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Prediction of inappropriate pre-hospital
transfer of patients suspected acute
myocardial infarction:
machine-learning analysis of data from
the National Emergency Department
Information System and the National
Fire Agency

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the National Emergency Department
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Directed by Professor Hyeon Chang Kim, M.D., Ph.D.

The Doctoral Dissertation submitted to the Department
of Medicine, the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Doctor of Philosophy

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I hope that this study, enriched with valuable data, will contribute to developing the emergency medical system so that the best medical care can be provided to everyone in need.

I dedicate this thesis to my beloved son and daughter, hoping that they will continue contributing to a healthy world.

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ABSTRACT

Prediction of inappropriate pre-hospital transfer of patients suspected acute myocardial infarction: machine-learning analysis of data from the National Emergency Department Information System and the National Fire Agency

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(Directed by Professor Hyeon Chang Kim, M.D., Ph.D)

Aims: As the importance of the pre-hospital stage in the treatment of suspected acute myocardial infarction (AMI) patients has become widely known, it is important to select a definite hospital with capability at the pre-hospital stage. However, inappropriate pre-hospital transfers still occur in South Korea. Therefore, we developed a predictive model for the inappropriate transfer of patients with suspected AMI at the pre-hospital stage using variables obtained from the integrated nationwide dataset, and analyzed the model's effectiveness.

Method and Results: The study included 68,742 fire-department-based emergency medical services (EMS) transferred patients, who were matched with the National Emergency Department Information System data (NEDIS), among patients with an EMS cardiovascular registry created at the pre-hospital stage in South Korea from September 2017 to December 2018. We developed the two-step predictive model utilizing a machine learning algorithm. The patient class prediction was performed by a three-layer MLP model and the final prediction including specific hospital factors was conducted using the XGBoost model. The area under

the receiver operating characteristic curve of the final predictive model was 0.793 (95% confidence interval, 0.776-0.807). We estimated avoidable deaths by using the number of inappropriate transfers that can be predicted with the developed model, which is 172 per year.

Conclusions: The present study investigated the potential clinical usefulness that can be obtained through the prediction of inappropriate pre-hospital transfer on suspected AMI patients. For our results to lead to the changes in the EMS system, communication facilities for collecting real-time information should be developed. The productivity loss cost calculated by avoidable death can be a guide for considering an EMS system policy.

Key words: acute myocardial infarction, pre-hospital transfer, productivity loss cost

Prediction of inappropriate pre-hospital transfer of patients suspected acute myocardial infarction: analysis of the nationwide dataset

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I. INTRODUCTION

Acute myocardial infarction (AMI) is a leading cause of mortality worldwide and has a well-established, standard treatment ^{1,2}. In particular, a guideline outlining that reperfusion therapy must be commenced in the case of ST segment elevation myocardial infarction has been published ³. Various studies have reported that early recognition of AMI at the pre-hospital phase and rapid treatment at the hospital are the key factors in improving survival rate ⁴⁻⁹. Therefore, it is most important to evaluate the possibility of AMI and select a hospital capable of managing the disease severity in the pre-hospital stage.

The guideline released by the European Resuscitation Council categorized those factors that delay the total ischemic time of AMI patients into patient and system delay, with system delay being divided into pre- and post-first medical contact. This guideline, thus, emphasized on preventing delays from the pre-hospital phase itself rather than solely focusing on the system after arrival to the hospital in order to prevent definitive treatment delay. It also emphasized the need for a system where in an electrocardiography is performed within 10 minutes and there is rapid transfer of the patient to a hospital where definite treatment is possible. This system should be in place at the community level for hospitals that cannot commence reperfusion treatment at the first medical contact or when emergency medical service (EMS) is used ¹⁰.

As the importance of the pre-hospital phase in the treatment of AMI patients has become well known, efforts have also been made in South Korea to establish an efficient EMS system. However, the rate of public ambulance use by AMI patients was only 51% as of 2017, in particular, the rate of improper transfer with delayed emergency treatment due to the inability to transfer of the patient to a capable hospital for definite care was as high as 30.7% as of 2015 ¹¹. Therefore, the basic plans for emergency medical care for 2018–2022, as announced by the Ministry of Health and Welfare, are to improve the arrival rate of severe emergency patients to the final treatment facility within the appropriate time frame to 60% by 2022 and to improve the EMS system. Various policies are in progress to address these issues. However, most of these improvement policies were arrived at based on consensus and lacked relevant evidence. There are several reasons for not securing evidence for community EMS policy on AMI response. First, it is difficult to complete an integrated dataset because the subjects handling data are separated into the pre-hospital stage and the hospital stage. Second, it is difficult to formulate a concrete improvement policy because there is insufficient data or research that calculate the effect of EMS improvement for AMI patients as a quantified cost. Thus, this study was performed to a) develop and validate models for the prediction of inappropriate pre-hospital transfer of suspected AMI patients using variables obtained from the integrated nationwide dataset, and b) investigate the potential clinical usefulness of this model.

