Failure to Rescue after Infectious Complications in a Statewide Trauma System

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Abstract

Background: The failure to rescue (FTR) rate, the rate of death after a complication, measures a center's ability to identify and manage complications by "rescuing" vulnerable patients. Infectious complications are common after trauma, but risk factors for death after infection are not established. We hypothesized that risk factors would differ for FTR after infectious complications, development of infections, and for development of and death after non-infectious complications.

Patients and Methods: We analyzed trauma registry data for adult patients admitted to all 30 level I and II Pennsylvania trauma centers, 2011–2014. We used multivariable regression to identify risk factors for infection, non-infectious complications, failure to rescue after infection (FTR-I), failure to rescue after non-infectious complications (FTR-N), and death. We compared secondary complication patterns among patients with an index infection.

Results: Of 95,806 admitted patients, at least one complication developed in 11.2%. Among these, 33.6% had an infection as the first complication. Mortality rates were 3.7% overall, 2.8% in patients with no complications, 7.2% after infection, and 13.5% after non-infectious complications. Urinary tract infection was the most common infection (41.7%), followed by pneumonia (37.5%) and wound infection (6.9%). Risk factors for infection included higher injury severity score (ISS), poor admitting physiology, female gender, cirrhosis, dementia, history of stroke, and drug abuse. Factors associated with FTR-I included male gender (odds ratio [OR] 1.6, 95% confidence interval 1.1–1.2), older age (OR 1.04, 1.03–1.05), increased ISS, cirrhosis, chronic renal insufficiency, and use of anticoagulation or steroids.

Conclusions: Infectious complications are common in trauma patients and are an important component of FTR. Risk factors for infection and FTR-I differ and may help identify patients who may benefit from close surveillance and early intervention. Half of all FTR deaths were preceded by only a single complication, highlighting that management of this index complication, along with any secondary complications, may be a fruitful area for intervention.

ALTHOUGH TRAUMA CENTERS have been demonstrated to reduce death after injury by 25% [1], assessing the performance of individual trauma centers remains challenging. Accurate measurement of quality of care is critical to ongoing improvement in trauma care. Likewise, as outcome metrics increasingly inform reimbursement, more accurate measurement is crucial [2,3]. Whereas death is the most reliably measured outcome, progression of injury causes many trauma deaths, and relying on even risk-adjusted mortality

rates may inappropriately penalize centers caring for high-risk populations with disproportionately severe injuries.

Complication rates are not always correlated with mortality rates and may contribute additional insights into quality of care [4]. Centers may make diagnoses and report complications differently, however, biasing this metric [5]. Moreover, complications have been shown to be strongly related to non-modifiable patient characteristics and as such may not represent optimal targets for improving clinical care [6,7].

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Failure to rescue (FTR) aims to combine the strengths of measuring mortality and complication rates and may be of particular relevance in the trauma population. FTR is defined as death following a complication [8] and has been shown to correlate better than complication rates with in-hospital mortality rates across many surgical disciplines [6,9,10]. FTR is also more closely associated with institutional characteristics that are likely to influence quality of care, such as nurse-to-bed ratios, hospital technology, and physician board certification, and less associated with patient characteristics such as age and co-morbidities [11,12].

Whereas FTR rates vary between trauma centers [13], this finding alone does not identify opportunities for improvement in care. The failures of care resulting in FTR may differ from patient to patient and from center to center [3], particularly in trauma, because patient characteristics and injury characteristics are heterogeneous [13,14]. Given that infections are common after injury [15,16], we set out to describe FTR after infection (FTR-I), the fractional contribution of infectious complications to FTR rates. We grouped patients according to whether their first complication was infectious or non-infectious and examined rates of and risk factors for FTR in both groups.

Patients and Methods

Setting and population

We identified adult patients admitted to level I and II trauma centers in Pennsylvania (n=30) from 2011 to 2014 using the Pennsylvania Trauma Outcomes Study (PTOS) registry. PTOS includes all patients admitted for ≥ 48 hours or ≥ 36 hours with an injury severity score (ISS) ≥ 9 ; all intensive care unit (ICU) and step-down unit admissions; all deaths (regardless of duration of admission); and all transfers. PTOS excludes patients with isolated hip fractures and injuries from drowning, poisoning, asphyxiation, or in-hospital injury [17]. We further excluded patients who died in or were discharged from the emergency department (ED) or whose primary mechanism of injury was burn. Patients who were transferred out of the trauma center were excluded, because their outcomes could not be determined. Patients transferred in from another institution were included at the receiving center. In addition to injury diagnoses, co-morbidities, and demographics, the PTOS registry records the diagnosis and date of each complication.

The PTOS registry is maintained by the Pennsylvania Trauma Systems Foundation (PTSF), the accrediting body for trauma centers in Pennsylvania. Each Pennsylvania trauma center retains trained coders responsible for abstracting patient data for the registry. Coders use specified criteria derived from the National Trauma Data Bank in documenting complications [17,18]. Data were received with no identifying patient information. Patients were linked to trauma centers, identified only by center number. This study was performed with the permission of PTSF, which specifically disclaims responsibility for any analyses, interpretations, or conclusions. The study was deemed exempt by the University of Pennsylvania Institutional Review Board.

