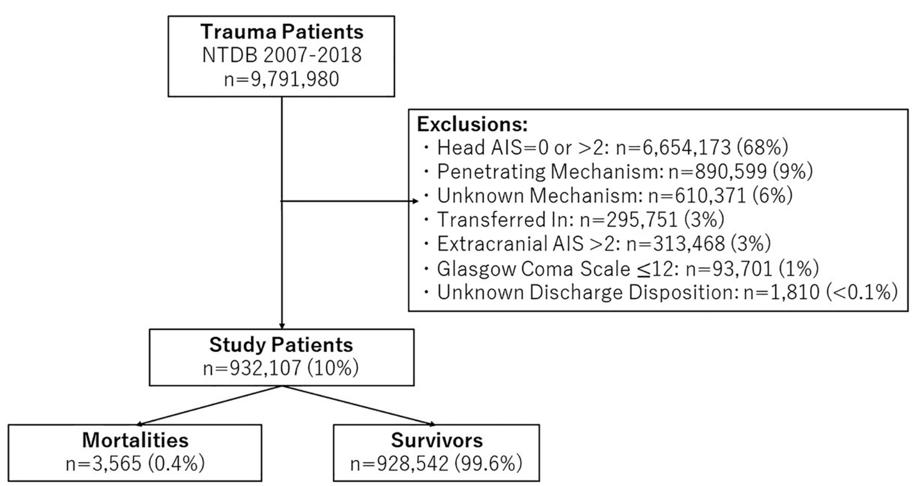

Fig. 1 Flow of Patients through Study. *NTDB* National Trauma Data Bank, *AIS* Abbreviated Injury Scale score

Table 1 Patient demographics, insurance status, comorbid conditions, and intoxicants on admission

	Survivors ($n=928{,}542$, 99.6%)	Mortalities ($n=3{,}565$, 0.4%)	p
Patient demographics			
Age, years	39 [22–60]	72 [50–82]	< 0.001
Sex, male	576,346 (62)	2,090 (59)	< 0.001
Insurance status			
Private/Commercial insurance	360, 063 (39)	722 (20)	< 0.001
Governmental insurance	332,061 (36)	1,955 (55)	< 0.001
Self-Pay	129,397 (14)	165 (5)	< 0.001
Not Billed	6,033 (1)	5 (0.1)	< 0.001
Other	100,988 (11)	718 (20)	< 0.001
Comorbidities			
Cardiac disease	216,175 (23)	1,806 (51)	< 0.001
Current Lmoker	117,527 (13)	237 (7)	< 0.001
Home anticoagulant medication*	24,955 (11)	283 (34)	< 0.001
Diabetes mellitus	83,181 (9)	720 (20)	< 0.001
Alcohol use	65,958 (7)	251 (7)	0.884
Psychiatric disease**	49,970 (8)	194 (8)	0.992
Illicit drug use**	34,418 (5)	62 (3)	< 0.001
COPD	48,832 (5)	489 (14)	< 0.001
Bleeding disorder	40,299 (4)	419 (12)	< 0.001
Functional dependent status	38,065 (4)	553 (16)	< 0.001
CVA with deficit	18,098 (2)	188 (5)	< 0.001
ESRD	6,764 (0.7)	185 (5)	< 0.001
Immunosuppression	5,041 (0.5)	99 (3)	< 0.001
Cirrhosis[£]	3,489 (0.5)	94 (3)	< 0.001
Intoxicants on admission			
Alcohol	137,534 (16)	185 (7)	< 0.001
Illicit Drug	100,650 (13)	271 (10)	< 0.001

Continuous variables listed as median [interquartile range]

Categorical variables presented as number (percentage)

COPD chronic obstructive pulmonary disease, *CVA*

*Variable available only for study years 2017–2018 (during which time the study population was $n=218{,}812$)

**Variable available only for study years 2012–2018 (during which time the study population was $n=644{,}319$)

[£]Variable available only for study years 2011–2018 (during which time the study population was $n=717{,}608$)

more common among Survivors ($n=137{,}534$; 16% vs. $n=185$; 7%, $p<0.001$; $n=100{,}650$; 13% vs. $n=271$; 10%, $p<0.001$). Admission hypotension was more frequent among Mortalities ($n=201$; 6% vs. $n=11{,}877$; 1%, $p<0.001$) (Table 2). Median GCS on arrival to hospital was significantly lower among patients who died (15 [14–15] vs. 15 [15–15], $p<0.001$).

Mortalities required admission to ICU ($n=996$; 28% vs. $n=89{,}158$; 10%, $p<0.001$) or transfer directly to the operating room ($n=109$; 3% vs. $n=21{,}952$; 2%, $p=0.006$) more frequently than did patients who survived (Table 2). Falls were the most frequent mechanism of injury among both study groups. Median ISS was higher among Mortalities (5 [4–6] vs. 5 [2–6], $p<0.001$). Patients who died were more likely to be intubated in the ED ($n=205$; 6% vs. $n=9619$; 1%, $p<0.001$). Operations and operations performed within 24 h of arrival were more common among Mortalities (Table 2).

