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Patterns of Palliation: A Review of Casualties That Received Pain Management Before Reaching Role 2 in Afghanistan

MAJ Ian L. Hudson, MC, USA, ‡; Amanda M. Staudt, PhD†; Matthew Burgess, BS‡; Carmen Hinojosa-Laborde, PhD‡; MAJ Steven G. Schauer, MC, USA*, ‡; MAJ Ryan K. Newberry, MC, USA*, ‡; Kathy L. Ryan, PhD‡; LTC Christopher A. VanFosson, AN, USA‡*

ABSTRACT

Introduction:

Battlefield pain management changed markedly during the first 20 years of the Global War on Terror. Morphine, long the mainstay of combat analgesia, diminished in favor of fentanyl and ketamine for military pain control, but the options are not hemodynamically or psychologically equivalent. Understanding patterns of prehospital analgesia may reveal further opportunities for combat casualty care improvement.

Materials and Methods:

Using Department of Defense Trauma Registry data for the Afghanistan conflict from 2005 to 2018, we examined 2,402 records of prehospital analgesia administration to assess temporal trends in medication choice and proportions receiving analgesia, including subanalysis of a cohort screened for an indication with minimal contraindication for analgesia. We further employed frequency matching to explore the presence of disparities in analgesia by casualty affiliation.

Results:

Proportions of documented analgesia increased throughout the study period, from 0% in 2005 to 70.6% in 2018. Afghan casualties had the highest proportion of documented analgesia (53.0%), versus U.S. military (31.9%), civilian/other (23.3%), and non-U.S. military (19.3%). Fentanyl surpassed morphine in the frequency of administration in 2012. The median age of those receiving ketamine was higher (30 years) than those receiving fentanyl (26 years) or nonsteroidal anti-inflammatory drugs (23 years). Among the frequency-matched subanalysis, the odds ratio for ketamine administration with Afghan casualties was 1.84 (95% CI, 1.30-2.61).

Conclusions:

We observed heterogeneity of prehospital patient care across patient affiliation groups, suggesting possible opportunities for improvement toward an overall best practice system. General increase in documented prehospital pain management likely reflects efforts toward complete documentation, as well as improved options for analgesia. Current combat casualty care documentation does not include any standardized pain scale.

INTRODUCTION

Battlefield pain management has undergone a marked evolution during the first 20 years of the 21st century, contemporaneous with ongoing military antiterrorist efforts. Although the vasodepressive impacts during hemorrhagic shock and respiratory effects of morphine have been long known, morphine has been a mainstay of military analgesia since the Crimean War (in the United States since the Civil War) and remained so through much of the most recent conflicts in Iraq and Afghanistan.[1–3] As a result of emerging research, the Tactical Combat Casualty Care guidelines (TCCC) were modified in 2014 to formalize what had been ad hoc use of oral transmucosal fentanyl lozenges as well as intravenous ketamine (for those in shock or at risk for shock), in addition to morphine (IV and intraosseous routes only); these guidelines cover analgesia administered near the point of injury as well as during en-route care.[4] Previous work has been done to explore trends in the use of these medications in combat, and concern has been raised that the TCCC guidelines have not been consistently followed.[5–7]

Early trauma analgesia is clearly part of compassionate care, although several studies have drawn attention to low proportions of combat trauma patients receiving prehospital analgesia of any kind.[7,8] Opiate analgesia (e.g., morphine and fentanyl) has been shown to reduce psychological complications; ketamine has been less consistent against psychological effects, perhaps owing to its use in more severely injured patients.[9–12] Prehospital analgesic use in civilian practice has been evaluated with studies demonstrating the frequency of use for various analgesics, most notably ketamine and its increase in use over the last decade.[13–15] This increase is likely attributable to minimal changes in spontaneous respirations, systolic blood support, and lower pain scores upon

*Brooke Army Medical Center, San Antonio, TX 78234, USA

†The Geneva Foundation, San Antonio, TX 78234, USA

‡US Army Institute of Surgical Research, San Antonio, TX 78234, USA

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arrival to the hospital compared to opioid use.[14] However, the effects of the chosen analgesia have a much larger impact in the management of combat casualties than civilian casualties, as balancing potential return to combat effectiveness against proper analgesia becomes a concern for the future warfighter, in addition to ongoing concerns about not exacerbating potential shock states with opiate analgesia.[6,13] As Army medicine prepares for future combat less conducive to urgent evacuation, minimizing iatrogenic resuscitative burdens to the greatest extent possible becomes a priority, thereby drawing attention to the effects and patterns of analgesic choices. Lastly, from an ethical standpoint, it is incumbent upon medical providers to maximize the benefit-to-risk ratio of any intervention; as analgesics vary in hemodynamic and psychological effects, the analysis would ideally reveal consistency across multiple patient categories.

Military casualty care consists of four roles. Role 1 is closest to the point of injury and is care rendered under fire and immediately after in the field, during the initial evacuation, and/or at a small/limited aid station (care while still under fire does not involve analgesia). Role 2 has some of the capabilities of a field hospital (e.g., basic radiology and laboratory) but is smaller, more portable, and still relatively near initial injury[16]; these are at times augmented by damage control surgical capabilities. Role 3 is larger, less portable, and affords more hospital capabilities (e.g., critical care, subspecialty surgery, and advanced imaging), but evacuation to Role 3 may require hours. Role 4 is a full capability, typically distant medical facility in a permanent building (U.S. base hospital or robust overseas facility). Given the nature of care in or near combat, details of care in the prehospital space tend not to get documented during the administration of care or while making a rapid, precise handoff for further evacuation.[8,17,18] Previous studies using the Prehospital Trauma Registry have examined military prehospital analgesia use, although typically with smaller sample sizes, and a recent, larger study using the Department of Defense Trauma Registry (DoDTR) relied on prehospital documentation known to be somewhat limited in quality and integration.[6,7,19] Ongoing efforts to connect prehospital documentation to the DoDTR have made it possible to use the Army's most comprehensive database to examine this critical but nebulous area of casualty care more closely, and the availability of these data afforded the opportunity to investigate certain aspects of combat prehospital analgesia.[20]

Our previous work suggested inconsistencies in prehospital airway manipulation across broad national categories during combat operations; whether similar inconsistencies exist in other clinical aspects merits investigation, and another retrospective analysis has demonstrated systematic inconsistencies in the application of analgesia.[21,22] In the current analysis, we sought to determine the proportion of casualties receiving analgesia over time, as well as examine for possible group disparities (hypothesizing that groups would exhibit differences in analgesia received after adjusting for other factors).