Statistical analysis

Patient-level outcomes of interest were development of an index infectious or non-infections complication; FTR-I; FTR

after non-infectious complications (FTR-N), and overall death. Infectious complications included pneumonia (including aspiration pneumonia), urinary tract infection (UTI), wound infection (including both traumatic wounds and surgical sites), septicemia, sepsis, soft tissue infection, empyema, sinusitis, and central nervous system (CNS) infection. PTOS uses the National Trauma Data Bank definition of pneumonia. This definition requires a combination of clinical or radiographic evidence of new chest infiltrate with a documented infectious organism in blood, tracheal or bronchial aspirate, on pathologic evaluation, or by antigen or antibody titer. Out of concern for overlapping definitions, we combined the PTOS category of pneumonia with a separate category of aspiration/aspiration pneumonia [17,18].

Complications related to burn wound healing were excluded. We evaluated co-variables including patient demographics; injury diagnoses; mechanism of injury; ISS; admission Glasgow Coma Scale (GCS) score, revised trauma score (RTS), and systolic blood pressure (SBP); and co-morbidities. For transferred patients, vital signs at admission to the referring hospital were used. We evaluated all co-morbidities reported by PTOS. Categorical variables were compared using chi-square tests. Continuous variables were compared using the Kruskal-Wallis test.

We conducted bivariate regression analyses on candidate predictors for each outcome and included predictors with a p value of <0.2 in bivariate analysis in final multivariable regression models, along with patient age and sex. Standard errors were adjusted for clustering at the center level. We used logistic regression to evaluate risk factors for death, FTR-I, and FTR-N. Only patients in whom the relevant index complication developed were included in the analysis for FTR-I and FTR-N. Because patients in whom pneumonia developed appeared to be at particularly elevated risk of death, we conducted additional regression analysis to identify risk factors in this sub-group.

Because complications take time to develop and to be diagnosed, patients who die early in their hospital course are less likely to have a complication diagnosed. Therefore, characteristics that put patients at high risk of death may appear to be associated falsely with decreased risk of complications [19]. To avoid this bias, we evaluated the risk of complications using competing risk regression according to the method of Fine and Gray [20]. Survival time was set to 0.5 days for patients in whom the outcome developed on the day of admission. For development of infection, both death and non-infectious complications served as competing risks. For non-infectious complications, infection and death were competing risks. We compared survival time for patients according to complication type with the Kaplan-Meier method. To gain further insight into patient trajectories that might lead toward or away from FTR-I, we tabulated the frequency of each infectious complication and the frequency of secondary complications for those who died and those who survived after infection.

Results

Of 95,806 admitted patients, at least one complication developed in 10,739 (11.2%). Among patients with complications, an infection developed as their first complication in

FIG. 1. Patient population and comparison groups for failure to rescue in trauma patients. ED=emergency department; FTR-I=failure to rescue after infection; FTR-N=failure to rescue after non-infectious complications.

3609 (33.6%), and an index non-infectious complication developed in 7130 (66.4%) (Fig. 1). Among index infectious complications, UTI (41.7%) was the most common infection, followed by pneumonia (37.6%), and wound infection (6.9%), as shown in Table 1. The death rate was 3.7% overall—2.8% in patients with no complications, 11.4% in patients with any complication, 7.2% in patients with infectious complications, and 13.5% in patients with non-infectious complications. Of deaths, 34.3% were preceded by complication.

TABLE 1. INCIDENCE OF PRIMARY INFECTIONS IN TRAUMA PATIENTS

Index complication	All infection patients	Survivors	Deaths	p
				<0.001
Pneumonia	1355 (37.6)	1187 (35.4)	168 (64.9)	
Sepsis	130 (3.6)	111 (3.3)	19 (7.3)	
Bacteremia	166 (4.6)	153 (4.6)	13 (5.0)	
STI	142 (4.0)	141 (4.2)	1 (0.4)	
UTI	1505 (41.7)	1448 (43.2)	57 (22.0)	
Wound infection	249 (6.9)	248 (7.4)	1 (0.4)	
Other	62 (1.7)	62 (1.9)	0 (0)	

STI=soft tissue infection; UTI=urinary tract infection.

Table 2 summarizes patient and injury characteristics for those with no complications, non-infectious complications, and infectious complications. More than 80% of patients in each category were white. Fall was the most common mechanism of injury, occurring in approximately half of all patients. Patients in whom complications developed had more severe injuries than those who did not and were more likely to have received blood transfusions in the ED or ≥ 2 L of fluid pre-hospital.

Nearly all co-morbidities were more common in patients with complications than in those without. Most co-morbidities were more common in the non-infectious complication group, including diabetes mellitus, chronic lung disease, cardiac disease, cirrhosis, and chronic renal insufficiency ($p < 0.001$ for all). Dementia, history of stroke, functional dependency, drug use, and thyroid disease were most common in the infection group ($p < 0.001$ for all). Smoking was most common in those with non-infectious complications and least common in those with infectious complications. There were no significant differences among groups in peptic ulcer disease, psychiatric disease, attention deficit disorder, steroid use, arthritis, or history of previous traumatic brain injury.