Hospital LOS was comparable between groups (2 [1–3] vs. 4 [1–8] days, $p<0.001$), although ICU LOS and ventilator days were shorter among survivors (2 [1–3] vs. 4 [2–8] days, $p<0.001$; 1 [1,2] vs. 3 [1–8] days, $p<0.001$) (Table 3). The hospital LOS among patients who died represents their time to death, which occurred at a median of the 4th day of hospitalization. Uniformly, complications were higher among patients who died (Table 3). The most

Table 2 Clinical data, injury data, and interventions

	Survivors (*n* = 928,542, 99.6%)	Mortalities (*n* = 3,565, 0.4%)	*P*
First ED vital signs			
SBP < 90	11,877 (1)	201 (6)	< 0.001
HR > 120	72,895 (8)	261 (8)	0.582
GCS	15 [15–15]	15 [14–15]	< 0.001
Disposition from ED			
Ward	415,331 (45)	973 (28)	< 0.001
Home	206,538 (23)	0 (0)	< 0.001
Stepdown unit	83,389 (9)	368 (11)	0.005
ICU	89,158 (10)	996 (28)	< 0.001
Operating room	21,952 (2)	109 (3)	0.006
Other	100,885 (11)	48 (1)	< 0.001
Mechanism of injury			
Fall	353,685 (38)	2,414 (68)	< 0.001
MVC	339,824 (37)	712 (20)	< 0.001
Assault	106,118 (12)	176 (5)	< 0.001
AVP	86,734 (9)	222 (6)	< 0.001
MCC	40,259 (4)	50 (1)	< 0.001
Other	18,988 (2)	37 (1)	< 0.001
Injury severity			
ISS	5 ± 3; 5 [2–6]	5 ± 3; 5 [4–6]	< 0.001
AIS head	2 ± 0; 2 [1, 2]	2 ± 0; 2 [1, 2]	< 0.001
AIS face	0 ± 1; 0 [0–1]	0 ± 1; 0 [0–1]	0.023
AIS neck	0 ± 0; 0 [0–0]	0 ± 0; 0 [0–0]	0.231
AIS chest	0 ± 0; 0 [0–0]	0 ± 1; 0 [0–0]	< 0.001
AIS abdomen	0 ± 0; 0 [0–0]	0 ± 0; 0 [0–0]	0.160
AIS spine	0 ± 1; 0 [0–0]	0 ± 1; 0 [0–0]	< 0.001
AIS upper extremities	0 ± 1; 0 [0–1]	0 ± 1; 0 [0–1]	0.035
AIS lower extremities	0 ± 1; 0 [0–0]	0 ± 1; 0 [0–1]	0.002
AIS external	0 ± 0; 0 [0–0]	0 ± 0; 0 [0–0]	0.033
Procedures			
ED intubation	9,619 (1)	205 (6)	< 0.001
PEG	860 (0.1)	69 (2)	< 0.001
Tracheostomy	348 (< 0.1)	20 (0.6)	< 0.001
Operations			
Craniotomy/Craniectomy	103 (< 0.1)	6 (0.2)	< 0.001
< 24 h	52 (51)	2 (33)	0.679
Intracranial pressure monitor insertion	25 (< 0.1)	8 (0.2)	< 0.001
< 24 h	17 (68)	6 (75)	1.000
Exploratory laparotomy	1,110 (0.3)	63 (1.8)	< 0.001
< 24 h	928 (84)	33 (52)	< 0.001
Thoracotomy/Sternotomy	21 (< 0.1)	2 (0.1)	0.004
< 24 h	8 (38)	1 (50)	1.000
Orthopedic (Pelvis, Femur)	5,952 (0.6)	34 (1)	0.020
< 24 h	2,205 (37)	11 (32)	0.572

Continuous variables listed as median [interquartile range]. Categorical variables presented as number (percentage)

ED emergency department, *SBP* systolic blood pressure in mmHg, *HR* heart rate in beats per minute. *GCS* Glasgow Coma Scale score, *MCV* motor vehicle collision. *AVP* auto vs. pedestrian collision, *MCC* motorcycle collision, *ISS* Injury Severity Score, *AIS* Abbreviated Injury Scale score, *PEG* percutaneous endoscopic gastrostomy. < 24 h, within 24 h of hospital arrival

