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Purposeful Variable Selection and Stratification to Impute Missing FAST Data in Trauma Research

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Abstract

Background—The Focused Assessment with Sonography for Trauma (FAST) exam is an important variable in many retrospective trauma studies. The purpose of this study was to devise an imputation method to overcome missing data for the FAST exam. Due to variability in patients' injuries and trauma care, these data are unlikely to be missing completely at random (MCAR), raising concern for validity when analyses exclude patients with missing values.

Methods—Imputation was conducted under a less restrictive, more plausible missing at random (MAR) assumption. Patients with missing FAST exams had available data on alternate, clinically relevant elements that were strongly associated with FAST results in complete cases, especially when considered jointly. Subjects with missing data (32.7%) were divided into eight mutually exclusive groups based on selected variables that both described the injury and were associated with missing FAST values. Additional variables were selected within each group to classify missing FAST values as positive or negative, and correct FAST exam classification based on these variables was determined for patients with non-missing FAST values.

Results—Severe head/neck injury (odds ratio, OR=2.04), severe extremity injury (OR=4.03), severe abdominal injury (OR=1.94), no injury (OR=1.94), other abdominal injury (OR=0.47), other head/neck injury (OR=0.57) and other extremity injury (OR=0.45) groups had significant ORs for missing data; the other group odds ratio was not significant (OR=0.84). All 407 missing FAST values were imputed, with 109 classified as positive. Correct classification of non-missing FAST results using the alternate variables was 87.2%.

Conclusions—Purposeful imputation for missing FAST exams based on interactions among selected variables assessed by simple stratification may be a useful adjunct to sensitivity analysis in the evaluation of imputation strategies under different missing data mechanisms. This approach has the potential for widespread application in clinical and translational research and validation is warranted.

Level of Evidence—Level II Prognostic or Epidemiological

Keywords

FAST exam; imputation; MCAR; MAR

Background

The use of ultrasound in emergency care advanced quickly and adapted well to evolving practices in trauma care. What began in 1970 as an exploration of ultrasound's efficacy in detecting fluid injected into the peritoneal cavity of a cadaver (1, 2), has developed into a widely used procedure known as the Focused Assessment with Sonography for Trauma (FAST) exam (1). Its original description and subsequent application involved the imaging of four points with ultrasound: the right upper quadrant, the left upper quadrant, the epigastrium, and the pelvic space. FAST was quickly adopted as a non-invasive and rapid option for detecting peritoneal or pericardial fluid, quickly replacing diagnostic peritoneal lavage (DPL) in many centers (3). In addition, recent research has identified a number of new uses of emergency ultrasound, including imaging of abdominal aortic aneurisms (4–6), pericardial effusions (7, 8), and renal tract disease (9, 10), among others (1). To support the continued growth of ultrasonography research, missing data must be kept to a minimum.

Missing data is a common problem with no perfect solution. The most appropriate method of accounting for missing data depends on its classification. Data sets with missing values can be analyzed under the assumption of missing completely at random (MCAR), missing at random (MAR), or missing not at random (MNAR). These assumptions are differentiated by the presumed mechanism underlying the missing data. If the missing data values are correlated with none of variables necessary for a valid analysis to answer the study question, the assumption of MCAR can be used. If they are correlated with variables necessary for valid analysis and sufficiently captured in the dataset, the assumption of MAR can be utilized. However, if they are correlated with necessary variables not captured in the dataset, the MNAR mechanism can be addressed only in sensitivity analyses that apply different hypothetical scenarios (11).

While the collection of ultrasound data was not the primary focus of the PROspective, Observational, Multi-center Major Trauma Transfusion (PROMMTT) study, the large number of trauma patients serves as a valuable resource for studies involving ultrasound in trauma. However, because PROMMTT did not alter patient care, the use of FAST among the ten clinical centers was not standardized and many patients did not undergo FAST. The present study sought to devise a method of “purposeful imputation” for missing FAST data, combining principles of purposeful variable selection (12) and multiple imputation (13–14). The goal of this analysis is not for prediction of a positive FAST exam, but to combine aspects of these techniques and account for risk factors of missingness, so that a simplified method of purposeful imputation can be designed which can be clearly presented to a target audience that does not specialize in statistical modeling.