Patients who died without a recorded complication had more severe injuries (median ISS 25, interquartile range [IQR] 14–30) than those with infectious (ISS 17, IQR 10–29) or non-infectious complications (ISS 18, IQR 10–26). They were physiologically more unstable (median RTS 4.8, IQR

TABLE 2. CHARACTERISTICS OF TRAUMA PATIENTS WITH NO COMPLICATIONS, NON-INFECTIOUS COMPLICATIONS, AND INFECTIOUS COMPLICATIONS

	<i>No complications</i> n = 85,067	<i>Non-infectious complication</i> n = 7,130	<i>Infectious complications</i> n = 3,609	p ^a
Male	49,296 (56.0)	4,699 (65.9)	2,081 (57.7)	<0.001
Age	57 (36 – 77)	62.5 (46 – 79)	58 (38 – 78)	<0.001
Race/ethnicity				0.004
White (non-Hispanic)	68,715 (82.2)	5,785 (82.4)	2,898 (82.0)	
Black (non-Hispanic)	10,202 (12.2)	915 (13.0)	441 (12.5)	
Hispanic	3,258 (3.9)	218 (3.1)	125 (3.5)	
Other	1,472 (1.8)	104 (1.5)	70 (2.0)	
Insurance				<0.001
Medicare	29,774 (35.0)	2,690 (37.6)	1,320 (36.6)	
Medicaid	12,206 (14.4)	983 (13.8)	559 (15.5)	
Private	19,951 (23.5)	1,505 (21.1)	724 (20.1)	
Uninsured/other	23,136 (27.2)	1,962 (27.5)	1,006 (27.9)	
Mechanism of injury				<0.001
Gunshot wound	2,833 (3.3)	480 (6.7)	223 (6.2)	
Cut/stab	2,204 (2.6)	114 (1.6)	38 (1.1)	
Fall	43,979 (51.7)	3,600 (50.5)	1,760 (48.8)	
Traffic	25,592 (30.1)	2,418 (33.9)	1,311 (36.3)	
Struck	3,390 (4.0)	93 (1.3)	54 (1.5)	
Other/unknown	7,069 (8.3)	425 (6.0)	223 (6.2)	
Injury severity score	9 (4 – 12)	14 (9 – 22)	14 (9 – 25)	<0.001
Moderate to severe injury to:				
Head/neck	20,670 (24.3)	2,843 (29.9)	1,666 (46.2)	<0.001
Chest	12,309 (14.5)	2,127 (29.8)	1,114 (30.9)	<0.001
Abdomen	3,278 (3.9)	766 (10.7)	419 (11.6)	<0.001
Extremities	9,162 (10.8)	1,472 (20.7)	596 (16.5)	<0.001
Co-morbidities	2 (1 – 4)	3 (1 – 4)	2 (1 – 4)	<0.001
Transfer patient	27,687 (32.6)	2,024 (28.4)	1,092 (30.3)	<0.001
Post-ED Destination				<0.001
Intensive care unit	24,080 (28.3)	3,531 (49.5)	1,887 (52.3)	
Operating room	7,896 (9.3)	1,385 (19.4)	701 (19.4)	
Ward	39,934 (15.3)	1,474 (20.7)	670 (18.6)	
Step-down unit	12,794 (15.0)	650 (9.1)	304 (8.4)	
Interventional radiology	359 (0.4)	90 (1.3)	47 (1.3)	
Revised trauma score	7.84 (7.84– 7.84)	7.84 (7.84– 7.84)	7.84 (6.9– 7.84)	<0.001
GCS on admission	15 (15 – 15)	15 (14 – 15)	15 (10 – 15)	<0.001
SBP on admission	140 (124 –158)	138 (116 –159)	138 (116 –158)	<0.001
Transfused in ED	1,824 (2.2)	809 (11.6)	339 (9.7)	<0.001
>2 L of fluid infused pre-hospital	8,058 (9.5)	1,222 (17.1)	651 (18.0)	<0.001

Continuous variables presented as median (interquartile range). Categorical variables presented as n (%).

^ap values for categorical variables from chi-square tests. p values for continuous variables from Kruskal-Wallis test.

ED=emergency department; GCS=Glasgow Coma Scale; SBP=systolic blood pressure.

2.9–7.8) than patients who died after infection (7.1, 4.1–7.8) or non-infectious complications (7.8, 6.0–7.8). Of patients who died without complications, 14.7% had firearm injuries, compared with 2.7% of patients in whom infections developed and 8.2% of patients with non-infectious complications. Head injuries were also most common in those who died without complications (74.2% vs. 65.6% for deaths after infection and 56.7% of deaths after non-infectious complications).

Figure 2 demonstrates survival time for each group. Patients who died without complications died in a median of 1.1 days (IQR 0.3–3.1). Patients with non-infectious complications died in a median of 6.3 days (IQR 2.1–11.7), whereas those with infections died after a median of 10.4 days (IQR 6.6–15.4). Likewise, the first non-infectious

complication was diagnosed in a median of three days (IQR 1–5), compared with five days (IQR 3–8) for infectious complications.

Multivariable regression results

Table 3 summarizes the results of competing risk regression analysis identifying independent predictors of infectious and non-infectious complications. Factors associated with increased hazard of infection included ISS (sub-hazard ratio [SHR] 1.01, 95% confidence interval [CI] 1.01–1.02), along with presence of moderate-severe injury to the head and neck, chest, or abdomen. Higher GCS score was associated with reduced hazard of infection (SHR 0.95, 95% CI 0.94–0.95).