II. MATERIALS AND METHODS

1. Study design and setting

This study was a retrospective observational study using a nationwide dataset from the National Fire Agency and National Emergency Medical Center in South Korea. In South Korea, the National Fire Agency, which consists of 18

provincial fire departments, oversees the public EMS system. All provincial fire departments operate on a single-tiered and fire-department-based EMS system. The paramedics working at the National Fire Agency comprise level-1 emergency medical technicians (EMTs), level-2 EMTs, and nurses, who are defined according to their qualifications and roles during the transportation of patients from the scene to the hospital. Level-1 EMTs and nurses provide a limited number of advanced treatment techniques, including intravenous fluid administration, such as normal saline and glucose solution, advanced airway placement, and injections of specific medications with the supervision of medical directors at the pre-hospital stage. All the patients assessed by the fire-department-based EMS are transported to one of the emergency departments (EDs) according to field first aid standard protocol produced by the National Fire Agency. This protocol covers standardized first aid procedures at the scene, and guidelines for selecting a transfer hospital. The protocol is updated annually under the supervision of medical advisors. A nationwide fire-department-based EMS quality management program was established in 2011 for major emergency conditions, namely, out-of-hospital cardiac arrest, severe trauma, AMI, and acute stroke. With this program, the performance of individual paramedics in each provincial fire department is evaluated, and feedback is provided by the medical director. According to the Rescue and Fire EMS Act, every year, all paramedics at the National Fire Agency are required to receive 40 h of mandatory training for medical skills and knowledge.¹²

In Korea, EDs are designated by the Ministry of Health and Welfare at levels 1, 2, or 3. This designation is based on the ED's human resources, emergency equipment, and availability of medical service and specialists. By law, level-1 and level-2 EDs must be staffed 24 h/day with board-certified emergency physicians.¹³ EDs rated at levels 1 and 2 are evaluated annually by the Ministry of Health and Welfare in accordance with the EMS Act to confirm whether they can provide high-level emergency medical care. The designation of levels 1 and

2 can change according to this result. In 2017, 36 sites were designated as level-1 and 119 were designated as level-2 EDs, while in 2018, 36 sites were designated as level-1 and 118 were designated as level-2 EDs .¹⁴

2. Selection of participants

Patients aged >15 years who were transferred by the fire-department-based EMS to EDs from September 2017 to December 2018 were enrolled. Among these, patients whose EMS cardiovascular registry had been activated were included, while patients who could not match hospital stage information were not included in the study.

3. Data collection and processing

The data for the present study were extracted from the following three datasets: EMS run sheets and the EMS cardiovascular registry, which are both managed by the National Fire Agency, and data from the National Emergency Department Information System (NEDIS), which is operated by the National Emergency Medical Center in South Korea. EMS run sheets are electronically filled out to provide basic EMS operation information storage in the National Fire Agency. The age, gender, past medical history, mental status, and vital signs of the patient at the pre-hospital stage are extracted from the EMS run sheets. If the patient's symptoms recorded in the EMS run sheet include chest pain, dyspnea, palpitations, syncope, or other suspected cardiovascular events at the pre-hospital stage, the fire department paramedics are additionally required to enter information into the EMS cardiovascular registry for AMI screening. The EMS cardiovascular registry consists of a two-step systematic entry. In the first step, chief complaints, accompanying symptoms, and the onset of symptoms, as well as the location, characteristics, intensity, radiation, duration, aggravating and relieving factors of chest pain, are evaluated. Based on this information, paramedics are required to record whether the patient is predicted to have

cardiovascular emergency diagnosis in the hospital, and in this case, additional information should be obtained from the patient and recorded. This additional information includes the following: response of sublingual nitroglycerin, 3-lead and 12-lead electrocardiographic findings, and thrombolysis in myocardial infarction risk score based on the exclusion of cardiac enzyme marker results. Since 2013, the EMS cardiovascular registry has been amended four times by the Expert Quality Management Committee. Based on data from this registry, an EMS quality management program is in progress.

