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Reviews

Civilian Gunshot Wounds to the Head: Prognostic Factors Affecting Mortality: Meta-Analysis of 1774 Patients

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Abstract

Civilian gunshot wounds to the head (cGSWH) are devastating, but there is no consensus regarding prognosis and management. Therefore, we conducted a meta-analysis to identify prognostic factors associated with mortality. PubMed, EMBASE, Scopus, Web of Science, and Cochrane Library were queried for retrospective cohort studies of isolated cGSWH reporting mortality prognostic factors. Meta-Analysis Of Observational Studies in Epidemiology (MOOSE) guidelines were followed. Study quality was assessed using the Newcastle–Ottawa scale. Primary outcome was mortality. Pooled estimates of odds ratios (ORs) and 95% confidence intervals (CIs) were derived using random-effects models. Seventeen (17) observational studies (1774 patients) were identified and included. Factors associated with mortality were: age >40 years (OR, 3.44; 95% CI [1.71–6.91]), suicide attempt (5.78; [3.07–10.87]), Glasgow Coma Scale (GCS) 3–8 compared with 9–15 (38.02; [21.98–65.77]), GCS 3–5 versus 6–8 (15.38; [6.72–35.23], bilateral fixed and dilated pupils versus normal (67.12; [16.67–270.22]), and versus unilateral fixed and dilated pupil (25.35; [5.82–110.41]), dural penetration (29.07; [4.30–196.53]) and bihemispheric (4.23; [2.32–7.68]), and multi-lobar injuries (6.53; [1.99–21.42]). Selection for operative management, according to expert neurosurgical opinion, was protective (0.06; [0.01–0.22]). This is the first meta-analysis on cGSWH mortality prognostic factors. Increasing age, suicide attempt, lower GCS, bilateral mydriasis, dural penetration, and bihemispheric and multi-lobar injury are associated with increased mortality. This study can serve as a guide to clinicians and will provide directions for future research to develop evidence-based management algorithms.

Keywords: gunshot wounds; meta-analysis; penetrating brain injuries; prognosis

Introduction

Gun violence accounts for 25 times more deaths in the United States than in other high-income countries.[1] Every day, 96 Americans are killed with guns, according to the Centers for Disease Control and Prevention.[2] In 2013, there were 73,505 nonfatal and 33,636 fatal gunshot injuries in the United States.[3,4] Civilian gunshot wounds to the head (cGSWH) were the most common cause for traumatic brain injury (TBI)-related deaths (34.9%), more than motor vehicle accidents (31.4%), in 2007.[5] Gunshot injuries from 2006 to 2010 cost the United States a total of $88 billion.[6] cGSWH are associated with roughly 91%[7] overall mortality, but selected cGSWH cases may have outcomes similar to nonpenetrating TBI with appropriate treatment.[8] More than 70% of victims die at the scene,[7,9–11] with survival of those hospitalized ranging from 7.69% to 69.70% in various studies.[7,9,10,12] Gunshot wounds to the head (GSWH) were first studied in military settings. Civilian and military cases differ in ammunition and weapons used, injury type, treatment, complications, and prognosis, necessitating an alternative approach in analysis.

Management of cGSWH remains elusive. Guidelines for penetrating brain injury (PBI) were published in 2001[13–20]; however, they were not limited to bullet injuries (they also contained shrapnel, stab wounds, etc.), and they were based on military reports and expert opinions, given the lack of high-quality evidence available at the time. No strict criteria exist for either surgical or conservative treatment approach. Surgical treatment modalities include craniotomy, necrotic tissue debridement, removal of bullet and bone fragments, hematoma evacuation, and decompressive craniectomy. Conservative management involves fluid resuscitation and intracranial pressure (ICP)-lowering measures, with or without ICP monitoring. Ethical and practical reasons preclude the utilization of randomized controlled trials to prospectively study outcomes in cGSWH. Most evidence comes from observational studies, which lack uniformity in data reporting.

Starting with the role of dural penetration described by Cushing 100 years ago,[21] multiple prognostic factors have since been proposed to predict mortality. Studies conducted in the early 1990s collectively studied Glasgow Coma Scale (GCS), pupillary abnormalities, age, suicide attempt, and imaging characteristics

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(multi-lobar, bihemispheric, and transventricular trajectory) as outcome prognosticators.[12,22–25] ICP has more recently been suggested as an important consideration.[7] This study aims to identify the prognostic factors associated with mortality in isolated cGSWH by utilizing meta-analysis tools and quality assessment of the literature. Further, we propose a template for data reporting and a management algorithm to assist in cGSWH triage.

Methods

Background

The clinical problem in question is identification of factors predicting outcome in cGSWH. We hypothesize that the following factors are associated with higher mortality in cGSWH: patient >40 years of age, male sex, suicide attempt, low GCS after initial resuscitation, pupillary abnormalities, ICP >20 mm Hg, penetration of the dura, perforating injury, trajectory through both hemispheres (bihemispheric), involving more than one lobe (multi-lobar), through the ventricles (transventricular), and type of management (conservative or surgical). The primary outcome studied is in-hospital mortality. We only included isolated bullet projectiles involving the skull and brain. Possible interventions are surgery, conservative management, and placement of an ICP monitor. Eligible study designs were observational cohort studies and randomized controlled trials. The population under study was civilians with GSWH, regardless of age, sex, and country.