TABLE 3. COMPETING RISKS REGRESSION RESULTS: INDEPENDENT RISK FACTORS FOR DEVELOPMENT OF COMPLICATIONS IN TRAUMA PATIENTS

	<i>Non-infectious complications</i>			<i>Infection</i>		
	<i>SHR</i>	<i>95% CI</i>	<i>p</i>	<i>SHR</i>	<i>95% CI</i>	<i>p</i>
Male	1.2	1.2 –1.3	<0.001	0.8	0.7 –0.9	<0.001
Age	1.01	1.01 –1.02	<0.001	1.0	1.0 –1.0	0.12
Mechanism (vs. fall)						
Gunshot wound	1.5	1.3 –1.7	<0.001	0.9	0.8 –1.1	0.48
Cut/stab	0.9	0.8 –1.1	0.52	0.6	0.4 –0.8	0.001
Traffic	1.1	1.1 –1.2	<0.001	1.0	0.9 –1.1	0.75
Struck	0.7	0.6 –0.8	<0.001	0.8	0.6 –1.0	0.10
Other/unknown	0.9	0.8 –1.0	0.15	0.9	0.7 –0.997	0.045
Injury Severity Score	1.01	1.01 –1.02	<0.001	1.01	1.01–1.02	<0.001
Moderate to severe injury (AIS ≥3):						
Head/neck	1.1	1.1 –1.2	<0.001	1.2	1.1 –1.3	<0.001
Extremities	1.5	1.3 –1.6	<0.001	0.9	0.8 –0.97	0.014
Chest	1.3	1.2 –1.3	<0.001	1.2	1.05–1.3	<0.001
Abdomen	1.3	1.1 –1.4	<0.001	1.2	1.05–1.4	0.010
GCS score on admission	0.98	0.97 –0.99	<0.001	0.95	0.94–0.96	<0.001
Transfused in ED	1.5	1.4 –1.7	<0.001	1.1	0.9 –1.2	0.31
Received >2L of fluid pre-hospital	1.2	1.1 –1.3	0.003	1.1	1.0 –1.2	0.07
Post-ED Destination (vs. ward)						
Intensive care unit	2.0	1.8 –2.1	<0.001	1.8	1.5 –2.1	<0.001
Operating room	2.1	1.9 –2.3	<0.001	1.9	1.6 –2.2	<0.001
Step-down unit	1.2	1.03 –1.4	0.021	1.2	1.1 –1.4	0.004
Interventional radiology	1.8	1.4 –2.3	<0.001	2.0	1.6 –2.4	<0.001
Number of co-morbidities						
1–2	1.0	1.0 –1.1	0.62			
≥3	1.1	1.004–1.2	0.041			
Drug abuse				1.3	1.2 –1.5	<0.001
Cirrhosis	1.5	1.3 –1.8	<0.001	1.3	1.1 –1.5	0.013
Dementia	0.8	0.7 –0.98	0.023	1.2	1.01–1.3	0.031
Stroke	1.0	0.9 –1.1	0.67	1.2	1.03–1.3	0.016
Smoking	1.2	1.1 –1.3	0.002	0.9	0.8 –1.1	0.24
Alcohol abuse	2.2	1.8 –2.5	<0.001	1.1	0.9 –1.2	0.37
Previous traumatic brain injury	1.0	0.9 –1.1	0.97	0.8	0.7 –0.9	0.010
Cancer	1.1	0.9 –1.2	0.29	0.8	0.6 –1.1	0.27
Chronic pulmonary disease	1.1	1.1 –1.2	<0.001			
Cardiac disease	1.1	1.02 –1.2	0.014			
Chronic renal disease	1.3	1.1 –1.6	<0.001			
Hypertension	1.1	1.02 –1.1	0.007			
Peripheral vascular disease	1.3	1.1 –1.5	<0.001			
Obesity	1.4	1.3 –1.6	<0.001			
Arthritis	0.9	0.8 –0.95	<0.001			

Admission blood pressure was included in both models but was not significant. Race/ethnicity, diabetes mellitus, anticoagulation, and thyroid disease were included in the model for non-infectious complications, but were not significant.

SHR=sub-hazard ratio; CI=confidence interval; AIS=abbreviated injury score; GCS=Glasgow Coma Scale; ED=emergency department.

Co-morbidities associated with development of infection included cirrhosis (SHR 1.3, 95% CI 1.1–1.5), dementia (SHR 1.2, 95% CI 1.01–1.3), history of stroke (SHR 1.2, 95% CI 1.03–1.3), and drug abuse (SHR 1.3, 95% CI 1.2–1.5).

Factors associated with development of non-infectious complications were similar, although in this case, age was an independent risk factor (SHR 1.01, 95% CI 1.01–1.02) and male gender was a positive risk factor (SHR 1.2, 95% CI 1.2–1.3). Patients who received transfusions in the ED or >2L of fluid pre-hospital had higher hazards of non-infectious complications, as did those with ≥3 or more co-morbidities. The individual co-morbidities that were independently as-

sociated with non-infectious complications also included cirrhosis, but also smoking, alcohol abuse, chronic lung disease, cardiac disease, chronic renal insufficiency, hypertension, peripheral vascular disease, and obesity. Both history of stroke and arthritis were associated with reduced hazard of non-infectious complications.