NEDIS is a nationwide computerized system used to collect and analyze the medical information of the patients who visit EDs in South Korea. This dataset includes various types of information, such as emergency care given and procedures performed, as well as the clinical outcome of each patient in the hospital phase. In particular, in NEDIS, real-time information regarding the availability of emergency resources is provided. This registry is managed according to the standardized protocol distributed by the National Emergency Medical Center and has been revised several times since its establishment in 2003 until January 2019; it has also been updated to version 3.2. The matching variables between the databases from the National Fire Agency and NEDIS are age, gender, the location of the patient, and time of arrival to the ED (± 10 min).

4. Model development

The predictive model for inappropriate pre-hospital transfers was developed by integrating three datasets (EMS run sheet, EMS cardiovascular registry, NEDIS). This model comprised two structures: the patient's class prediction and matching hospital factors (Fig. 1). The patient class was composed of 13 classes according to the examination and treatment codes the patient received in the ED (Table 1).

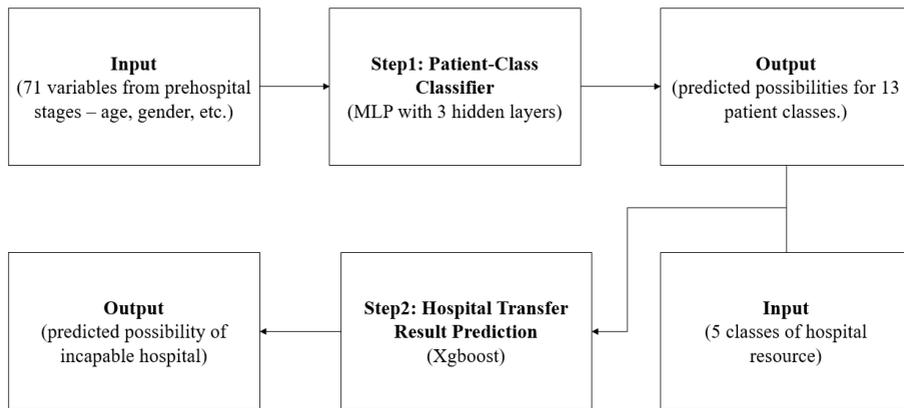


Figure 1. Flow chart of model development

Table 1. Patient class and definition

Class	Definition
Class 1	Predicted cardiopulmonary resuscitation in the ED ¹
Class 2	Predicted intubation in the ED
Class 3	Predicted central catheterization in the ED
Class 4	Predicted massive transfusion in the ED
Class 5	Predicted emergency percutaneous coronary intervention
Class 6	Predicted intensive care unit admission after ED process
Class 7	Predicted emergency operation
Class 8	Predicted performed magnetic resonance imaging in the ED
Class 9	Predicted performed echocardiography in the ED
Class 10	Predicted performed computed tomography angiography in the ED
Class 11	Predicted psychiatric manage in the ED
Class 12	Predicted admission after ED process
Class 13	Predicted discharge after ED process

¹ ED: emergency department

The matching hospital factors consisted of five classes: management quality, resource availability, ED crowding, hospital occupancy, and distance from scene

to hospital. Table 2 shows the components of hospital classes to be connected with each patient class.

Table 2. The components of hospital classes and matched patient classes

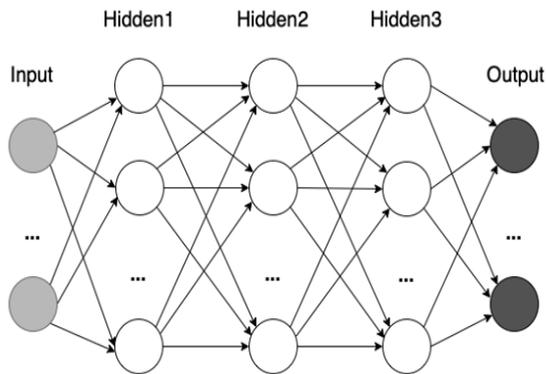
Class	Component	Matched patient classes
Quality	Annual mortality within matched patients classes	Class 1-7
	Annual admission rate within matched patient classes	Class 1-7
Availability	Availability for percutaneous coronary intervention	Class 5
	Availability for Echocardiography	Class 9
	Availability for computed tomography angiography	Class 10
	Availability for magnetic resonance imaging	Class 8
	Availability for psychiatric treatment	Class 11
	Availability for emergency operation	Class 7
ED crowding	ED bed occupancy	All classes
	Relative crowding	All classes
Hospital occupancy	Hospital bed occupancy	All classes
	Available bed in intensive care unit	All classes
Distance	Distance from scene to hospital	All classes