Search strategy

A search of PubMed, EMBASE, Scopus, Web of Science, and Cochrane Library was performed on March 1, 2017 for human studies after 2000 in English by one investigator (G.M.) and a qualified librarian (M.S.). The complete list of search terms and medical headings is presented in Supplementary Digital Content 1 (see online supplementary material at http://www.liebertpub.com). Two investigators (G.M. and A.F.) independently screened all abstracts, full-text articles, and reference lists in duplicate. We attempted to contact authors of studies with incomplete data to obtain any available unreported data.

Inclusion/exclusion criteria

Inclusion criteria were isolated craniocerebral gunshot wounds, reporting patient data associating studied prognostic factors with mortality. Exclusion criteria were: war setting, shrapnel injuries, concomitant injuries to the body, injuries to the face or orbits without penetration of the dura, fewer than 10 participants, and animal and experimental models. Patients dead on arrival were excluded.

Data collection

The prognostic factors (exposures) studied can be seen in Table 2. The primary outcome was mortality. Data were extracted independently by two reviewers (G.M. and A.F.) using a data collection form devised beforehand, according to current clinical principles. Study quality assessment was conducted as recommended by the Meta-Analysis Of Observational Studies in Epidemiology (MOOSE) guidelines (please see Supplementary Digital Content 2 (see online supplementary material at http://www.liebertpub.com), for the completed MOOSE checklist),[26–29] using the Newcastle–Ottawa Scale for observational cohort studies (please see Supplementary Digital Content 3 (see online supplementary material at http://www.liebertpub.com) for the criteria and Supplementary Digital Content 4 (see online supplementary material at http://www.liebertpub.com) for scoring of each included study).

Statistical analysis

Quantitative data synthesis was performed using the software package Review Manager (Version 5.3 (RevMan, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Odds ratios (ORs) were used for dichotomous data, with 95% confidence intervals (CIs), using random-effects models, because of expected methodological variability. The null hypothesis for each potential prognostic factor was that there is no association with mortality.

Heterogeneity

The I^2 test, Q value, and funnel plots were used to assess between-study statistical heterogeneity. The influence of study characteristics on statistically significant ($p(Q) < 0.05$) heterogeneity was evaluated through metaregression[30] (StataCorp 2013, Stata Statistical Software: Release 13; StataCorp LP, College Station, TX). Covariates used were the Newcastle–Ottawa Scale, inclusion of pediatric patients, and year of publication. The Monte Carlo permutation test was used to account for multiple covariates being tested simultaneously. The proportion of observed heterogeneity explained by covariates is expressed as the adjusted R^2 statistic.

Results

Our search strategy yielded 873 studies, excluding duplicates. Based on titles and abstracts, 64 articles were relevant. One study was added through manual searching. Seventeen studies encompassing 1774 patients met the criteria for quantitative meta-analysis.[7,10,31–45] We were unable to track three full-text articles. The study selection flow chart is presented in Figure 1.

Study characteristics

Descriptive characteristics of the included studies are presented in Table 1. All identified studies were observational cohorts, 15 retrospective and two prospective. The majority of patients were from North America (41.7%). Ten studies ($n = 1136$ patients) included both adult and pediatric patients, four studies ($n = 489$) excluded pediatrics, and three studies ($n = 149$) excluded adults. Of the total 1774 included patients, 674 had surgery (excluding ICP monitor placement) and 602 conservative management. There was no report regarding operative versus conservative management for the remaining 498 patients, who were excluded from analysis of surgical outcomes.

Prognostic factors

Table 2 presents number of studies, number of patients, OR summary estimates with 95% CIs and *p* values for overall effect on mortality for each prognostic factor, as well as I^2 and *p* values for between-study heterogeneity. Forest plots for all prognostic factors are presented in Supplementary Digital Content 5 (see online supplementary material at http://www.liebertpub.com). The prognostic factors found to have statistically significant association with mortality were: age >40 years, suicide attempt, GCS <9, bilateral fixed and dilated pupils, dural penetration, bihemispheric, multi-lobar and transventricular injury, and ICP >20 mm Hg. Patients undergoing operative management were found to have lower mortality than conservatively managed patients, but no conclusion can be reached whether this reduction in mortality is an effect of the surgery itself or if a lower mortality group was selected for surgery.