Methods

Data for this study originated from PROMMTT, a prospective cohort study lasting from July 2009 to October 2010 and involving ten Level 1 trauma centers in the United States. PROMMTT investigators recorded treatment procedures and patient outcomes among patients that met the inclusion criteria of triggering the highest level of trauma activation, requiring at least 1 unit of blood in the first six hours after admission, and being at least 16 years of age. Exclusion criteria for the study included pregnancy, inhalation injury, transfer, death in the first 30 minutes after ED arrival, status as a prisoner, greater than 5 minutes of CPR received before admission or within 30 minutes of admission, and burn injury affecting more than 20% of the body's surface area. Data were actively collected during resuscitation efforts, and later, daily from the medical record. PROMMTT was approved by all appropriate parties, including the Institutional Review Boards for each of the ten sites and

the Human Research Protection Office of the U.S. Army. A more detailed description of PROMMTT has previously been published (15–16).

Database variables of relevant treatment procedures or injury characteristics were identified. A number of indicators, including 24-hour mortality, time to death within 24 hours, proportion of massive transfusion (MT) patients, and injury severity score (ISS), were calculated for both the patients with available FAST data and the patients with missing FAST data. These statistics were utilized to shed light on possible explanations for the large proportion of missing data. Patients with a missing FAST exam were first classified into groups defined by injury type and severity. The patients that were not described by any injury group were categorized as “other.” The patients classified by injury were then stratified into subgroups by clinically important variables that predicted FAST data absence. The subgroup combinations were selected in a heuristic manner, and are listed in Table 1. Selected variables represented events that occurred both before and after a FAST exam is typically performed.

Once these subgroups were defined, non-missing data for subjects who received a FAST exam (complete cases) were analyzed. Clinically relevant variables were examined alone and in combination to identify those most strongly associated with positive FAST exams. These factors were used to impute positive FAST values for missing data assuming a MAR mechanism (i.e., valid surrogate variables were captured in the PROMMTT data set and considered). All subjects that did not meet the criteria were assigned a negative value. The variables and corresponding values used to impute positive FAST values are listed in Table 2. The accuracy of this method, adjusting for group, was estimated by calculating the proportion of missing data that each group accounted for and summing the products of these group proportions and group-specific accuracies. All tabulations, regressions, and variable generations in this study were completed with STATA MP 12 (17). A p-value of 0.05 or less was considered significant.

Results

Of the 1,245 patients enrolled in the PROMMTT study, 838 received a FAST exam, with 407 (32.7%) of the subjects missing FAST results. Ninety-four percent (N=381) of those missing FAST results were due to the test not being ordered or performed. The remaining 6% (N=26) were genuinely missing with no information regarding whether a FAST exam had been ordered or not. Other critical values used to guide resuscitation and serve as surrogates of illness were also absent in more than 10% of patients (13% missing International Normalized Ratio [INR] and 23% missing base deficit) usually because the test had not been ordered or performed.

The 24-hour mortality for patients missing FAST data was 13.3% compared with 11.2% for patients with FAST results (not significant, NS). Time to death within 24 hours was also slightly shorter for patients missing FAST data (1.3 hours vs. 1.9 hours for the 25th percentile, and 3.0 vs. 3.3 hours for the 50th percentile). Comparing patients with missing FAST with their non-missing counterparts, the proportion of MT patients was lower (22% vs. 25%, NS). However, 24-hour mortality among those who received a MT was greater in those with missing FAST data (31% vs. 26%, NS), while Injury Severity Score (ISS) was lower overall for patients missing FAST data (mean=22.6 vs. 27.8, $p<0.0001$). Finally, there was high site variability in performing FAST exams which is demonstrated in Table 3.

Eight injury groups were selected heuristically based on strong associations with missing FAST results. All injury groups selected had strong and significant associations with missing FAST results, except for the group classified as “Other,” likely because this

category was relatively heterogeneous. The definitions of each injury group are listed in Table 1, and odds ratios (OR) and 95% confidence intervals (CI) as well as group totals for missing, not missing and proportion having positive or negative FAST results among the non-missing can be found in Table 4. More broadly classified, there appeared to be three groups: relatively uninjured patients classified as no injury (6.6%), patients with severe injuries to the head/neck, abdomen, or extremities (46.7%), and patients with less severe injuries to the head/neck, abdomen/chest, extremities, or classified as other (46.7%).