¹ ED: emergency department

In the patient class prediction step, we trained a three-layer MLP model with dropout and batch normalization using the 99 variables obtained from the pre-

hospital stage (Fig. 2). Since one patient can be categorized to multiple classes (multi-label classification problem), the loss function was constructed by the mean of each class's binary cross-entropy loss. In this way, the model was trained to capture the correlation of class labels and predict all class labels correctly in the same time. The dataset was divided by train and test set in 7:3 using the iterative stratification method, in order to split train and test with similar positive ratio in every class label. Then, the train dataset was split into 10-folds, and the area under the receiver operating characteristic curve (AUROC)/average precision (AP) score was calculated in the validation set in every epoch. We chose the best model that showed the highest AUROC and AP scores in validation fold. Next, in the final model to predict inappropriate transfer, we trained an XGBoost model (Fig 3). This final model was developed by connecting the results of the prediction model for patient class and the hospital class data. In the same procedure as that followed for patient class prediction, the final model was developed and selected by 10-fold cross validation.

For model interpretation, we adopted Shapley Additive Explanations (SHAP), proposed by Lundberg and Lee in 2017.¹⁵ SHAP can provide explanation of any machine learning model's output, by calculating each feature's impact on model prediction based on game theory. By this process, we can understand three things: (1) which feature is the most important to model prediction, (2) the positive or negative direction of feature impact, (3) the relation of importance score (SHAP value) and feature value. Applying SHAP to our developed models, we used the Deep Explainer module, which enables the fast approximation of SHAP values in the deep learning model, and the Tree Explainer module, which optimizes the SHAP algorithm for tree ensemble methods such as XGBoost.¹⁶



Input (# features: 99)

Hidden Layer 1 (# nodes: 128) – Dense + Batch Normalization + ReLU

Hidden Layer 2 (# nodes: 256) – Dense + Batch Normalization + ReLU + Dropout

Hidden Layer 3 (# nodes: 512) – Dense + Batch Normalization + ReLU + Dropout

Output (# logits: 13) – Dense + Sigmoid

Figure 2. Patient-class classifier (3-Layer MLP)

- Ensemble of Decision Trees

- K: number of decision trees
- F: set of all possible classification and regression trees (CART)

$$\hat{y}_i = \sum_{k=1}^K f_k(x_i), f_k \in \mathcal{F}$$

- Additive Training

- Step by step (t), fix the learned tree & add new tree

$$\begin{aligned} \hat{y}_i^{(0)} &= 0 \\ \hat{y}_i^{(1)} &= f_1(x_i) = \hat{y}_i^{(0)} + f_1(x_i) \\ \hat{y}_i^{(2)} &= f_1(x_i) + f_2(x_i) = \hat{y}_i^{(1)} + f_2(x_i) \\ &\dots \\ \hat{y}_i^{(t)} &= \sum_{k=1}^t f_k(x_i) = \hat{y}_i^{(t-1)} + f_t(x_i) \end{aligned}$$

- Optimization Function

- l: cross-entropy loss
- Omega: restriction term for model complexity

$$\begin{aligned} \text{obj}^{(t)} &= \sum_{i=1}^n l(y_i, \hat{y}_i^{(t)}) + \sum_{i=1}^t \Omega(f_i) \\ &= \sum_{i=1}^n l(y_i, \hat{y}_i^{(t-1)} + f_t(x_i)) + \Omega(f_t) + \text{constant} \end{aligned}$$

- Model Complexity (of tree)

- T: number of leaves
- w: vector of scores on leaves

$$\Omega(f) = \gamma T + \frac{1}{2} \lambda \sum_{j=1}^T w_j^2$$

Figure 3. Final predictive model for the inappropriate transfer (XGBoost)

5. Calculation for productivity loss cost

Avoidable deaths were estimated based on inappropriate transfer from the present model to derive the productivity loss cost. Then, we estimated the potential benefit (reduction in productivity loss cost) following the avoidable deaths. The productivity loss cost due to premature death caused by the

inappropriate transfer was identified from a societal perspective. The human capital approach was utilized to estimate the productivity loss cost due to premature deaths of the working-age population (15–64 years old) based on the number of deaths by gender and age groups at the time of death. The human capital approach is the most commonly used method to assess time loss in monetary units. The general formula is as follows (Fig. 4).