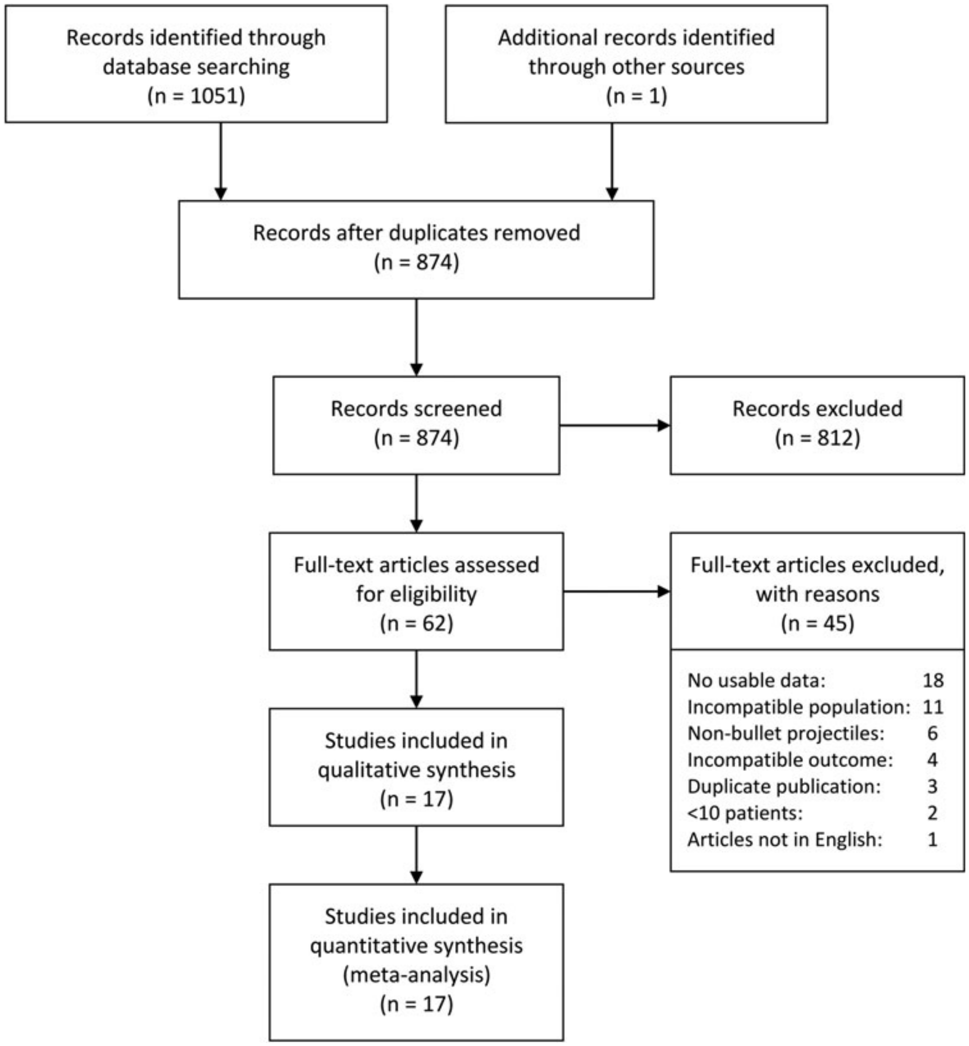

FIG. 1. Study selection flow chart. Regarding reasons for full-text article exclusion: ''No usable data'' means there was no cross-tabulation of outcome with any of the studied prognostic factors to be included in meta-analysis. ''Incompatible patient population'' included studies with war GSWH, dead-on-arrival patients, polytrauma, and only nonfatal injuries. ''Incompatible outcome'' included arterial injury, infection, functional outcomes, etc., with no subgrouping to assess mortality. GSWH, gunshot wounds to the head.

Epidemiology

Overall reported in-hospital mortality ranged from 7.69% to 69.70% among the included studies. Mean overall hospital mortality was 33.72 ± 19.67%. Patients >40 years of age had significantly higher mortality than those <40 years of age ($n = 229$; OR, 3.44; 95% CI [1.71–6.91]; $p < 0.0001$; $I^2 = 0\%$). There were insufficient data to assess mortality differences between pediatric and adult patients. No association was found between sex and mortality ($n = 302$; [0.36–1.43]; $p = 0.35$). Suicide attempts were more lethal than assaults and accidents ($n = 264$; OR, 5.78; [3.07–10.87]; $p < 0.0001$; $I^2 = 0\%$).

Initial assessment

Lower GCS, measured after resuscitation, was associated with higher mortality. Patients with GCS 3–8 had higher mortality than patients with GCS 9–15 ($n = 974$; OR, 38.02; [21.98–65.77]; $p < 0.0001$; $I^2 = 20.88\%$). GCS 9–12 patients had no statistically significant difference in mortality than GCS 13–15 ($n = 217$; [0.96–5.44]; $p = 0.06$). GCS 3–5 patients had higher mortality than GCS 6–8 ($n = 402$; OR, 15.38; [6.72–35.23]; $p < 0.0001$; $I^2 = 0\%$). Pupillary abnormalities on arrival were associated with increased mortality. Bilateral fixed and dilated pupils were associated with higher mortality than bilateral reactive pupils ($n = 224$; OR, 67.12; [16.67–270.22]; $p < 0.0001$; $I^2 = 0\%$) and higher mortality than a unilateral fixed and dilated pupil ($n = 137$; OR, 25.35; [5.82–110.41]; $p < 0.0001$; $I^2 = 0\%$). Having a unilateral fixed and dilated pupil had no statistically significant difference in mortality, compared to bilateral reactive pupils ($n = 279$; [0.74–7.98]; $p = 0.14$; $I^2 = 67.58\%$). Meta-regression attributed between-study heterogeneity to differences in study quality per Newcastle–Ottawa Scale ($R^2 = 100\%$; $p = 0.25$).