METHODS

The DoDTR, managed by the Joint Trauma System and previously known as the Joint Theater Trauma Registry, is the aggregate of traumatic injury data regarding patients treated at military facilities or by forward surgical teams, including both battle and non-battle injuries, and represents over 80,000 unique trauma patients; it has been thoroughly described elsewhere.[20,23] Originally limited to patients treated at Role 3 facilities (which are sometimes bypassed or not reached), Joint Trauma System staff have been increasingly integrating prehospital and en-route care documentation over time, retroactively enhancing the resolution of the registry closer to the point of injury.

This study specifically focused on pain management during transport from the point of injury to Role 2 facilities. Given the intrinsic capabilities of Role 2 facilities (e.g., laboratory, radiology, and sometimes surgeons), only care provided before Role 2 arrival was regarded as "prehospital."[21] Role 2 facilities treat U.S. military, non-U.S. military, and host nation civilians. All patients treated at Role 2 facilities in Afghanistan from October 1, 2005 to June 5, 2018 were initially eligible for analysis. For the primary analysis, we included patients with (1) an abbreviated injury scale (AIS) score greater than 1 in any of the six injury severity score (ISS) body regions and (2) a transport time less than or equal to 1 day.

Patient demographics included age, gender, and affiliation (Afghanistan forces [AFG], U.S. military [USM], non-U.S. coalition military [NUSM], or civilian/other [C/O]). Patient injury characteristics included classification of injury (battle versus non-battle injury), type of injury (penetrating, blunt, burn, or other), ISS, and maximum AIS for each ISS body region (head or neck, face, chest, abdominal or pelvic contents, extremities or pelvic girdle, and external/skin). ISS was calculated using the sum of squares of the three highest AIS scores in three separate ISS body regions. Vital signs (temperature, pulse, respiratory rate, systolic blood pressure, oxygen saturation, Glasgow coma scale [GCS], and shock index) were collected in the prehospital environment. Patient disposition was the status of patients upon discharge from the Role 2 facility.

Primary Analysis: Combat Analgesia Trends

In the primary analysis, study groups were stratified by receipt of pain management. Pain management meant that the patient's documentation noted administration of analgesia, paralytics, or sedatives at the point of injury, Role 1, or during transport to Role 2. Documented analgesia included acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), fentanyl, ketamine, morphine sulfate, hydrocodone, hydromorphone, oxycodone, and tramadol. NSAIDs included acetylsalicylic acid, "combat pill pack" (Combat Wound Medication Pack, which contains meloxicam and acetaminophen, as well as the antibiotic moxifloxacin), diclofenac, ibuprofen, ketorolac, meloxicam, and naproxen.[24] Paralytics included rocuronium, succinylcholine, and vecuronium. Sedatives included etomidate, propofol, lorazepam, and midazolam.

Subgroup Analysis 1: Pain Management Without Clear Contraindication

Patients included in the primary analysis subsequently qualified for a subgroup analysis intended to identify patients who required pain management without clear contraindication. No data element was available to explicitly identify patients who may have contraindicated pain management, so prehospital vital signs (i.e., shock index $\leq$1 and GCS $\geq$14) served as a proxy to create the study group of "stable wounded." Although these exclusion criteria were regarded as likely to exclude ketamine administrations by deliberately precluding those with evidence of shock, the purpose was to isolate a group of casualties maximally likely to receive analgesia for comparison with previous analyses. In the "stable wounded" analysis, study groups were stratified by TCCC-recommended medications (NSAIDs, fentanyl, ketamine, and morphine) to demonstrate medication selection patterns among a group most likely to have analgesia indications and having fewer contraindications within the data afforded by the registry.

Subgroup Analysis 2: Ketamine Administration Comparison

To determine whether there may be systematic inconsistencies in the administration of battlefield prehospital analgesia, an exploratory analysis was conducted to determine if ketamine use was higher in Afghanistan force patients after frequency matching these patients to non-Afghanistan force patients on the following factors: Injury type (penetrating, burn, blunt); age group ($\leq$18, 19-30, 31-40, >40 years); maximum AIS among all six ISS body regions[1–6]; need for a prehospital procedure requiring analgesia; and shock risk. The need for a procedure requiring analgesia use was defined as having documentation of an airway, fracture stabilization, tourniquet, or ventilation. To determine shock risk, we dichotomized patients by receipt of any prehospital blood, receipt of >1 L of prehospital fluid, or a prehospital shock index $\geq$0.9 versus none of those treatments/conditions. Unique combinations of these five matching factors created the stratum.

Only patients injured after 2011 were eligible for the exploratory analysis, as that was the year ketamine use began to increase. Patients with prehospital procedures that contraindicated ketamine use (i.e., Cardiopulmonary Resuscitation, pericardiocentesis, or thoracotomy) were excluded from this exploratory analysis, as they did not have the opportunity to receive the outcome variable. Only patients with non-missing values for the five matching factors were included in the exploratory analysis.