$$\text{Cost of Productivity Loss due to Premature Death} = \sum_j \sum_j \sum_k^n (N_{ij} \times \frac{Y_{ij(t+k)} \times P_{ij(t+k)}}{(1+r)^k})$$

i = Sex

j = Age

k = 1, 2, ..., n (n equals the difference between life expectancy and age of death)

t = Age at death

r = Discount rate

N_{ij} = Number of deaths from the disease by gender and age group

Y_{ij(t+k)} = Average annual income generated at the time of t+K by gender and age group

P_{ij(t+k)} = Employment rate at the time of t+K by gender and age group

Figure 4. Cost of productivity loss due to premature death

In this study, the cost of productivity loss was estimated by adopting a narrow perspective including only time loss in paid work. For the average annual employment rate by gender and age group, data from the Economically Active Population Survey of the National Statistical Office of Korea were utilized. The wage data were derived from the Survey of Labor Status by Employment Type by the Ministry of Employment and Labor. The employment rate and annual salary information to estimate the productivity loss costs are presented in Table 3. The discount rate of future costs experiencing productivity loss was applied at 4.5% and converted to costs at the time of death (2017–2018), while wage growth rates were not applied. The employment rate was assumed to be maintained at the value at the time of death.

Table 3. Employment rate and annual salary information

Age	Employment rate (%)				Annual salary (1,000 won)			
	2017		2018		2017		2018	
	Male	Female	Male	Female	Male	Female	Male	Female
15-19	7.6	9.3	6.4	8.5	20,472	18,324	20,892	19,284
20-24	55.6	59.4	56.1	59.6	24,228	23,220	26,184	24,576
25-29	55.6	59.4	56.1	59.6	32,796	29,988	34,320	31,440
30-34	90.2	59.4	89.7	60.7	40,980	35,076	42,708	36,756
35-39	90.2	59.4	89.7	60.7	48,228	36,744	50,232	38,748
40-44	92.6	66.0	91.9	65.7	54,240	34,644	56,568	37,296
45-49	92.6	66.0	91.9	65.7	59,628	31,440	61,536	33,828
50-54	87.7	62.9	86.9	63.5	59,628	29,088	61,740	33,852
55-59	87.7	62.9	86.9	63.5	52,608	26,028	54,720	28,056
60-64	51.5	30.6	51.7	30.7	34,788	19,944	37,080	22,440

6. Outcome measurement

The primary outcome was inappropriate pre-hospital transfer. In the NEDIS, the disposition of patients visiting the ED was classified into four categories: admission, discharge, transfer to other hospital, and death. Inappropriate pre-hospital transfer was defined as death or transfer to another hospital at the initial ED. Availability, which is one of the hospital classes, was defined as the presence of a real-time signal of emergency resource sent to the NEDIS from the transferred hospital. Relative crowding was defined as the number of patients in the ED compared to the average number of patients in the same time point of the same ED.

7. Statistical analysis

All statistical analyses, model fitting and validation were conducted with the R statistical package (www.R-project.org). The statistical significance criterion was set as two-sided, and P values < 0.05 were considered statistically significant. The model performance was evaluated by calculating the AUROC. The cut-off threshold for calculating inappropriate transfer was selected as the point that maximizes the Youden's J- score in the final model.

III. RESULTS

1. Baseline characteristics of study subjects

During the study period, a total of 68,742 fire-department-based EMS transferred patients were matched with NEDIS data among patients with the EMS cardiovascular registry created at the pre-hospital stage. Among the patients, the final study subjects were 68,623 patients after excluding the missing data.

The final study subjects were categorized into train and test sets. Among enrolled patients in the train set, 3,097 transfers (6.4%) were inappropriate. Among the 20,601 enrolled patients in the test set, 1,154 (5.6%) transfers were inappropriate (Fig 5). The baseline characteristics of the study subjects are summarized in Tables 4-7.