Imaging

Three injury types are defined based on bullet penetration. Tangential injuries do not penetrate the dura matter, penetrating injuries penetrate the dura and brain tissue, and perforating injuries also have an exit wound.[46] Perforating injuries had similar mortality as penetrating ($n = 148$; [0.37–2.28]; $p = 0.85$). Penetrating

TABLE 1. DESCRIPTIVE STUDY CHARACTERISTICS

Included studies	N	Surgery (n [%])	Expired (n [%])	Male (n [%])	Age (years; Mean ± SD, range)	Follow-up (months)
Aarabi, 2014[7]	48	28 (58)	24 (92)	?	38.2 ± 18.0	Mean 40.6
Ambrosi, 2012[31]	110	110 (100)	27 (92)	102 (92)	26.9 ± 11.0	Discharge
Bandt, 2012[32]	48	48 (100)	31 (87)	42 (87)	14.1 ± 4.7	Unspecified
Coughlan, 2003[33]	30	14 (47)	6 (76)	23 (76)	6.8 ± 4.0 (1–13)	Minimum 6
DeCuypere, 2016[34]	71	39 (55)	34 (80)	57 (80)	14 (1–18)	Unspecified
Glapa, 2009[35]	72	70 (97)	42 (80)	58 (80)	34 (18–73)	3
Gressot, 2014[36]	119	80 (67)	58 (87)	104 (87)	(12–73)	6
Hofbauer, 2010[37]	85	24 (28)	53 (81)	69 (81)	48 (17.8–98.4)	Discharge
Joseph, 2014[38]	132	20 (15)	92 (34)	46 (34)	32.5 ± 17.5	Discharge
Khan, 2014[39]	51	45 (88)	11 (84)	43 (84)	28.92 ± 2.33	3
Kim, 2005[40]	37	9 (24)	10 (91)	34 (91)	26 (13–49)	6–12
Kim, 2007[41]	13	1 (8)	1 (84)	11 (84)	24.1 (8–39)	Unspecified
Liebenberg, 2005[42]	125	27 (22)	87 (88)	111 (88)	24.9 ± 10.9	Mean 4
Martins, 2003[43]	319	156 (49)	172 (93)	297 (93)	26 (3–27)	Discharge
Stoffel, 2009[44]	214	?	58 (85)	183 (85)	30 ± 11	Discharge
Tsuei, 2005[45]	16	13 (81)	5 (93)	15 (93)	30.9 (14–68)	Discharge
Zafonte, 2001[10]	284	?	168 (86)	245 (86)	28.4	Discharge

SD, standard deviation.

injuries were more lethal than tangential ($n = 477$; OR, 29.07; [4.30–196.53]; $p = 0.0005$; $I^2 = 56.75\%$). Between-study heterogeneity was partially explained by differences in inclusion of pediatric patients ($R^2 = 36.43\%$; $p = 0.66$). Bihemispheric injuries, defined as bullet trajectory involving both hemispheres, were more lethal than unihemispheric ($n = 449$; OR, 4.23; [2.32–7.68]; $p < 0.0001$; $I^2 = 35.54\%$). Bullet trajectories involving more than one lobe (multi-lobar) were more lethal than those involving only one lobe (unilobar; $n = 108$; OR, 6.53; [1.99–21.42]; $p = 0.002$; $I^2 = 0\%$). Transventricular injuries, that is, bullet trajectories through the

TABLE 2. PROGNOSTIC FACTORS FOR MORTALITY IN cGSWH

Prognostic factor	Studies	Patients (N)	Odds ratio[a]	95% confidence interval	p value for overall effect	I^2 (Q)
Age						
≥40 years	2	229	3.44	1.71–6.91	<0.0001	0%
Sex (male vs. female)	3	302	0.72	0.36–1.43	0.35	0%
Intention (suicide vs. other causes)	3	264	5.78	3.07–10.87	<0.0001	0%
Glasgow Coma Scale						
3–8 versus 9–15	9	974	38.02	21.98–65.77	<0.0001	20.88%
9–12 versus 13–15	7	217	2.29	0.96–5.44	0.06	0%
3–5 versus 6–8	7	451	15.38	6.72–35.23	<0.0001	0%
Pupillary abnormalities						
Bilateral fixed and dilated pupils versus bilateral reactive	4	224	67.12	16.67–270.22	<0.0001	0%
Unilateral fixed and dilated pupil versus bilateral reactive	5	279	2.44	0.74–7.98	0.14	67.58%
Bilateral fixed and dilated versus unilateral	4	137	25.35	5.82–110.41	<0.0001	0%
High ICP (>20 mm Hg)	2	75	3.51	1.24–9.95	0.02	0%
Penetration of the dura						
Perforating versus penetrating	2	148	0.92	0.37–2.28	0.85	16.41%
Penetrating versus tangential	5	477	29.07	4.30–196.53	0.0005	56.75%
Bihemispheric injury	7	449	4.23	2.32–7.68	<0.0001	35.54%
Multi-lobar injury	4	108	6.53	1.99–21.42	0.002	0%
Transventricular injury	5	319	7.68	1.60–36.92	0.01	78.30%
Operative management	5	512	0.06	0.01–0.22	<0.0001	72.20%

[a]Odds ratios reflect the comparison of the first versus the second statement in the Prognostic factor column, that is, OR >1 denotes that expired patients were more likely to be older than 40 years than younger.
[b]Insufficient evidence for meta-analysis.
[c]GSWH, civilian gunshot wounds to the head; ICP, intracranial pressure; OR, odds ratio.

ventricles, had higher mortality than wounds not involving the ventricles ($n = 319$; OR, 7.68; [1.60–36.92]; $p = 0.01$; $I^2 = 78.30\%$). Heterogeneity was explained by differences in inclusion of pediatric patients ($R^2 = 100\%$; $p = 0.225$).