Statistical Analysis

Descriptive statistics were used. To answer the primary objective (i.e., primary analysis and subgroup analysis 1), differences between study groups were determined using χ^2, Fisher's exact, and analysis of variance tests as appropriate; significance was set at $P < .05$. For the exploratory analysis (i.e., subgroup analysis 2), multilevel mixed-effects logistic regression was used; the fixed-effects model included ketamine use as the dependent variable and patient affiliation (Afghanistan force versus not) as the independent variable, although the random-effect model equation included stratum. As a sensitivity analysis, another logistic regression was repeated, but the dependent variable was changed to ketamine use or the use of etomidate, propofol, fentanyl, or morphine as patients who received these other medications may not have had the opportunity to receive ketamine, which would bias our results. This analysis was conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC) and Stata version 15.1 (StataCorp).

Ethics

This analysis was conducted as part of a study using secondary analyses of de-identified data from the DoDTR. The study was reviewed and approved using expedited procedures by the U.S. Army Medical Research and Development Command Institutional Review Board.

RESULTS

Primary Analysis: Combat Analgesia Trends

A total of 8,134 trauma patients were recorded in the DoDTR across the period of October 2005 through June 2018 meeting the inclusion criteria, of whom 2,402 (29.5%) received documented prehospital analgesia (Table I). The median age of casualties was 25 (interquartile range [IQR] 21-30), and they were generally male (7,798 [95.9%]). Documented prehospital analgesia administration followed unbalanced proportions across national affiliation groups (AFG 53.0% [576/1,087] of casualties received analgesia, USM 31.9% [912/2,855], C/O 23.3% [615/2,642], and NUSM 19.3% [299/1,550]), battle injuries (31.0% [1,979/6,382] battle versus 25.0% [423/1,692] non-battle), and wound type (penetrating 33.4% [1,721/5,147], blunt 22.3% [615/2,761], and burn 32.0% [66/206]). A minority of patients who died before or at Role 2 had documented analgesia (23.3% [87/374] versus survivors 29.8% [5,444/7,759]). While in terms of the global ISS, those who received analgesia had a statistically higher median score (analgesia patients had a median score of 13, those without analgesia 10); for most AIS regions, there was not a statistical difference in injury severity between casualties who received analgesia and those who did not. Proportions of casualties receiving documented pain medication generally increased throughout the study period (Fig. 1). There were nine (0.4%) instances of adverse drug reactions documented among the 2,402 patients who received analgesia of interest;

TABLE I. Demographics, Injury Characteristics, and Disposition of Study Patients by Medication Status ($N = 8{,}134$)

	Total		Pain management		None		
	n	%	*n*	%	*n*	%	*P*-value
Total population	8,134	100.0	2,402	29.5	5,732	70.5	<.0001
Age							.0004
No. of patients with non-missing data	8,130	100.0	2,401	100.0	5,729	99.9	
Median (IQR)	25	21, 30	25	21,30	25	21,30	
Gender							.0003
No. of patients with non-missing data	8,134	100.0	2,402	100.0	5,732	100.0	
Male	7,798	95.9	2,332	97.1	5,466	95.4	
Patient affiliation							<.0001
No. of patients with non-missing data	8,134	100.0	2,402	100.0	5,732	100.0	
U.S. military	2,855	35.1	912	38.0	1,943	33.9	
Afghanistan forces	1,087	13.4	576	24.0	511	8.9	
Non-U.S. military	1,550	19.1	299	12.4	1,251	21.8	
Civilian/other	2,642	32.5	615	25.6	2,027	35.4	
Classification of injury							<.0001
No. of patients with non-missing data	8,074	99.3	2,402	100.0	5,672	99.0	
Battle	6,382	79.0	1,979	82.4	4,403	77.6	
Type of injury							<.0001
No. of patients with non-missing data	8,120	99.8	2,402	100.0	5,718	99.8	
Penetrating	5,147	63.4	1,721	71.6	3,426	59.9	
Blunt	2,761	34.0	615	25.6	2,146	37.5	
Burn	206	2.5	66	2.7	140	2.4	
Other	6	0.1	0	0.0	6	0.1	
Discharge status							.0088
No. of patients with non-missing data	8,133	100.0	2,402	100.0	5,731	100.0	
Died	374	4.6	87	3.6	287	5.0	
ISS							<.0001
No. of patients with non-missing data	8,134	100.0	2,402	100.0	5,732	100.0	
Median (IQR)	10	6, 17	13	9,21	10	5,17	
Maximum AIS by the ISS body region—head or neck							.9611
No. of patients with non-missing data	3,579	44.0	1,015	42.3	2,564	44.7	
Median (IQR)	2	2, 3	2	2,3	2	2,3	
Maximum AIS by the ISS body region—face							.0393
No. of patients with non-missing data	2,367	29.1	796	33.1	1,571	27.4	
Median (IQR)	2	1, 2	2	1,2	2	1,2	
Maximum AIS by the ISS body region—chest							.0749
No. of patients with non-missing data	2,149	26.4	705	29.4	1,444	25.2	
Median (IQR)	3	2, 3	3	2,3	3	2,3	
Maximum AIS by the ISS body region—abdominal or pelvic contents							.1037
No. of patients with non-missing data	2,180	26.8	726	30.2	1,454	25.4	
Median (IQR)	2	2, 3	2	2,3	2	2,3	
Maximum AIS by the ISS body region—extremities or pelvic girdle							<.0001
No. of patients with non-missing data	4,803	59.0	1,596	66.4	3,207	55.9	
Median (IQR)	3	2, 3	3	2,3	3	2,3	
Maximum AIS by ISS the body region—external							<.0001
No. of patients with non-missing data	5,691	70.0	1,862	77.5	3,829	66.8	
Median (IQR)	1	1, 1	1	1,1	1	1,1	

Abbreviations: AIS, abbreviated injury scale; ISS, injury severity score; IQR, interquartile range.

the character of reaction was indeterminate in the constraints of the registry.