Table 3 Secondary outcomes

	Survivors ($n = 928{,}542$, 99.6%)	Mortalities ($n = 3{,}565$, 0.4%)	p
Hospital LOS	2 ± 4; 2 [1–3]	4 ± 9;4 [1–8]	< 0.001
ICU LOS	2 ± 3; 2 [1–3]	4 ± 8; 4 [2–8]	< 0.001
Ventilator days	1 ± 5; 1 [1, 2]	3 ± 9; 3 [1–8]	< 0.001
Complications			
Unplanned return to ICU*	1,745 (0.2)	229 (7)	< 0.001
AKI	1,491 (0.2)	220 (6)	< 0.001
Pneumonia	1,535 (0.2)	188 (5)	< 0.001
DVT	999 (0.1)	42 (1)	< 0.001
ARDS	583 (0.1)	130 (4)	< 0.001
PE	465 (0.1)	22 (0.6)	< 0.001
Severe sepsis*	308 (< 0.1)	126 (5)	< 0.001
Unplanned return to OR*	217 (< 0.1)	11 (0.4)	< 0.001
SSI, superficial	195 (< 0.1)	8 (0.2)	< 0.001
SSI, organ space	150 (< 0.1)	4 (0.1)	0.003
SSI, deep	74 (< 0.1)	1 (< 0.1)	0.250
Discharge disposition£			
Home	582,879 (85)	–	–
Skilled nursing facility	47,137 (7)	–	–
Rehabilitation facility	25,755 (4)	–	–
Left AMA	12,221 (2)	–	–
Outside hospital	7,358 (1)	–	–
Legal facility¥	2,602 (0.7)	–	–
Psychiatric facility¥	1,772 (0.5)	–	–
Intermediate care facility	3,434 (0.5)	–	–
Other	4,356 (0.6)	–	–

Continuous variables listed as median [interquartile range]. Categorical variables presented as number (percentage)

LOS length of stay in days, *ICU* intensive care unit, *AKI* acute kidney injury, *VAP* ventilator-associated pneumonia, *DVT* deep vein thrombosis, *ARDS* acute respiratory distress syndrome, *PE* pulmonary embolism, *OR* operating room, *SSI* surgical site infection

*Variable available only for study years 2011–2018 (during which time the study population was $n = 717{,}608$)

£Among survivors only

¥Variable available only for study years 2014–2018 (during which time the study population was $n = 358{,}247$)

common discharge destination for Survivors was home ($n = 582{,}879$; 85%).

Variables independently associated with in-hospital mortality are given in Table 4. Age ≥ 65 was most strongly associated with death (odds ratio [OR] 26.43, $p < 0.001$), followed by ED intubation (OR 10.08, $p < 0.001$), admission hypotension (OR 4.55, $p < 0.001$), and comorbidities, particularly end-stage renal disease (ESRD) (OR 3.03, $p < 0.001$) and immunosuppression (OR 2.18, $p < 0.001$).

Discussion

In this study, in-hospital mortality following isolated mild TBI was fortunately low and occurred among less than 1% of study patients. Nonetheless, this is an important population of patients to examine as one would expect mortality to be exceedingly rare given the low injury severity sustained. We found that patients who died following isolated mild TBI tended to be older and more comorbid than their surviving counterparts. They were more likely to have government-sponsored health insurance, which aligns with the existing literature demonstrating worse outcomes after trauma for underinsured patients, particular after TBI [10–12]. When compared with survivors, patients who died were more likely to be hypotensive on arrival to hospital and have a lower GCS score on presentation to the ED. After controlling for potential confounders, the factors most strongly associated with mortality after isolated mild TBI were age ≥ 65 years, intubation in the ED, admission hypotension, and comorbidities including end-stage renal disease and immunosuppressed status.

Our findings support the concept that the elderly and comorbid are at particularly high risk for adverse outcomes after injury [1–8]. In general, this is related to a diminished ability of these individuals to manifest physiologic compensation for traumatic injuries including blood loss and head injuries. Especially related to the clinical manifestation of head injuries is the fact that elderly patients experience cerebral volume loss as they age. Consequently, their craniums can accommodate a greater volume of blood and shift before these changes become symptomatic. Therefore, one might expect that the elderly would have worse outcomes after mild head injuries, in part because they are able to accommodate a larger volume of intracranial blood before their cerebral contents are compressed. Patient comorbidities have been demonstrated to have a significant negative impact on outcomes following trauma, especially among patients with cirrhosis, cardiac disease, and pulmonary disorders [4–8].