Management

Surgery was offered at the discretion of the treating physician to patients thought to have better survival chances. Surgery was associated with lower mortality rates ($n = 512$; OR, 0.06; [0.01–0.22]; $p < 0.001$; $I^2 = 72.20\%$). Studies published later chronologically seemed to have better surgical results than previous ones. There was high heterogeneity, explained by differences in year of publication ($R^2 = 100\%$; $p = 0.739$). Insufficient data exist for decision to place an ICP monitor (extraventricular drainage device or intraparenchymal pressure monitor). For patients who did have an ICP monitor, ICP >20 mm Hg was associated with increased mortality ($n = 75$; OR, 3.51; [1.24–9.95]; $p = 0.02$; $I^2 = 0\%$).

Risk of bias assessment

Most included cohort studies scored 5 on the 8-point Newcastle–Ottawa Scale (Supplementary Digital Content 4) (see online supplementary material at http://www.liebertpub.com). Rigorous follow-up for more than 6 months was rarely achieved, because most studies evaluated mortality at discharge. Publication bias assessment by funnel plots is presented in Supplementary Digital Content 6 (see online supplementary material at http://www.liebertpub.com).

Discussion

The guidelines for penetrating brain injury published in 2001 were the first major effort to systematically approach all PBIs, including cGSWH.[13–20] They offer navigation in a field inherently difficult to study, attributable to ethical dilemmas in conducting prospective randomized controlled trials and lack thereof, multiple confounding parameters, and lack of consensus for gathering, reporting, and objectively assessing data. For these reasons, data currently available in the literature are solely derived from observational studies. Most studies before the guidelines were from military settings and included expert opinions with no clear focus on isolated civilian gunshot wounds to the head. Civilian and military GSWH differ in many respects, including caliber of bullets, shrapnel injuries, and wound contamination. Over the past years, cGSWH hospitalizations have increased,[5] calling for a systematic approach. Observational data may be problematic in assessing and guiding surgical treatment; however, they can help estimate the effect of prognostic factors on mortality. To refine the quality of conclusions derived from these studies, we utilize quality assessment checklists, meta-analysis, and metaregression tools. We limited our search to studies published after 2000, the last year that the PBI guidelines included in their search.[13–20] We aimed to study modern-day management of cGSWH, largely influenced by the PBI guidelines being publicly available.

Age

Patients >40 years of age had higher mortality than younger patients. The choice of age 40 years as the cutoff was made mainly because of data availability, that is, the identified published series used this cutoff for comparisons. cGSWH happen predominantly to young males.[5,47] Older age is associated with more comorbidities, therefore worse surgical outcome and survival through acute care. This may clarify the controversies in the literature about whether age predicts mortality[25,38,48] or not.[49,50]

Suicide

Suicide attempts were approximately 6 times more lethal than assaults and accidents. Our findings validate previous author comments about the lethality of attempted suicides,[9,24,40,50–52] as well as the PBI guidelines.[20] Attempted suicide is a consistent prognosticator of mortality in cGSWH, possibly attributed to proximity and better aim at the central cerebral structures.[53] According to the latest TBI surveillance data in the United States,[5] suicide accounts for 74.2% of cGSWH-related deaths, followed by homicides (22.2%) and accidents (3.6%).

Glasgow Coma Scale

Several authors agree that post-resuscitation GCS is one of the most reliable predictors of mortality.[24,31,35,43,54–57] In this meta-analysis, GCS 3–8 patients invariably had higher mortality than those with GCS 9–15 (OR, 40). There was even higher mortality in patients with GCS 3–5 than those with GCS 6–8 (OR, 15). Clearly, patients with GCS 5 or less had the worst mortality rates. Around 38–81% of cGSWH patients had admission GCS between 3 and 5,[7] whereas 48–94% had GCS 8 or less.[54,58] Aggressive fluid resuscitation for all patients, irrespective of pre-resuscitation GCS, may lead to survival in up to 28% of patients with initial GCS 3–5.[38] Pediatric patients arriving with even GCS 3 have been shown to survive, necessitating additional prognostic factors to predict outcome.[32] Part of the increased mortality in low GCS may be attributed to the Pygmalion effect, that is, clinicians not operating on patients in perceived bad clinical condition. Our group advocates aggressive medical and fluid resuscitation for all patients arriving with cGSWH, and assessment of GCS and prognostic factors after the initial resuscitation effort. In patients presenting with GCS >9, our meta-analysis did not detect a statistically significant difference in mortality between GCS 9–12 and GCS 13–15 ($p = 0.06$; CI [0.96–5.66]). Our results are marginal, with a p value of 0.06. It is not clear whether, in this group, lower GCS plays a detrimental role in patient prognosis. According to the TBI literature, GCS may underperform in patients with aphasia or intubation because of lack of verbal assessment. Therefore, clinicians should not rely solely on GCS to predict mortality in cGSWH, despite strong association with high mortality rates.