Subgroup Analysis 1: Pain Management Without Clear Contraindication

Of the 2,402 patients who received analgesia, only 569 had documented prehospital vital signs consistent with inclusion/exclusion criteria for the "stable wounded" cohort, as described in our methods. In this group, between 2006 and 2018, 58.7% (334/569) received documented prehospital analgesia, ranging from 41.7% to 72.7% by year (Fig. 2). Morphine was the most common documented analgesic (149/569 instances, 26.2%), followed closely by fentanyl (139/569, 24.4%) (Table II). Fentanyl surpassed morphine as the most administered medication beginning in 2012. The median age of those receiving ketamine was markedly higher, at 30 years old versus 23 (NSAIDs) to 26 (fentanyl). A higher proportion of AFG casualties received ketamine (13.9% [16/115]) as

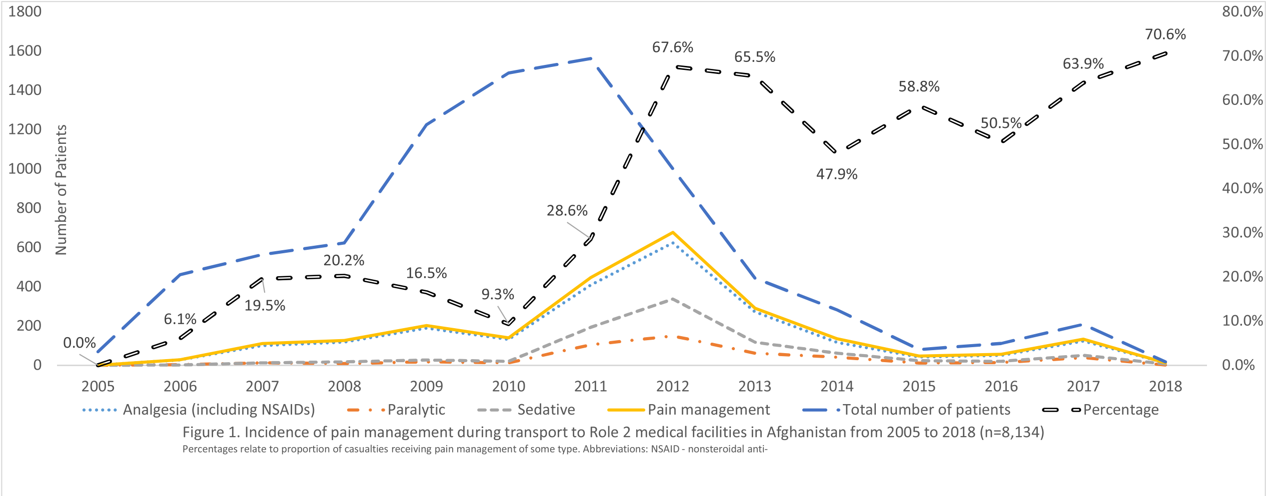

FIGURE 1. Incidence of pain management during transport to Role 2 medical facilities in Afghanistan from 2005 to 2018 ($n = 8,134$). Percentages relate to proportion of casualties receiving pain management of some type. Abbreviations: NSAID - nonsteroidal anti.

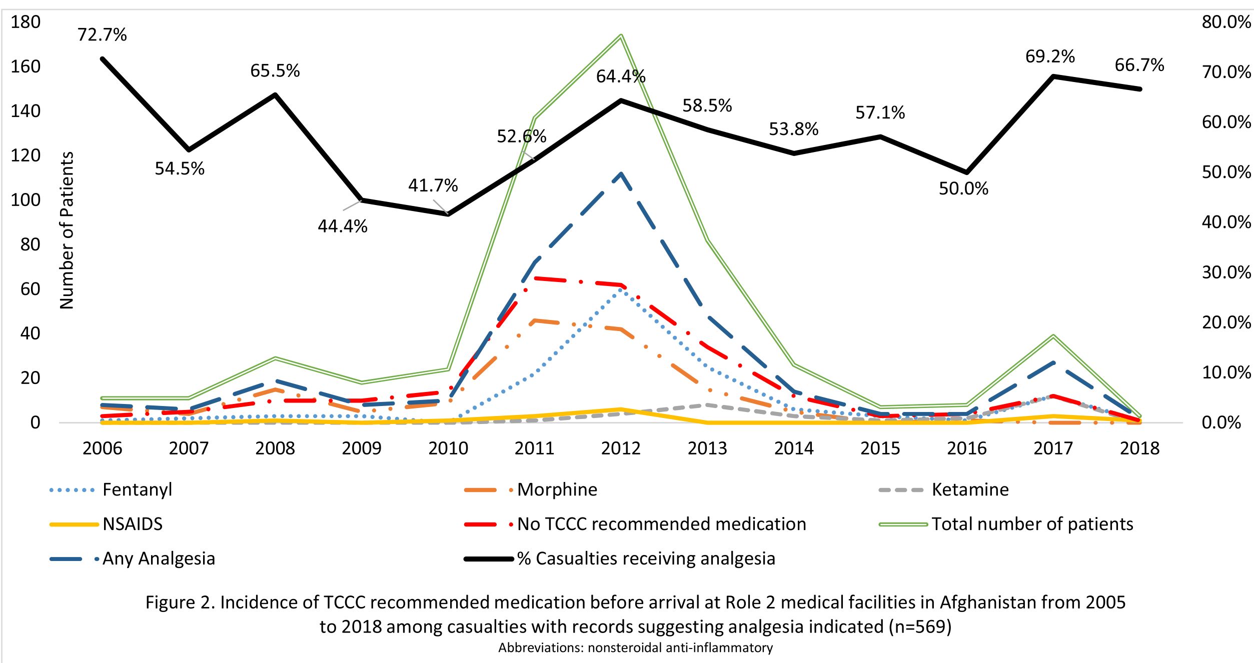

FIGURE 2. Incidence of TCCC-recommended medication before arrival at Role 2 medical facilities in Afghanistan from 2005 to 2018 among casualties with records suggesting analgesia indicated ($n = 569$). Abbreviations: NSAID, nonsteroidal anti-inflammatory drug; TCCC, Tactical Combat Casualty Care.