The variables and corresponding values selected to impute a positive FAST exam result for each patient group can be found in Table 2. Within each previously-defined injury group, we estimated the accuracy of our indicators of a positive FAST by analyzing data from patients who were not missing FAST results. The estimated group-specific accuracy of an imputed positive FAST ranged from 75% (other abdominal injury) to 100% (severe head/neck injury, severe extremity injury, no injury) and total accuracy was 87% (Table 5). This technique predicted 109 positive FAST results among the 407 (26.7%) subjects with missing data, and an overall proportion of 29.2% (364/1245) positive FAST exams compared with the 30.4% (255/838) estimated from a complete case analysis.

Discussion

This analysis of missing FAST data provides a new method to purposefully impute missing values using multiple variables in combination to classify patients by injury type and severity and predict what FAST exam results would have been if performed. In this study, FAST exam results were missing in 32.7% of patients, generally due to the exam not being ordered or performed by their physician. Missing FAST values were not confined to a single mechanism, demographic, or injury group. Overall patients with missing FAST results were less severely injured than those who had a recorded FAST result. However, within the group of patients missing a FAST exam result, there appeared to be three groups: relatively uninjured patients (6.6%), patients with severe injuries (46.7%), and patients with less severe injuries (46.7%). In the most severely injured and/or hemorrhaging patients, more urgently-needed therapeutic interventions may have preempted diagnostic procedures like the FAST exam. In relatively uninjured patients, defined here as patients having all AISs less than 3, no surgery performed, and discharge within two days, physicians may have omitted the FAST exam because they decided a FAST exam would not assist with diagnosis. Additionally, different hospitals and physicians had different criteria for performing FAST exams. Some centers did not perform FAST exams on truncal penetrating injuries, while others performed them regardless of injury type or location. Clinical sites varied widely in the proportion of patients missing FAST results (13.6–76.4%), however, the site variation did not appear to be independent of the patient and intervention characteristics evaluated for this purposeful imputation approach.

We used the purposeful imputation approach for missing FAST values in order to accommodate the complicated relationships among variables in this dataset and to avoid using black-box imputation methods that do not take full advantage of clinical knowledge. In a 2008 paper, Bursac et al. described a method of statistical modeling which allowed the analyst, rather than a computer algorithm, to ultimately select the variables (12). This method, termed purposeful selection, was found especially effective in identifying the important risk factors for the occurrence of an event, rather than simply predicting outcome (12). The approach presented in this study utilizes clinically relevant variables and simple stratification and does not require extensive statistical modeling experience. Because the approach includes variables that suggest the reason for missing data values, it can serve a complementary role to more complex multiple imputation methods and sensitivity analyses.

Unfortunately, the terms used for statistical classifications of missing data can be misleading. The assumption of “missing at random” does not imply that FAST data are missing randomly, but rather that the missing values are correlated with variables recorded in the dataset. Data that are not significantly correlated with any other variables (whether recorded or unrecorded in the dataset) are classified as MCAR and are assumed to be truly missing randomly so that simply ignoring missing values (i.e., performing a complete case analysis) can still provide a valid estimate of the parameter of interest. The popularity of complete case analysis is largely based on its simplicity and its validity under the MCAR assumption (11, 20). However, when the MAR assumption is likely to be more appropriate (e.g., when one or more non-missing variables is associated with the presence of missing values on the variable of interest), the validity of complete case analysis decreases, and this method is frequently replaced by multiple imputation, which has the added advantage of increasing statistical power (11, 20). Finally, “missing not at random” does not describe all data that are not “missing randomly.” Instead, MNAR refers to missing data that are correlated with important variables necessary for valid imputation and estimation of the desired parameter, but not recorded in the dataset.

When a large proportion of data are missing, there may be no satisfying solution to resolve whether the assumption of MAR (inherent in standard imputation methods) or a MNAR mechanism is appropriate (13, 18–19). The purposeful imputation approach as outlined in this study is a practical method for dealing with missing data under a MAR assumption. By utilizing some of the principles of purposeful selection of variables and multiple imputation, this method allowed for compromise between statistical and clinical validity of the surrogate definition. Because some of the variables selected occurred after the FAST exam is typically performed, this approach may also shed light on the reasons for a missing data value (i.e., the missing data mechanism). One limitation of using these downstream variables is that this particular classification of patients cannot be used to predict FAST exam results in new patients prospectively at the bedside. However, the purpose of this analysis was not prediction, but imputation to gain better understanding of missing data mechanisms and inform future analyses that may depend upon FAST exam results.