Table 4 shows multivariable logistic regression results identifying risk factors for death. Table 5 shows results for FTR-N and Table 6 shows results for FTR-I. Each table includes significant predictors for the respective outcome. Insurance status, dementia, stroke, diabetes mellitus, and peripheral vascular disease were included in all three models

TABLE 4. MULTIVARIABLE LOGISTIC REGRESSION RESULTS: INDEPENDENT RISK FACTORS FOR OVERALL MORTALITY

	<i>All deaths (n=87,461)</i>			
	<i>OR</i>	<i>95% CI</i>		<i>p</i>
Male	1.3	1.1	–1.4	<0.001
Age	1.04	1.04	–1.05	<0.001
Mechanism (vs. fall)				
Gunshot wound	3.5	2.7	–4.5	<0.001
Cut/stab	0.7	0.5	–1.1	0.16
Traffic	0.7	0.6	–0.8	<0.001
Struck	0.3	0.1	–0.6	<0.001
Other/unknown	0.7	0.5	–0.9	0.003
Injury severity score	1.1	1.1	–1.1	<0.001
Moderate to severe injury (AIS ≥3):				
Head/neck	1.3	1.2	–1.5	<0.001
Extremities	0.9	0.7	–1.0	0.11
Chest	0.8	0.7	–0.97	0.018
GCS score on admission	0.8	0.8	–0.8	<0.001
Admission SBP, per 10 mm Hg	0.96	0.94	–0.97	<0.001
Transfused in ED	2.4	2.1	–2.9	0.001
Post-ED destination (vs. ward)				
Intensive care unit	2.6	2.0	–3.3	<0.001
Operating room	3.6	2.7	–4.8	<0.001
Step-down unit	1.0	0.7	–1.2	0.73
Interventional radiology	3.4	2.0	–5.8	<0.001
Co-morbidities				
Cirrhosis	3.8	2.8	–5.2	<0.001
Smoking	0.5	0.4	–0.6	<0.001
Drug abuse	0.4	0.3	–0.6	<0.001
Cardiac disease	1.3	1.1	–1.4	<0.001
Anticoagulation	1.4	1.2	–1.6	<0.001
Chronic renal insufficiency	2.5	2.0	–3.1	<0.001
Hypertension	0.8	0.7	–0.9	0.002
DNR status	1.5	1.1	–2.0	0.005
Psychiatric disease	0.8	0.7	–0.9	0.003
Alcohol abuse	0.7	0.6	–0.9	0.010
Previous traumatic brain injury	0.7	0.5	–0.9	0.012
Cancer	1.8	1.4	–2.4	<0.001

OR=odds ratio; CI=confidence interval; AIS=abbreviated injury score; GCS=Glasgow Coma Scale; SBP=systolic blood pressure; ED=emergency department; DNR=do not resuscitate.

but were not significant in any. Thyroid disease was included in models for FTR-N and FTR-I but was not significant in either. Attention deficit disorder, moderate-to-severe abdominal injury, and pre-hospital fluid resuscitation were included in models for FTR-N and death but were not significant. Transfer status was included in the model for death but was not significant. Functional dependency, ulcer disease, and obesity were included in the model for FTR-N but were not significant.

Model performance was good to excellent for all outcomes. Area under the receiver-operator curve (AUC) for the final, multi-variable logistic regression model was 0.80 for FTR-I with a chi square value of 10.7 for the Hosmer-Lemeshow test ($p=0.22$). For FTR-N, the AUC was 0.79 with a chi square value of 8.4 for the Hosmer-Lemeshow test ($p=0.39$). For overall death, the AUC was 0.93. The Hosmer-Lemeshow statistic for this model was significant (chi

TABLE 5. MULTI-VARIABLE LOGISTIC REGRESSION RESULTS: INDEPENDENT RISK FACTORS FOR FAILURE TO RESCUE AFTER NON-INFECTIOUS COMPLICATIONS

	<i>FTR-N (n = 6,614)</i>			
	<i>OR</i>	<i>95% CI</i>		<i>p</i>
Age	1.02	1.02	–1.03	<0.001
Mechanism (vs. fall)				
GSW	1.7	1.1	–2.6	0.008
Cut/stab	0.9	0.4	–1.9	0.77
Traffic	0.8	0.7	–1.1	0.17
Struck	1.0	0.4	–2.2	0.99
Other/unknown	0.5	0.3	–0.8	0.003
Injury Severity Score	1.03	1.02	–1.04	<0.001
Moderate to severe injury (AIS ≥3):				
Head/neck	1.4	1.1	–1.7	0.003
Extremities				
Chest	0.9	0.7	–1.1	0.18
GCS score on admission	0.9	0.9	–0.9	<0.001
Admission SBP, per 10 mm Hg	0.96	0.94	–0.99	0.002
Transfused in ED	2.1	1.5	–2.9	<0.001
Post-ED destination (vs. ward)				
Intensive care unit	1.4	1.02	–1.9	0.035
Operating room	1.8	1.2	–2.6	0.002
Step-down unit	0.7	0.5	–1.1	0.17
Interventional radiology	1.6	0.8	–3.3	0.20
Number of co-morbidities				
1–2	1.1	0.8	–1.4	0.74
≥3	1.5	1.1	–2.1	0.015
Cirrhosis	2.6	1.8	–3.8	<0.001
Smoking	0.4	0.3	–0.6	<0.001
Drug abuse	0.4	0.2	–0.7	0.003
Chronic renal insufficiency	2.4	1.8	–3.2	<0.001
Hypertension	0.8	0.6	–1.0	0.016
Alcohol abuse	0.7	0.5	–0.9	0.006
Cancer	1.4	1.1	–1.9	0.016