compared with other affiliation groups (USM 4.8% [13/270], C/O 1.7% [2/118], and NUSM 0.0% [0/66]), and the ketamine was predominantly administered between 2011 and 2013 and in 2017 (Fig. 2). AFG casualties also more frequently received fentanyl (44/115, 38.2%) than other groups. Conversely, AFG casualties were least likely to receive no TCCC analgesia in this subgroup; only 22.6% (26/115) of these casualties received no documented TCCC analgesic, compared with NUSM 40.9% (27/66), USM 46.3% (125/270), or C/O 48.3% (57/118). Of the 11 casualties in this group with burn injuries, 9 received some TCCC analgesia (81.8%), although 61.3% (223/364) of those with penetrating injuries and 52.6% (102/194) of casualties with blunt injuries received TCCC analgesia. In this subgroup with lower prehospital shock index and higher GCS scores, there were only two documented adverse drug reactions (0.4%) and ultimately only four deaths (2.3%).

When paralytics were given, the majority of the time fentanyl was a co-administered medication (62.5% [20/32]), and fentanyl was often co-administered with sedative medications as well (61.5% [48/78]) (Table S1). Among this cohort of those for whom prehospital data was suggestive of

TABLE II. Incidence of TCCC recommended medication before arrival at Role 2 medical facilities in Afghanistan from 2005 to 2018 among casualties with records suggesting analgesia indicated ($n = 569$). Abbreviations: nonsteroidal anti-inflammatory.

	Total		Fentanyl		Morphine		Ketamine		NSAIDs		No TCCC-recommended medication		
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*P*-value
Total population	569	100.0	139	24.4	149	26.2	31	5.4	15	2.6	235	41.3	<.0001
Age													.0059
No. of patients with non-missing data	569	100.0	139	100.0	149	100.0	31	100.0	15	100.0	235	100.0	
Median (IQR)	25	22,30	26	22, 30	25	22, 30	30	24, 32	23	21, 27	25	21, 27	
Gender													.8785
No. of patients with non-missing data	569	100.0	139	100.0	149	100.0	31	100.0	15	100.0	235	100.0	
Male	559	98.2	137	98.6	147	98.7	31	100.0	15	100.0	229	97.4	
Patient affiliation													<.0001
No. of patients with non-missing data	569	100.0	139	100.0	149	100.0	31	100.0	15	100.0	235	100.0	
U.S. military	270	47.5	56	40.3	67	45.0	13	41.9	9	60.0	125	53.2	
Afghanistan forces	115	20.2	44	31.7	27	18.1	16	51.6	2	13.3	26	11.1	
Non-U.S. military	66	11.6	15	10.8	23	15.4	0	0.0	1	6.7	27	11.5	
Civilian/other	118	20.7	24	17.3	32	21.5	2	6.5	3	20.0	57	24.3	
Classification of injury													.0040
No. of patients with non-missing data	569	100.0	139	100.0	149	100.0	31	100.0	15	100.0	235	100.0	
Battle	445	78.2	120	86.3	111	74.5	24	77.4	7	46.7	183	77.9	
Type of injury													<.0001
No. of patients with non-missing data	569	100.0	139	100.0	149	100.0	31	100.0	15	100.0	235	100.0	
Penetrating	364	64.0	107	77.0	94	63.1	19	61.3	3	20.0	141	60.0	
Blunt	194	34.1	25	18.0	54	36.2	11	35.5	12	80.0	92	39.1	
Burn	11	1.9	7	5.0	1	0.7	1	3.2	0	0.0	2	0.9	
Discharge status													.8682
No. of patients with non-missing data	569	100.0	139	100.0	149	100.0	31	100.0	15	100.0	235	100.0	
Died	4	0.7	1	0.7	2	1.3	0	0.0	0	0.0	1	0.4	
ISS													.0
No. of patients with non-missing data	569	100.0	139	100.0	149	100.0	31	100.0	15	100.0	235	100.0	
Median (IQR)	9	5,14	10	6,17	9	5,12	9	5,14	5	4,9	9	5,13	

Abbreviations: AIS, abbreviated injury scale; NSAIDs, nonsteroidal anti-inflammatory drugs; TCCC, Tactical Combat Casualty Care.

analgesia indication without clear contraindication, there was no statistically significant difference between TCCC analgesia medications in terms of shock index, pulse, systolic blood pressure, respiratory rate, oxygen saturation, temperature, or GCS.

Subgroup Analysis 2: Ketamine Administration Comparison

Two hundred seventy-eight AFG casualties met the exploratory analysis eligibility criteria. There were 13 AFG who were unable to be matched, leaving 265 AFG matched to 497 non-AFG. Unique combinations of the five matching factors for these 762 patients resulted in 55 strata. The ratio of the matched non-AFG to the AFG per stratum ranged from 0.25 to 18 with a median ratio of 1.75. In the non-AFG group, patient count ranged from 1 to 37 with a median of five patients per stratum. In the AFG group, patient count ranged from 1 to 32 with a median of three patients per stratum.

In the exploratory multilevel mixed-effects model among the 762 matched study patients, an association of ketamine use with patient affiliation was statistically significant ($P = .001$). The odds ratio for ketamine use was 1.84 (95% CI, 1.30-2.61) for the AFG (81 instances of ketamine use among 265) versus the matched non-AFG (95 instances of ketamine use among 497).