The association between ED intubation and mortality after isolated mild TBI identified by this study is intuitive but provocative. These intubations may be reflective of rapidly declining mental status as a result of head injury and may be necessary for airway protection. Conversely, the intubation and ensuing mechanical ventilation may independently bring an increased risk of death, which would be an important reason to avoid liberal intubation of these patients. A recent study showed that trauma patients with isolated head injuries and arrival GCS of 7–8 who were intubated within an hour of admission had increased risk of mortality and in-hospital complications [13]. Those study authors suggested that ED intubation for TBI

Table 4 Binary logistic regression of factors associated with in-hospital mortality

	Odds ratio	95% CI	*p*
Age			
< 18 years	Reference		
18–64 years	5.25	3.21–8.57	< 0.001
≥ 65 years	25.54	15.63–41.73	< 0.001
Sex, male	1.52	1.38–1.69	< 0.001
Admission vital signs			
SBP < 90 mmHg	4.57	3.77–5.54	< 0.001
HR > 120 bpm	2.07	1.74–2.48	< 0.001
ED Intubation	10.12	8.44–12.13	< 0.001
Intoxicants on admission			
Alcohol	0.49	0.41–0.59	< 0.001
Illicit drugs	1.21	1.02–1.45	0.032
Comorbidities			
ESRD	3.01	2.49–3.64	< 0.001
Immunosuppression	2.21	1.72–2.84	< 0.001
Alcohol use disorder	2.06	1.73–2.46	< 0.001
COPD	1.96	1.73–2.23	< 0.001
Functional dependent status	1.66	1.46–1.89	< 0.001
Cardiac disease	1.30	1.16–1.46	< 0.001
Diabetes mellitus	1.26	1.13–1.42	< 0.001
Bleeding disorder/Home anticoagulant	1.19	1.05–1.34	0.005
CVA with deficit	1.06	0.87–1.29	0.571
Current smoker	0.75	0.63–0.89	0.001
Mechanism of injury			
Fall	1.89	1.14–3.14	0.013
AVP	1.07	0.62–1.84	0.820
MVC	1.01	0.60–1.68	0.983
Assault	0.91	0.55–1.49	0.702
MCC	0.35	0.17–0.74	0.006
ISS	1.10	1.09–1.12	< 0.001

AUROC 0.852, 95% CI 0.846–0.858, $p < 0.001$

SBP systolic blood pressure in mmHg, *AKI* acute kidney injury, *ARDS* acute respiratory distress syndrome, *ED* emergency department, *VAP* ventilator associated pneumonia, *HR* heart rate in beats per minute, *ISS* Injury Severity Score

patients should be approached more selectively instead of routinely in the context of their findings of potentially imparted harm.

Our study findings also support the vices paradox observed among trauma patients, wherein those intoxicated with alcohol or drugs at the time of injury appear to have decreased mortality [14]. In the current study, alcohol and drug intoxication on admission were significantly more common among patients who survived to hospital discharge. Further work into the vices paradox in trauma is needed to understand the potential mechanism of protective action of drugs or alcohol following injury.

The study limitations must be acknowledged. This retrospective dataset-driven study is hindered by this type of study design and a lack of granularity that accompanies registry data. Particularly related to this study, it would be of interest to visualize the computed tomography scans of the head for patients who died vs. survived and to map patient clinical course in more detail, but this is not possible from the NTDB and can be an area of further investigation for the future. Furthermore, the NTDB does not code cause of death, which would be valuable to more completely understand the patients who died. For example, the distinction between a mild TBI that progressed and was the immediate cause of death as opposed to a mild TBI incurred by a comorbid patient who died from organ failure related to the underlying comorbidities would allow for a more complete grasp of patients with mild TBI who die. This cannot be ascertained in the current study. Next, owing to large patient numbers, this study may be overpowered. It must therefore be emphasized that statistically significant differences between groups do not uniformly translate to clinically relevant differences between patients. This should be considered in the interpretation of our results. In addition, the study results concerning insurance status are relevant only to the United States and are of limited generalizability for this reason. Although the mortality rate in this series was low, we were unable to capture functional or cognitive disability incurred from mild head injuries. Therefore, the low mortality rate among study patients should not be interpreted as a low burden of morbidity among these patients. Last, the possibility of coding errors must always be considered with a registry-based study and therefore a multicenter study to examine this concept in greater detail will be useful moving forward.

To conclude, we demonstrated that advanced age, intubation in the ED, and patient comorbidities were associated with mortality following isolated mild head injury. At a minimum, these data imply that a period of in-hospital clinical observation of patients with mild TBI may be necessary, particularly among patients with the delineated risk factors for mortality. Furthermore, identification of these risk factors for in-hospital death should alert clinicians to be increasingly vigilant in the clinical care of such patients and could be used to inform discussions with patients and families about prognostication.

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Declarations

Conflict of interest Authors Schellenberg, Arase, Wong, and Demetriades declare that they have no conflict of interest.

Ethical approval All procedures performed in this retrospective observational study involving human participants were in accordance with the ethical standards of the Institutional Review Board of the University of California (HS-19-00625) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent This study received a waiver for informed consent by the Institutional Review Board of the University of Southern California (HS-19-00625).

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