FTR-N=failure to rescue after non-infectious complications; OR=odds ratio; CI=confidence interval; GSW=gunshot wound; AIS=abbreviated injury score; GCS=Glasgow Coma Scale; SBP=systolic blood pressure; ED=emergency department.

square=39.8, $p<0.001$), but visual comparison of observed to expected events revealed excellent calibration. Independent predictors of overall death included male gender (odds ratio [OR] 1.3, 95% CI 1.1–1.4), increased age (OR 1.04, 95% CI 1.04–1.05) and ISS (OR 1.1, 95% CI 1.1–1.1). Higher admission SBP and GCS score were associated with lower odds of death.

Compared with falls, gunshot wounds (GSW) were associated with higher risk of death (OR 3.5, 95% CI 2.7–4.5), whereas traffic and struck by/against injuries were associated with lower odds of death. Co-morbidities associated with increased odds of death included cirrhosis, cancer, cardiac disease, anticoagulation, chronic renal insufficiency, and do not resuscitate (DNR) status at admission. Smoking, alcohol abuse, drug abuse, psychiatric disease, and history of traumatic brain injury were all associated with lower odds of death. Independent predictors of FTR-N were similar, and included male gender, older age, GSW or other mechanism of injury, along with higher ISS, lower SBP or GCS score, being transfused in the ED, being admitted to the ICU or operating

TABLE 6. MULTI-VARIABLE LOGISTIC REGRESSION RESULTS: INDEPENDENT RISK FACTORS FOR FAILURE TO RESCUE AFTER INFECTIOUS COMPLICATIONS

	FTR-I n = 3,392		
	OR	95% CI	p
Male	1.6	1.2–2.2	0.004
Age	1.04	1.03–1.05	<0.001
Race/ethnicity (vs. white)			
Black (non-Hispanic)	0.7	0.4–1.2	0.21
Hispanic	1.2	0.7–2.4	0.52
Other	0.2	0.03–0.9	0.033
Mechanism (vs. fall)			
GSW	0.8	0.3–2.2	0.72
Cut/stab	0.9	0.1–6.3	0.91
Traffic	0.6	0.4–0.9	0.006
Struck	0.3	0.03–2.5	0.26
Other/unknown	0.7	0.3–1.4	0.30
Injury Severity Score	1.04	1.06–1.05	<0.001
Moderate to severe injury (AIS ≥ 3):			
Head/neck	1.1	0.7–1.7	0.71
Extremities	0.8	0.6–0.95	0.017
Chest			
GCS score on admission	0.9	0.8–0.9	<0.001
Co-morbidities			
Cirrhosis	3.9	1.5–9.6	0.004
Anticoagulation	1.7	1.1–2.5	0.019
Chronic renal insufficiency	2.9	2.0–4.4	<0.001
Steroids	2.7	1.2–6.3	0.021

FTR-I=failure to rescue after infectious complications; OR=odds ratio; CI=confidence interval; GSW=gunshot wound; AIS=abbreviated injury score; GCS=Glasgow Coma Scale.

room, and head injury. Increased number of co-morbidities was associated with FTR-N, as were several individual co-morbidities.

We identified the fewest independent risk factors for FTR-I. These included male gender (OR 1.6, 95% CI 1.1–1.2), older age (OR 1.04, 95% CI 1.03–1.05), and increased ISS (OR 1.04, 95% CI 1.03–1.05). Traffic injuries were associated with lower odds of FTR-I (OR 0.6, 95% CI 0.4–0.8). The co-morbidities significantly associated with FTR-I were cirrhosis (OR 3.6, 95% CI 1.4–9.1), chronic renal insufficiency (OR 2.9, 95% CI 1.9–4.3), and use of anticoagulation (OR 1.6, 95% CI 1.1–2.5) or steroids (OR 2.7, 95% CI 1.1–6.2). Sub-group analysis of patients whose first complication was pneumonia (n = 1356) identified older age, lower GCS score, and higher ISS as risk factors for death. Patients with a history of dementia were at increased odds of death, as were those receiving anticoagulants or steroids. Admission DNR status was associated with a three-fold increase in death in this sub-group (p < 0.001). Chest and extremity injuries were associated with decreased risk of death in patients with pneumonia.

Secondary complications

Table 1 shows the incidence of index infections, comparing FTR-I patients with survivors. The incidence of pneumonia in deaths was nearly twice that in survivors (64.9% vs. 35.4%), whereas UTI was half as common in deaths as in survivors (22.0% vs. 43.2%). Table 7 shows the incidence of

secondary complications in this population. Median number of complications was two (IQR 1–2) for FTR-I patients, compared with one (1–2) for infection survivors. Among survivors, 31.1% had at least one secondary complication, compared with 51.4% of FTR-I patients.