In the sensitivity analysis, the association of ketamine or other medication use (etomidate, propofol, fentanyl, or morphine) with patient affiliation remained statistically significant ($P < .001$). The odds ratio for ketamine or other medication use was 2.60 (95% CI, 1.73-3.89) for the AFG (225 instances of ketamine or other medication use among 265) versus the matched non-AFG patients (339 instances of ketamine or other medication use among 467).

DISCUSSION

The present analysis of combat prehospital analgesia administration demonstrates trends both somewhat reassuring and problematic within combat casualty care, which require closer scrutiny. Only 29.5% of the DoDTR casualties in our study for whom there are prehospital data available received prehospital pain management over the entire period of study. However, positively, the DoDTR reflects increasing proportions of combat casualties receiving some type of prehospital analgesia from zero in 2005 (this almost certainly reflects deficiencies in documentation practices and lack of granularity at this early point in the database) to a high of 70.6% in 2018 (low-tempo at that late stage and with documentation practices long implemented). Notable is the rapid increase from 9.3% to 67.6% from 2010 to 2012. In isolation, this trend may illustrate a dual effort in both improving prehospital documentation and increasing attention to prehospital analgesia benefited by new options, culminating in the revision of the TCCC guidelines.[4] We attempted to examine this, ideally to determine more valid proportions of administered analgesia in combat casualty care.

To confidently assess prehospital analgesia trends, remove the ongoing issue of missing prehospital documentation, as well as remove the component of clinical status/procedural needs precluding TCCC-recommended analgesia, we defined a cohort of those with a higher GCS and demonstrable injury but without elevated prehospital shock index scores. The average proportion of 58.7% who received prehospital analgesia in our cohort is notably higher than those previously reported by Maddry et al (8.7%) or Kotwal et al (16.4%) and slightly higher than Robinson (53%).[8,17,25] The latter study examined only 49 casualties in 2013 with excellent documentation as that was material to the other efforts of the work and thus reasonably fits near the middle of our annual range. As further corroboration, a 2011 report on the 75th Ranger regiment featured an aggregate of 100% net documentation and demonstrated that 54% of trauma casualties received some type of prehospital analgesia.[26] This would seem to suggest that the primary improvement seen in proportions of recorded prehospital pain medication may be attributable to improved documentation quality as opposed to a paradigm shift in prioritization of analgesia among other care issues; improving documentation should be a continual effort—as stated by Gerhardt, "absence [of adequate documentation] is tantamount to substandard care."[19] We recognize that not all of the current TCCC medications were in wide use early in the Afghanistan conflict; however, morphine represented a significant fraction of early analgesia and remained a TCCC-approved medication despite a noted decline in utilization in our cohort. Completeness and validity of documentation is an issue that has been well described elsewhere; improvements seen over the course of the recent conflicts will hopefully be retained, avoiding a comparable "Walker dip" (phenomenon wherein quality of casualty care falls between wars/conflicts) in casualty care data.[8,27,28] The benefits of maintaining high performance in prehospital documentation from the very beginning of the next conflict would include continuity of care on and near the battlefield, improving the quality of available data for casualty care research and guideline development, and ultimately facilitating granular assessment of disability claims for wounded service members.[29] Automating prehospital vital sign collection, as with the Army's Medical Hands-free Unified Broadcast System, would represent a significant leap forward in documentation, research capability, and real-time resource requirements.[30]

As described above, our previous work suggested inconsistencies in how combat casualty care is applied, and a similar inconsistency in prehospital analgesia administration was also suggested here.[21] Without the capacity to evaluate individual cases as they developed, determining the reasons for this observation is difficult. Our consensus is that this discrepancy is likely multifactorial: Cultural differences, language barriers, possible tolerance issues, and risk reduction for safe transport from the point of injury by U.S. forces. A 2004 study describing the excess propensity of English-speaking providers to intubate Spanish-speaking patients illustrated a similar situation in that language barriers and cultural differences may have resulted in aggressive and unnecessary medical management, and Hewes' 2018 work reported a systematic racial disparity in the provision of analgesia.[22,31] U.S. personnel, or other English-speaking military allies, may not have received ketamine due in part to the TCCC providers' ability to accurately assess the combat wounded's pain level and identify their goals of care. The use of analgesic medications that also have a sedating effect to decrease the risk from an agitated or combative patient to the care team or the patient themselves is also well established.[32] Combat wounded may be suffering from life-threatening injuries causing or coinciding with their mental status changes. Rapid sedation combined with chemical restraint is an essential component of the treatment to prevent morbidity and mortality in these patients.[33] The impetus toward this treatment strategy is also likely stronger in a combat zone as the risk of "Green-on-Blue" violence (assaults by putative allies) has been reported.[34] Given how integrated opiates are in the Afghan economy and life, there may have been increased tolerance to opiates among the AFG forces; a 2012 analysis of Afghan police found 15.5% positive for active opiate use.[35,36]

Despite our attempt to adequately match Afghan casualties with other patients based on clinically relevant characteristics, it is possible they remained systematically different in some unaccounted-for way, meriting a higher proportion of ketamine administration despite equivalent levels of shock risk, injury severity, or procedural requirements. However, the odds of AFG receiving ketamine was almost double that of non-AFG and was robust (stronger) in sensitivity analysis, suggesting that the phenomenon is genuine. If present, the rationale should be explored at the guideline level, as not all prehospital analgesia is equal from psychological standpoints, in addition to long-held hemodynamic concerns. We suspect that a language barrier and cultural differences may have inadvertently resulted in the TCCC provider mistakenly interpreting the pain level of the AFG combat wounded as higher than a similarly wounded U.S. or English-speaking non-U.S. combat casualty, necessitating a more aggressive analgesic treatment strategy. The current and previous TCCC guidelines vaguely describe pain levels as indications for the various analgesic modalities, but without a validated pain scale as a component of the patient's assessment. Future TCCC iterations may consider the addition of a standardized pain scale tool, such as a visual analog scale or a numerical rating scale, to remain consistent with current U.S. prehospital analgesia protocols for the administration of opioid and non-opioid medications.[37] Further consideration in prolonged conflicts may include cultural consideration and language-barrier tools for the assessment of high probability non-English-speaking combat casualties. Overall, we contend that the systematic application of best practices is the objective of quality casualty care, and inconsistencies should be scrutinized to find opportunities for improvement.