Multiple imputation uses associations between the values of known variables and a Bayesian approach to create multiple plausible data sets for the prediction of the values of missing data; the results of these data sets are then pooled to determine the most valid complete data set (11, 20–21). This method has been positively reviewed by a number of professional associations, including the American Statistical Association, the American Medical Informatics Association, and the International Statistical Institute (14). Rubin proposes that the validity of multiple imputation relies on the appropriate application of concepts by the user (14). But because not all clinical investigators are trained in multiple imputation (21), appropriate application often necessitates close collaboration between the clinician and the analyst (14). For example, imputation models assume that data are MAR. If this assumption is not true, the imputation model may introduce bias (14). Clinicians should help identify potential associations among variables both recorded and unrecorded in the study dataset based on clinical knowledge so that the mechanism of missing data can be validated.

Other unexpected problems may arise when using multiple imputation even when the investigator is trained in statistical modeling. For example, a recent study used multiple imputation in the development of a cardiovascular disease risk predictor. In the original analysis, the investigators unexpectedly found no correlation between cardiovascular disease risk and cholesterol. However, after revising the multiple imputation model to correctly incorporate the outcome when computing imputed values for a covariate predictor, the expected association was found (21–22). Recognizing problems with imputation models is more difficult in analysis settings where the magnitude or direction of the association is not

known. Again, clinicians can assist a data analyst or statistician in validating imputation models when anomalies like these are recognized.

In addition to risks associated with use of multiple imputation, the audiences of medical journals may not be well versed in complex statistical models. Not only is an understanding of analysis methods important to the peer review process, but it is also important to readers for complete understanding of a study. For journals with non-statistically trained physicians as the target audience, a more tangible, less model-based method of dealing with missing data may be more informative. Our new purposeful imputation method is not model-based and thus may be easier for non-statistically trained investigators, reviewers, and readers to understand.

A limitation of this study is that a cross-validation of the method was not performed. The decision was made to take advantage of the data from all of the 838 patients that had a FAST exam in the development of the purposeful imputation method, as many of the relevant variables would likely be overlooked due to small sample size and low power if only half of the data had been utilized. Future research should focus on validating or refining this method using cross-validation techniques in datasets with a large portion of missing data. Additionally, this method is not meant to be used as a predictive tool for future FAST exam results. Because many of the variables used to impute the missing FAST results were collected after the FAST exam is typically done, the predictive value of this technique is confounded by the outcome. However, when utilized for the purposes of imputation, the use of outcome variables adds valuable information about the missing data mechanism.

The strengths of this study lie in its relative simplicity, transparency, generalizability, and its use of clinical knowledge. In addition, by utilizing variables in combination, stronger surrogates are identified, further reducing potential bias. The calculated accuracy estimation of 87%, along with the strengths of the imputation method and the relative face validity of the surrogate definition, provide promising evidence in support of the method outlined in this study.

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Table 1

Injury categories chosen for strong association with having a missing FAST result

Injury Category	Definition
Severe head/neck injury	Head injury only (AIS: Head 3 and all other AIS <3) or
Severe abdominal injury	To OR in 30 min and no "Severe head/neck injury" and no "Severe extremity injury" and
	Penetrating mechanism or
Severe extremity injury	SI: Intestines
	AIS: Abdomen<3 and SI extremity: suture of artery or vein and no "Severe Head/Neck Injury"
No injury	Discharged within 2 days or
Other head/neck injury	No "Severe Injury" and not "No Injury" and no "Other Abdominal Injury" and
	Head bleeding or Scalp bleeding or Neck bleeding
Other abdominal/chest injury	No "Severe Injury" and not "No Injury" and
	Abdominal bleeding or Chest bleeding or Abdominal surgery or Chest surgery or Damage control surgery or AIS: abdomen 3
Other extremity injury	No "Severe Injury" and not "No Injury" and no "Other Abdominal Injury" and no "Other Head/Neck Injury" and Extremity bleeding
Other injury	Does not fall into other categories

Abbreviations:

AIS= Abbreviated Injury Scale

SI= Surgical intervention

OR= Operating Room

Table 2

Indicators of a positive FAST exam result among patients with non-missing FAST results