The most common secondary complications overall were pneumonia (9.1%), UTI (8.3%), acute respiratory failure (7.2%), deep vein thrombosis (5.9%), decubitus ulcer (4.9%), and sepsis (4.7%). For FTR-I patients, the most common complications were pneumonia (22.0%), acute respiratory failure (18.2%), sepsis (12.5%), arrhythmia (8.9%), and acute kidney injury (8.1%). Pneumonia, acute respiratory failure, sepsis, arrhythmia, myocardial infarction, coagulopathy, cardiopulmonary arrest, acute kidney injury, and stroke were all significantly more common in FTR-I patients than in survivors (p < 0.001 for all), as was unplanned intubation (p = 0.004). Iatrogenic pneumothorax was rare in both groups, but more common among FTR-I patients (p = 0.013), as was CNS infection (p = 0.027). There were no differences in incidence of additional secondary infections (empyema, bacteremia, sinusitis, UTI, soft tissue infection, or wound infection).

Discussion

By focusing attention on the management of adverse events, FTR aims to identify contributors to avoidable death and may be a better explanation of the variation in death among trauma centers than complication rates [21]. Failure to rescue may offer more insight into the relative value and importance of institutional characteristics and practices than either complication rates or overall death after trauma, but mechanisms underlying FTR remain largely unexamined [3,22]. In this analysis, we begin to address this gap by identifying a sub-set of the population who experienced infectious complications. Whereas patients with complications were more likely to die than those without, those with an index infection were less likely to die and had longer survival times than those with non-infectious index complications.

Although we identified patient and injury factors associated with each outcome, we found the fewest factors to be significant for FTR-I, consistent with the idea that FTR is more related to clinical rather than patient factors. More severe injuries and worse admitting physiology were associated with worse outcomes across the board, consistent with previous research from our group and others [23]. Presence of specific body region injuries, however, was more strongly associated with development of complications than with death or FTR-I.

Mechanism of injury was associated primarily with overall death, which may indicate that high-energy injuries such as GSWs were associated with early deaths that occurred without complication. If patients survived their initial injury, mechanism had a lesser role to play in risk of developing complications, FTR-I, or FTR-N. Whereas male gender was associated with reduced hazard of infection, male patients had higher odds of FTR-I. Likewise, older patients were no more likely have an infection develop, but were more likely to die if they did. On the other hand, patients who required admission to the ICU, operating room, or interventional radiology were more likely to have infections develop, but were no more likely to die after infection.

TABLE 7. INCIDENCE OF SECONDARY COMPLICATIONS AFTER INFECTION IN TRAUMA PATIENTS

	<i>All infection patients</i>	<i>Survivors</i>	<i>Deaths</i>	<i>p</i>
Total complications ^a	1 (1–2)	1 (1–2)	2 (1–2)	<0.001
Secondary complications ^b				
Pneumonia ^c	205 (9.1)	185 (8.6)	20 (22.0)	<0.001
Acute respiratory failure	259 (7.2)	212 (6.3)	47 (18.2)	<0.001
Sepsis ^c	164 (4.7)	134 (4.1)	30 (12.5)	<0.001
Arrhythmia	141 (3.9)	118 (3.5)	23 (8.9)	<0.001
Acute kidney injury	50 (1.4)	29 (0.9)	21 (8.1)	<0.001
UTI ^c	175 (8.3)	159 (8.4)	16 (7.9)	0.83
Unplanned intubation	114 (3.2)	98 (2.9)	16 (6.2)	0.004
DVT	211 (5.9)	196 (5.9)	15 (5.8)	0.97
Decubitus ulcer	175 (4.9)	162 (4.8)	13 (5.0)	0.90
Stroke	22 (0.6)	11 (0.3)	11 (4.3)	<0.001
Cardiopulmonary arrest	28 (0.8)	19 (0.6)	9 (3.5)	<0.001
Unplanned return to ICU	134 (3.7)	125 (3.7)	9 (3.5)	0.83
Bacteremia ^c	87 (2.5)	81 (2.5)	6 (2.4)	0.93
Myocardial infarction	21 (0.6)	15 (0.5)	6 (2.3)	0.001
Coagulopathy	13 (0.4)	9 (0.3)	4 (1.5)	<0.001
Iatrogenic pneumothorax	25 (0.7)	20 (0.6)	5 (1.9)	0.013
CNS infection ^c	13 (0.4)	10 (0.3)	3 (1.2)	0.026
Wound infection ^c	96 (2.9)	93 (3.0)	3 (1.2)	0.09

UTI=urinary tract infection; DVT=deep vein thrombosis; ICU=intensive care unit; CNS=central nervous system.

^aMedian (interquartile range).

^bn (%).

^cExcluding patients with the infection in question as an index complication.

Additional complications occurred in <2% of patients after infection and were not significantly different among deaths and survivors: Alcohol or drug withdrawal, unplanned re-operation, pulmonary embolism, dehiscence, empyema, sinusitis, soft tissue infection, and gastrointestinal bleed.