As for future, multidomain, large-scale combat operations, analgesic impact on the ability to continue warfighter tasks will become more critical. Although one well-controlled and battlefield-relevant study found little difference between low-dose intramuscular ketamine and morphine on performance impact, few data exist to guide a compassionate but mission-focused medic; more research focused on the battlefield-relevant impact of analgesics on warfighter performance would be welcome.[38]

LIMITATIONS

This is a retrospective study using data inconsistently entered during the early phases of casualty care, a period known for inconsistent documentation.[39] As discussed above, the DoDTR does not yet have a uniform caliber of prehospital data across all periods, and may never, given the on-the-ground trends of documentation across the span of conflict. The interconnectivity between clinical severity, care rendered, time of transport, and documentation quality creates a system of bias for which it is difficult to account. Although we attempted to do so by examining smaller groups of patients with specific parameters and other factors suggesting higher-quality documentation, it remains possible that some proportion of patients received undocumented analgesia. Patients may also have received analgesia from non-U.S. personnel (e.g., Afghan allies) before transport by U.S. forces, increasing the possibility that culturally unique training and customs may have influenced patterns of pain treatment. Given the heavy influence of U.S. personnel on training Afghan allies, we view it as unlikely to account for the full observed disparity.

CONCLUSION

In DoDTR data pertaining to combat operations in Afghanistan, there were several systematic disparities regarding the administration of analgesic medications. We again observe heterogeneity of care afforded to different patient groups in the prehospital environment; such phenomena merit further research to identify opportunities to implement best practices where they may be lacking. Optimal analgesia might be served by the inclusion of a standardized pain scale in TCCC documentation, consistent with civilian prehospital standards. The prevalence of missing prehospital data remains an issue for retrospective military casualty research; the automation of vital sign collection would represent a tremendous advance in combat casualty care and subsequent research. Examinations of analgesic administration trends in the military prehospital space could improve future research, training, therapeutics development, and treatment algorithms.

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SUPPLEMENTARY MATERIAL

Supplementary material is available at *Military Medicine* online.

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CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Lee RE, Zweifach BW: Vasodepressor responses to morphine following hemorrhagic hypotension. Am J Physiol Legacy Content 1949; 157(2): 259–64.
2. Thompson PI, Joel SP, John L, Wedzicha JA, Maclean M, Slevin ML: Respiratory depression following morphine and morphine-6-glucuronide in normal subjects. Br J Clin Pharmacol 1995; 40(2): 145.
3. Brook K, Bennett J, Desai SP: The chemical history of morphine: an 8000-year journey, from resin to de-novo synthesis. J Anesth Hist 2017; 3(2): 50–5.
4. Butler FK, Kotwal RS, Buckenmaier CC 3rd, et al: A triple-option analgesia plan for Tactical Combat Casualty Care: TCCC guidelines change 13-04. J Spec Oper Med 2014; 14(1): 13–25.
5. De Rocquigny G, Dubecq C, Martinez T, et al: Use of ketamine for prehospital pain control on the battlefield: a systematic review. J Trauma Acute Care Surg 2020; 88(1): 180–5.
6. Schauer SG, Mora AG, Maddry JK, Bebarta VS: Multicenter, prospective study of prehospital administration of analgesia in the US combat theater of Afghanistan. Prehosp Emerg Care 2017; 21(6): 744–9.
7. Schauer SG, Robinson JB, Mabry RL, Howard JT: Battlefield analgesia: TCCC guidelines are not being followed. J Spec Op Med 2015; 15(1): 85.
8. Robinson JB, Smith MP, Gross KR, et al: Battlefield documentation of Tactical Combat Casualty Care in Afghanistan. US Army Med Dep J 2016; (2–16): 87–94.
9. Holbrook TL, Galarneau MR, Dye JL, Quinn K, Dougherty AL: Morphine use after combat injury in Iraq and post-traumatic stress disorder. N Engl J Med 2010; 362(2): 110–7.
10. Melcer T, Walker J, Sechriest VF 2nd, Lebedda M, Quinn K, Galarneau M: Glasgow Coma Scores, early opioids, and posttraumatic stress disorder among combat amputees. J Trauma Stress 2014; 27(2): 152–9.
11. Mion G, Le Masson J, Granier C, Hoffmann C: A retrospective study of ketamine administration and the development of acute or post-traumatic stress disorder in 274 war-wounded soldiers. Anaesthesia 2017; 72(12): 1476–83.
12. Highland KB, Soumoff AA, Spinks EA, Kemezis PA, Buckenmaier CC 3rd: Ketamine administration during hospitalization is not associated with posttraumatic stress disorder outcomes in military combat casualties: a matched cohort study. Anesth Analg 2020; 130(2): 402–8.