Category	FAST Positive if:											
Severe head/neck injury:	Fall and history of warfarin and transported to ED by helicopter or			Motorcycle accident and SI: damage control or		Car crash and		or stab and chest bleeding and SI: occlusion of head/neck vessels or		Bicycle accident or	Gunshot wound and died in 24 hours	
						Abdominal Bleeding or						
Severe abdominal injury:	SI: intestines and		or stab and		or shotgun wound and SI: abdomen		SI: damage control		or gunshot wound and			
											Blunt mech or	
	Unk mech		SBP <90 or		Vasopr in OR or		SI: thorax		Suture of abdominal artery or		To OR <15 min and abdominal bleeding	
Severe extremity injury:	General abdominal exploratory laparotomy and SI: damage control and										or motorcycle accident and to OR or death in 60 min	
	Abdominal bleeding or				To OR or death in 30 min							
No injury:	AIS: abdomen=2 and motor vehicle accident and transferred to ED by ambulance and received abdominal CT in ED											
Other head/neck injury:	Thoracotomy in ED											
Other abdominal/chest injury:	Stab and AIS: abdomen 3 and				or gunshot wound and		or blunt and		or unk mech and			
	ED heart Rate 120 or	Pelvic bleeding or	SI: liver and abdominal bleeding		SI: intestines or		SI: liver and SI: damage control		SI: general abdominal and AIS: abdomen 3 and to OR or death in 90 min		To OR or death in 90 min	
Other extremity injury:	Heart rate in ED 120 and pre-hospital intubation and motor-vehicle accident											
Other:	Motor-vehicle accident and SI and LSI in ED or					Death and						
	Transported to ED by helicopter or					Heart rate in ED 120						

Abbreviations:
ED= Emergency Department
Mech= Mechanism
SBP= Systolic blood pressure
LSI= Life-saving intervention
SI= Surgical Intervention
Unk= Unknown
Vasopr= Vasopressors
Pericard= Pericardiocentesis
OR= Operating Room
AIS= Abbreviated Injury Scale

Table 3

FAST exams missing by site in PROMMTT

Site Number	Number of FAST exams performed	Number of FAST exams missing	Total	% FAST missing
1	266	42	308	13.6
2	83	55	138	39.9
3	40	21	61	34.4
4	66	62	128	48.4
5	113	30	143	21.0
6	26	84	110	76.4
7	86	21	107	19.6
8	56	65	121	53.7
9	79	22	101	21.8
10	23	5	28	17.9
Total	838	407	1,245	32.7

Table 4

Characteristics of chosen injury groups

Category	OR (95% CI)	N Missing FAST	N Not Missing FAST	Total N	Among patients with non-missing FAST	
					FAST + N (%)	FAST – N (%)
Severe head/neck injury	2.04 (1.39–2.99)	56	61	117	8 (13.1)	53 (86.9)
Severe abdominal injury	1.94 (1.40–2.68)	80	94	174	61 (64.9)	33 (35.1)
Severe extremity injury	4.03 (2.55–6.38)	54	31	85	4 (12.9)	27 (87.1)
No injury	1.94 (1.14–3.31)	27	30	57	1 (3.3)	29 (96.7)
Other head/neck injury	0.57 (0.37–0.89)	28	96	124	5 (5.2)	91 (94.8)
Other abdominal/ chest injury	0.47 (0.36–0.60)	132	425	557	163 (38.4)	262 (61.6)
Other extremity injury	0.45 (0.25–0.81)	14	62	76	5 (8.1)	57 (91.9)
Other	0.84 (0.46–1.52)	16	39	55	8 (20.5)	31 (79.5)

Odds ratio refers to odds of missing FAST exam results vs. not missing.

Table 5

Predictive value of the surrogate definition of missing FAST exams in the PROMMTT data set by category

Category	True +	True -	False +	False -	Total	Accuracy % ¹	N Imputed +	N Missing (% of total)
Severe Head/Neck Injury	8	53	0	0	61	100	11	56 (13.8)
Severe Abdominal Injury	52	24	9	9	94	81	58	80 (19.7)
Severe Extremity Injury	4	27	0	0	31	100	1	54 (13.3)
No Injury	1	29	0	0	30	100	1	27 (6.6)
Other Head/Neck Injury	2	91	0	3	96	97	0	28 (6.9)
Other Abdominal Injury	110	210	52	53	425	75	37	132 (32.4)
Other Extremity Injury	2	55	2	3	62	92	0	14 (3.4)
Other	5	29	2	3	39	87	1	16 (3.6)
Total	184	518	65	71	838	87²	109	407

¹The Group-Specific Accuracy is calculated by dividing the sum of the group-specific true positives and negatives by the group-specific total

²The total accuracy is calculated as the sum of the multiplications of the group-specific accuracies by the group-specific proportions of total missing