Risk factors for FTR-I in the sub-group of patients with pneumonia were similar to those noted in the larger cohort, and differences between this analysis and the larger FTR-I analysis may relate to the smaller sample size (n = 1356). It is notable, however, that DNR status at admission was associated with significantly increased odds of death in those with pneumonia, but not in FTR-I overall. This may imply that patients who were not intubated because of DNR status might have survived with ventilator support. Alternatively, this may simply identify an additional group of frail patients at particular risk for respiratory compromise. Interestingly, chest

injury was associated with decreased risk of death after pneumonia, when controlling for ISS. DuBose et al. [24] found lower FTR after ventilator-associated pneumonia at level I compared with level II trauma centers, but the contributors to this advantage remain unclear. This is a fruitful area of investigation, and more research into the diagnosis, treatment, and outcomes of pneumonia after trauma should explore these issues.

Relatively few co-morbidities were associated with FTR-I, but those that were significant are suggestive: Cirrhosis, chronic renal insufficiency, and steroid use may all be associated with an immunocompromised state, making infections more difficult to manage. A previous single-center study from our group [23] identified chronic renal insufficiency as the only co-morbidity predictive of both complications and FTR. Cirrhosis has been identified as a major risk factor for death after trauma, both overall and after laparotomy; our findings indicate that FTR may be the mechanism of death in this combination [23,25,26]. Likewise, whereas FTR analysis identifies deaths after complication, in some patients, the complication itself may not have led directly to death, but rather serves as a marker of a high-risk, complicated patient deserving of special attention.

Because we are not able to examine clinical care directly, we sought insight into patients' clinical trajectories by examining secondary complications after infection. Secondary complication rates have been shown to vary among centers and to be associated with death, and have been proposed as a more sensitive metric than FTR [22]. Although patients who died were more likely to have a secondary complication than survivors, nearly half died after only a single complication.

FIG. 2. Kaplan Meier survival estimates: Time to death in trauma patients, by type of complication. CI=confidence interval.

Whereas this may represent failure to record ensuing complications, it may also indicate that a substantial portion of the FTR rate may hinge on management of the initial complication. In the other half of deaths, however, secondary complications included additional infections (most commonly pneumonia) as well as respiratory failure, arrhythmia, and stroke. These secondary complications may represent failure to treat the index complication successfully, as well as additional opportunities to intervene to prevent deaths.

As with any retrospective analysis, this study has certain limitations. Whereas registry coding is monitored for completeness and accuracy, certain complications are challenging to diagnose, and errors are possible. In particular, patients who remained in the hospital longer before death or discharge might have been more likely to have a complete medical history recorded.

Nearly one-third of patients were transferred to the trauma center from another facility, but few had recorded complications that occurred at the referring facility. Under-reporting of complications in transfer patients could bias our results, because patients are not transferred at random. We separated patients according to type of index complication, but our categorization into infectious versus non-infectious complications may not be optimal. For example, we categorized pneumonia as an infectious complication, because the treatment for patients with pneumonia can include both anti-infective measures and pulmonary support. A recent analysis of National Surgical Quality Improvement Program data grouped wound complications with infections, and septic shock and pneumonia with pulmonary complications [27].

We defined FTR as death after any recorded complication, separated into infectious and non-infectious groups. The majority of deaths were not preceded by a complication, however. Many of these deaths may have been attributable to progression of injury and may not have been preventable even with optimal care. Some deaths, however, that occurred without complications and that are attributed to the primary injury may have been preventable by optimal intervention—to control hemorrhage, for example, or to prevent neurologic deterioration after head injury. Still other deaths may have resulted from complications that were not diagnosed or recorded. Future research could include comparisons of injury diagnoses and complication diagnoses with cause-of-death data, which are not available from PTOS.

The FTR has been shown to be more strongly associated with institutional characteristics such as teaching status, nurse-to-bed ratio, and nurse education levels than complication rates or mortality rates [8,9]. Patient factors, as identified here, also play a role in determining the outcome, and institutional factors may well have differential impacts on patient sub-groups at varying levels of vulnerability. For example, trauma centers caring for higher proportions of elderly patients have lower FTR rates [14]. Although PTOS does not include this type of institutional information, we hope that research such as ours can support both individual institutions and collaborative systems to compare institutional resources and practices that may contribute to differing outcomes across centers, to identify patients at high risk, and the processes that affect them the most.

Our findings point to areas that may be especially high yield in preventing FTR, such as the care of patients in who, pneumonia develops after trauma, as well as those patients

with infectious complications who go on to have secondary complications develop. Patients with cirrhosis, chronic renal insufficiency, and steroid use deserve targeted attention, and infection may be a particularly worrisome sign in male patients and older patients. Whereas this analysis implies that institutional and clinical factors may bear more responsibility for FTR than patient factors do, we do not identify institutional factors directly. Moreover, previous studies suggest that system factors such as hospital teaching status explain only a small proportion of the variation in FTR, suggesting that hospital culture, protocols, and practice habits may play a major role [28,29]. Future research should focus on identifying specific practices and protocols key to preventing these failures and reducing avoidable death after trauma.

Conclusions

Infectious complications are common in patients with trauma and are an important component of FTR. Patients in whom infections developed were more likely to die, and died later, than those in whom infections did not develop. Variation in management after infectious complications may contribute to preventable deaths at some centers, and state trauma systems can share best practices to prevent primary and secondary complications and to improve care for patients after complications occur.

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