13. Zietlow J, Berns K, Jenkins D, Zietlow S: Prehospital use of ketamine: effectiveness in critically ill and injured patients. Mil Med 2019; 184(Suppl 1): 542–4.
14. Hollis GJ, Keene TM, Ardlie RM, Caldicott DG, Stapleton SG: Prehospital ketamine use by paramedics in the Australian Capital Territory: a 12 month retrospective analysis. Emerg Med Australas 2017; 29(1): 89–95.
15. Losvik OK, Murad MK, Skjerve E, Husum H: Ketamine for prehospital trauma analgesia in a low-resource rural trauma system: a retrospective comparative study of ketamine and opioid analgesia in a ten-year cohort in Iraq. Scand J Trauma Resusc Emerg Med 2015; 9(23): 94.
16. Mann-Salinas EA, Le TD, Shackelford SA, et al: Evaluation of role 2 (R2) medical resources in the Afghanistan combat theater: initial review of the joint trauma system R2 registry. J Trauma Acute Care Surg 2016; 81(5 Suppl 2 Proceedings of the 2015 Military Health System Research Symposium): S121–7.
17. Kotwal RS, Staudt AM, Trevino JD, et al: A review of casualties transported to role 2 medical treatment facilities in Afghanistan. Mil Med 2018; 183(suppl_1): 134–45.
18. Gerhardt RT, Reeves PT, Kotwal RS, Mabry RL, Robinson JB, Butler F: Analysis of prehospital documentation of injury-related pain assessment and analgesic administration on the contemporary battlefield. Prehosp Emerg Care 2016; 20(1): 37–44.
19. Schauer SG, Naylor JF, April MD, Fisher AD, Bynum J, Kotwal RS: 16 years of role 1 trauma care: a descriptive analysis of casualties within the prehospital trauma registry. Med J US Army Med Center Excellence (MedCoE) 2021: 44–9.
20. Schauer SG, Naylor JF, Maddry JK, Hinojosa-Laborde C, April MD: Trends in prehospital analgesia administration by US forces from 2007 through 2016. Prehosp Emerg Care 2019; 23(2): 271–6.
21. Hudson IL, Blackburn MB, Staudt AM, Ryan KL, Mann-Salinas EA: Analysis of casualties that underwent airway management before reaching role 2 facilities in the Afghanistan conflict 2008-2014. Mil Med 2020; 185(Suppl 1): 10–8.
22. Hewes HA, Dai M, Mann NC, Baca T, Taillac P: Prehospital pain management: disparity by age and race. Prehosp Emerg Care 2018; 22(2): 189–97.
23. Joint Trauma System: (Updated 13MAY2021). Registries - Joint Trauma System. JTS. Available at https://jts.amedd.army.mil/index.cfm/data/registries; accessed December 29, 2020.
24. Schauer SG, Naylor JF, Ahmed YM, Maddry JK, April MD: Prehospital combat wound medication pack administration in Iraq and Afghanistan: a Department of Defense Trauma Registry Analysis. J Spec Oper Med 2020; 20(3): 76–80.
25. Maddry JK, Mora AG, Savell S, Reeves LK, Perez CA, Bebarta VS: Combat MEDEVAC: a comparison of care by provider type for en route trauma care in theater and 30-day patient outcomes. J Trauma Acute Care Surg 2016; 81(5Suppl 2 Proceedings of the 2015 Military Health System Research Symposium): S104–10.
26. Kotwal RS, Montgomery HR, Kotwal BM, et al: Eliminating preventable death on the battlefield. Arch Surg 2011; 146(12): 1350–8.
27. Eastridge BJ, Mabry RL, Blackbourne LH, Butler FK: We don't know what we don't know: prehospital data in combat casualty care. US Army Med Dep J 2011; 11–5.
28. Knudson MM: A perfect storm: 2019 scudder oration on trauma. J Am Coll Surg 2020; 230(3): 269–82.
29. Chase RP, Nevin RL: Population estimates of undocumented incident traumatic brain injuries among combat-deployed US military personnel. J Head Trauma Rehabil 2015; 30(1): E57–64.
30. Patil S, Cholewcynski A, Krohn E, et al: Developmental test and evaluation of medical hands-free unified broadcast system. In: Presented at Military Health Systems Research Symposium. August 19-22, 2019, Kissimmee, Florida.
31. Bard MR, Goettler CE, Schenarts PJ, et al: Language barrier leads to the unnecessary intubation of trauma patients. Am Surg 2004; 70(9): 783–6.
32. Riddell J, Tran A, Bengiamin R, Hendey GW, Armenian P: Ketamine as a first-line treatment for severely agitated emergency department patients. Am J Emerg Med 2017; 35(7): 1000–4.
33. Kitch BB: Out-of-hospital ketamine: review of a growing trend in patient care. J Am Coll Emerg Physicians Open 2020; 1(3): 183–9.
34. Shortland N, Nader E, Sari H, Palasinski M, Hilland C: Murder on Maneuver: exploring green-on-blue attacks in Afghanistan. Armed Forces Soc 2019; 45(2): 368–88.
35. Omelicheva MY, Markowitz L: Does drug trafficking impact terrorism? Afghan opioids and terrorist violence in Central Asia. Stud Conflict Terrorism 2019; 42(12): 1021–43.
36. Arfsten DP, Moralez JF 2nd, Chester LL Jr, Mohamad P, Weber TH: Drug use among the Afghanistan National Police: a national assessment. Mil Med 2012; 177(1): 85–90.
37. Gausche-Hill M, Brown KM, Oliver ZJ, et al: An evidence-based guideline for prehospital analgesia in trauma. Prehosp Emerg Care 2014; 18(Suppl 1): 25–34.
38. Gaydos SJ, Kelley AM, Grandizio CM, Athy JR, Walters PL: Comparison of the effects of ketamine and morphine on performance of representative military tasks. J Emerg Med 2015; 48(3): 313–24.
39. Mabry RL, DeLorenzo R: Challenges to improving combat casualty survival on the battlefield. Mil Med 2014; 179(5): 477–82.