Pupillary abnormalities

The effects of pupillary defects on mortality are still controversial. In our meta-analysis, we detected a clear association of bilateral fixed and dilated pupils with mortality (approximately 67 times higher than bilateral normal pupils). Pupils unreactive to light have been associated with increased mortality in some studies,[12,22,36,54,59–61] whereas other researchers do not find statistical significance.[42,62,63] Bilateral pupillary defects may indicate damage to the brainstem or cerebral edema and could possibly be a precursor to brain death. Some researchers suggest that pupils should be assessed for patients with GCS 3–5,[37,51] to identify those with higher chances of survival. When patients with a unilateral fixed and dilated pupil (UFDP) were compared to those with both pupils normal, no significant mortality difference was detected. Because of the introduction of a foreign body, the mechanism of a UFDP may not be the same as that causing uncal herniation in space-occupying lesions (subdural hematomas, tumors). Rather, it

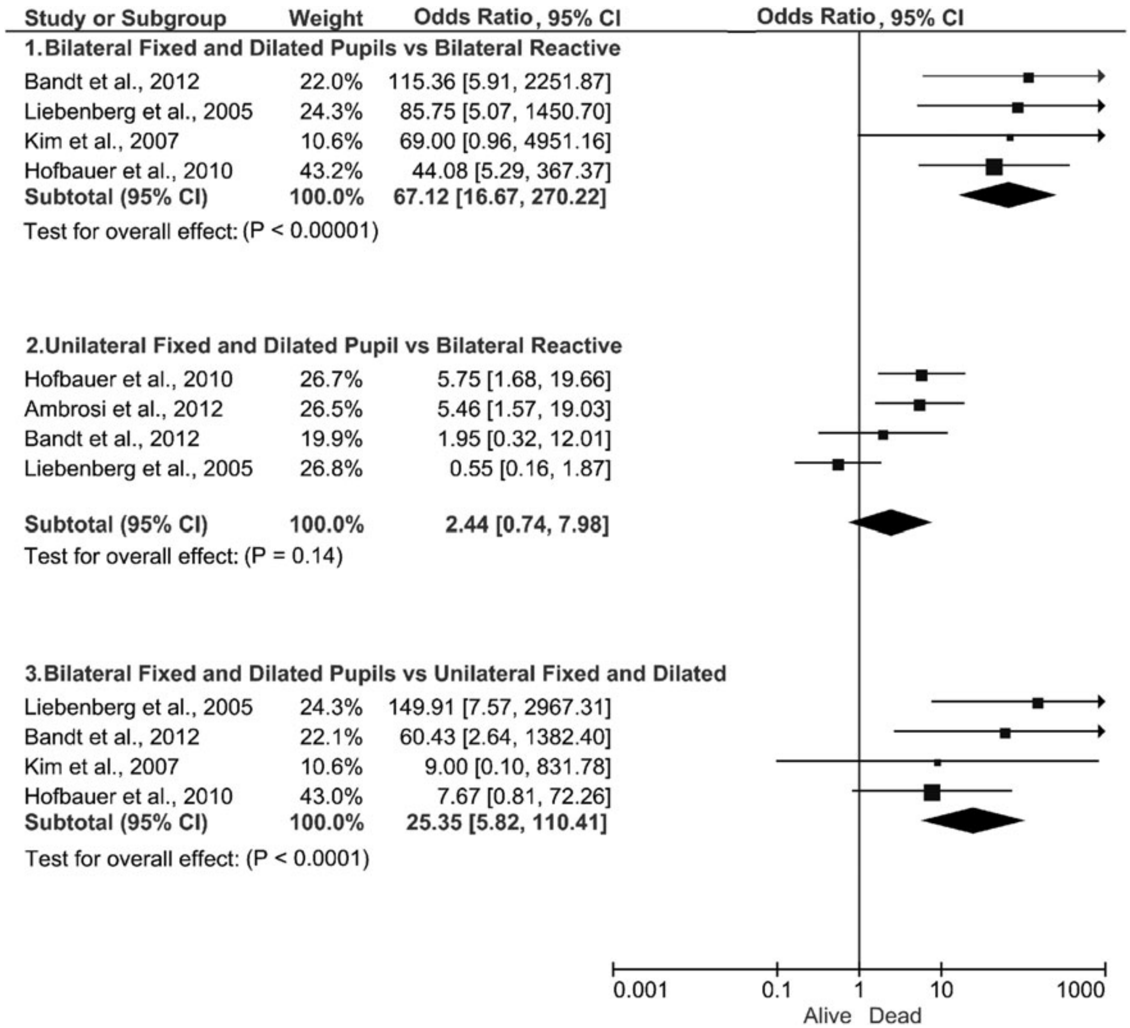

FIG. 2. Forest plot for pupillary abnormalities and mortality. The horizontal axis represents the odds ratio for patients to expire. All included studies in each comparison are mapped on the vertical axis. The boxes represent the mean of each study, and the horizontal line is the 95% confidence interval. Study weight is represented by the size of each box. The diamond is the mean and 95% confidence interval for the cumulative odds ratio. Comparisons 1 (bilateral fixed and dilated pupils vs. bilateral normal pupils) and 2 (bilateral fixed and dilated vs. unilateral fixed and dilated) are statistically significant, because the 95% CI does not include the value of 1 (vertical axis). Comparison 2 (unilateral dilated pupil vs. bilateral normal) is not statistically significant, because 1 is included in the confidence interval. CI, confidence interval.

may be caused by pressure of the oculomotor nerve by localized mass effect (e.g., hematoma), direct ocular or optic nerve damage (bullet impingement), or facial injury.[43] Such factors may be reversible and not as immediately life-threatening as in uncal herniation. There was high heterogeneity in this comparison, which metaregression attributed to quality differences between studies. Previous researchers have advocated surgery for patients with a UFDP regardless of GCS status, without commenting on long-term outcomes.[59] The relationship of the unilateral fixed and dilated pupil with mortality warrants further investigation.

Dural penetration

Patients arriving with cGSWH should be evaluated by computed tomography (CT) scan to identify bullet trajectory. If there is penetration of the cranium, but not the dura, the injury is termed tangential (Types I and II by Matson Classification).[64] We found that penetrating injuries were 30 times more lethal than tangential ones. Penetrating injuries are associated with direct damage inflicted on brain tissue, the possibility of affecting deep brain structures, and higher projectile energy. Tangential wounds cannot be considered trivial, however, because of possible meningeal artery injury, hematoma formation, and wound infection or bullet migration.[35,65] cGSWH that exit the skull, defined as ''perforating'' injuries, were not associated with higher mortality rates than those where the bullet stayed inside the cranium. A bullet exiting the skull cavity will not impact all its stored energy to the brain tissue, making this an unreliable prognosticator for mortality.

Trajectory

The trajectory of the bullet is also important in identifying patients more likely to die. Trajectories involving both hemispheres (OR, 4.23), or involving more than one lobe (OR, 6.53), and those involving the ventricles (OR, 7.68) are more lethal. Our findings agree with previous studies,[12,22,24,37,63,66,67] and the PBI

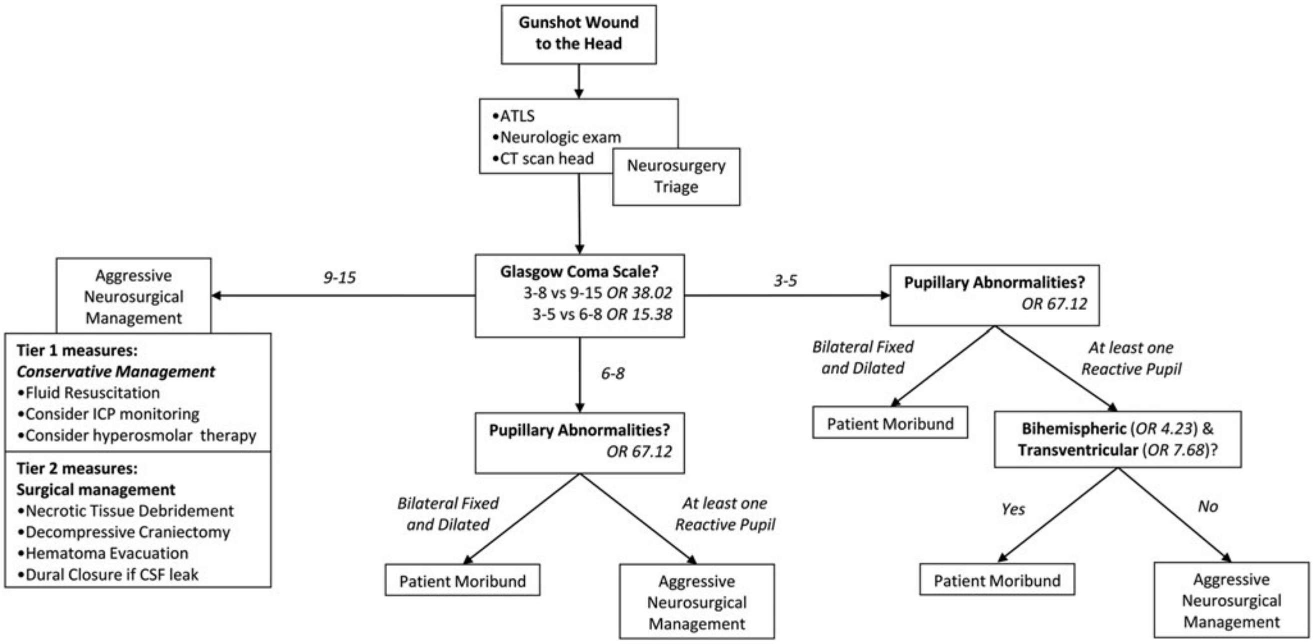

FIG. 3. Flow diagram for management of cGSWH. We propose this algorithm for management of civilian gunshot wounds to the head based on GCS, pupil assessment, and radiographical features. Please note that GCS evaluation should be considered valid only after fluid resuscitation of the patient, otherwise it may be underestimated. ATLS, Advanced Trauma Life Support; cGSWH, civilian gunshot wounds to the head; CSF, cerebrospinal fluid; CT, computed tomography; GCS, Glasgow Coma Scale; ICP, intracranial pressure; OR, odds ratio.

guidelines.[20] Bilateral injuries may involve larger areas of brain tissue, and may disrupt thalamocortical projections, or affect both cerebral cortices and brainstem. Midline structures may also be involved. Injury to midline structures, like the superior and inferior sagittal sinuses, the ventricular system, the diencephalon and brainstem, as well as the circle of Willis and the deep venous system, may lead to significant complications. The ''GSW zona fatalis,'' an area 4 cm above the dorsum sellae involving the mid-body of the corpus callosum, third ventricle, and cingulate gyrus, has previously been associated with high mortality rates.[40]

Intracranial hypertension

Our analysis showed an association of increased ICP with mortality, in agreement with previous researchers showing that intracranial hypertension is frequent and associated with worse outcomes in cGSWH.[23,63,68] However, ICP monitors may be selectively placed in patients suspected to have high ICP, causing selection bias.[7,54] To date, there is no established ICP cutoff for cGSWH. The two studies identified for meta-analysis used a cutoff of 20 mm Hg, and we excluded studies that did not report ICP monitor placement or thresholds. ICP monitor placement has been advocated for all pediatric patients by one study,[32] and for adult patients with GCS less than 10 or obscure neurological exam attributed to sedation or coma in another.[40] We suggest that ICP monitoring placement be left to physician discretion, according to the standard of care for severe TBI, given the paucity of evidence to make a conclusive recommendation.[69]

Surgery

Our meta-analysis validates the increased survival of patients receiving operative treatment, compared to those treated conservatively. The included studies utilize neurosurgical expert opinion to decide for or against surgery on select patients deemed salvageable,[16,20] introducing considerable selection bias to this outcome. Our finding should be viewed as validation that the previously used selection criteria have merit and successfully assist in patient selection, and do not by any means suggest that surgery should be offered for all cGSWH patients. Other authors have also suggested that timing is of importance in cGSWH, but we had insufficient evidence to comment on this.[70] Reliable recommendations about which patients should receive operative treatment are not currently possible, because of the lack of randomized controlled trials and clear inclusion or exclusion criteria for surgery. However, our meta-analysis solidifies which factors most substantially influence outcome since the introduction of the latest PBI guidelines in 2001. Decisions for operative versus conservative treatment can be guided by these prognostic factors. Studies should be conducted in the future, to ascertain what forms of operative treatment are most viable for these patients.

Future research recommendations

We suggest that future studies in cGSWH assess association of mortality with: age, sex, suicidal intent, post-resuscitation GCS, pupillary abnormalities, and radiological findings, including: penetration of the dura, number of hemispheres and lobes affected, whether the frontal lobes, ventricles, brainstem, and cerebellum are penetrated, and hematoma formation (please see Supplementary Digital Content 7 (see online supplementary material at http://www.liebertpub.com), for a table with a reporting list). We suggest a minimum follow-up period of 6 months to evaluate morbidity and mortality.

Management algorithm

We propose a simple-to-use management algorithm (Fig. 3), assessing clinical and imaging findings on admission, to rapidly ascertain whether a patient is highly likely to be moribund. This is not intended as an inclusive guideline to direct management of cGSWH, because of lack of high-quality studies in the literature, but more as an informative piece on prognostic factors, to assist in patient triage, decisions regarding transport, and discussion with families.

Limitations

Several features may limit the generalizability of this meta-analysis. First, most included studies were observational, retrospective cohorts. Therefore, there are multiple confounding factors that are not stated and cannot be eliminated from the results, such as past medical history, previous trauma, laboratory values, hypoxia on the field, transfer from outside hospital, etc. Lack of individual patient data led to inability to perform multi-variate analysis to identify confounders. Some of the included studies managed all included patients surgically, whereas others operated only on part of the patient population. Sensitivity analysis using studies exclusively including surgically treated patients was not possible because of their small number (Table 1). Studies reporting concomitant injuries were excluded. Inclusion of studies with minor polytrauma could potentially improve generalizability, but the identified studies included both minor and major concomitant trauma and would confound the results regarding GSWH, if they were included. Differences in hospital setting, patient population and selection, management algorithms, type and severity of injury and selection, report bias, and lack of consensus in reporting data were the main sources for heterogeneity. These studies are the only available evidence. In this study, we address this by utilizing the Newcastle–Ottawa Scale,[27] MOOSE guidelines,[26] and metaregression[30] for quality assessment, in addition to a meta-analysis random-effects model approach to assess the cumulative OR for mortality.

Conclusions

Shot wounds to the head patients have high mortality rates even before reaching the hospital. When such patients arrive alive in the emergency department, the treating physician needs to decide whether the patient is salvageable for either conservative or operative treatment, or moribund. Some patient characteristics, clinical signs, and imaging techniques can assist in the decision-making process. This meta-analysis suggests that age >40 years, suicide attempts, GCS <9, bilateral fixed and dilated pupils, penetration of the dura, and bihemispheric, multi-lobar, and transventricular trajectories have significantly worse prognosis than their counterparts.

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