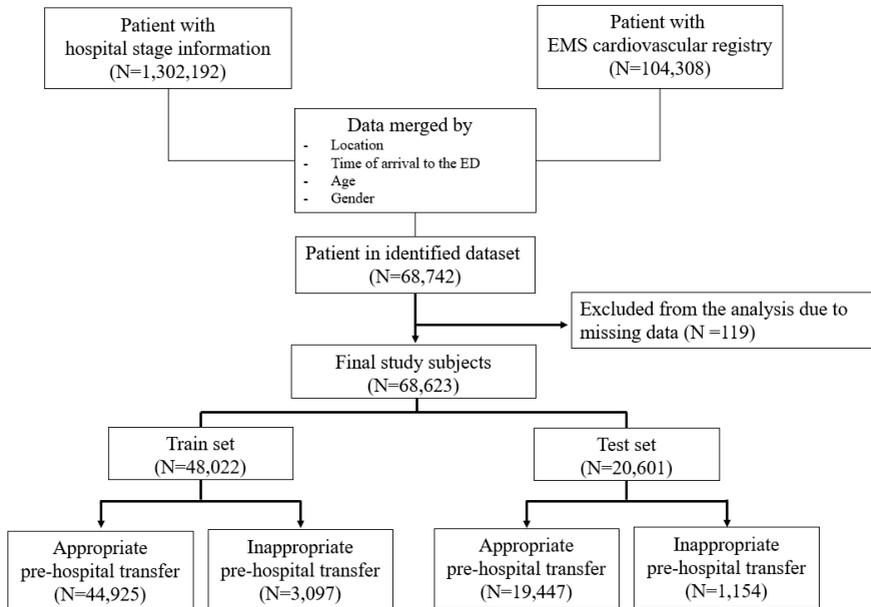


Figure 5. Flow chart of patient selection

Table 4. The baseline characteristics of the study subjects (n=68,623)

Variables	Mean ± SD ¹ or N(%)
Sex	
Female	29,563 (43.1)
Male	39,060 (56.9)
Age, years	61.69 ± 19.16
Patient's symptoms	
Chest pain	24,813 (36.2)
Dyspnea	37,012 (53.9)
Palpitation	4,846 (7.1)
Chest discomfort	829 (1.2)
Syncope	11,581 (16.9)
Nausea	5,326 (7.8)
Emesis	5,053 (7.4)
Dizziness	6,523 (9.5)
Cold sweating	6,477 (9.4)
Consciousness fluctuation	2,585 (3.8)
Past medical history	
Hypertension	23,413 (34.1)
Diabetes	12,457 (18.2)
Cerebral vascular disease	3,824 (5.6)
Lung disease	7,315 (10.7)
Cardiovascular disease	18,162 (26.5)
Tuberculosis	260 (0.4)
Hepatitis	174 (0.3)
Liver cirrhosis	590 (0.9)

(Continue)

Table 4. The baseline characteristics of the study subjects

Variables	Mean \pm SD ¹ or N(%)
Tuberculosis	260 (0.4)
Hepatitis	174 (0.3)
Liver cirrhosis	590 (0.9)
Allergic disease	196 (0.3)
Cancer	5,008 (7.3)
Kidney disease	2,354 (3.4)

¹SD: Standard deviation;

Table 5. The clinical characteristics of the study subjects

Variables	Mean ± SD ¹ or N(%)
Levels of Consciousness	
Alert	62,799 (91.5)
Verbal Stimuli	3,241 (4.7)
Response to pain/pressure	1,930 (2.8)
Unresponsive to stimuli	653 (1.0)
Vital signs	
Diastolic blood pressure, mmHg	
60-90	47,075 (68.6)
< 60	4,042 (5.9)
> 90	17,506 (25.5)
Systolic blood pressure, mmHg	
90-140	23,135 (33.7)
< 90	2,638 (3.8)
> 140	42,850 (62.4)
Pulse rate, minute⁻¹	
60-100	42,679 (62.2)
< 60	3,579 (5.2)
> 100	22,365 (32.6)
Respiratory rate, minute⁻¹	
12-20	50,685 (73.9)
< 12	398 (0.6)
> 20	17,540 (25.6)

(Continue)

Table 5. The clinical characteristics of the study subjects

Variables	Mean \pm SD ¹ or N(%)
Body temperature, °C	
35.5-36.6	30,529 (44.5)
< 35.5	1,133 (1.7)
> 36.5	36,961 (53.9)
Peripheral oxygen saturation, %	
≥ 94	48,452 (70.6)
< 94	20,171 (29.4)
Blood sugar level, mg/dl	
≥ 70	68,253 (99.5)
< 70	370 (0.5)

¹SD: Standard deviation;

Table 6. The chest pain profile of the study subjects

Variables	Mean ± SD ¹ or N(%)
Location of chest pain	
Left	8,123 (11.8)
Right	2,128 (3.1)
Substernal	4,449 (6.5)
Pit of the stomach (anticardium)	8,523 (12.4)
Other	2,213 (3.2)
Type of Chest Pain	
Pressing pain	3,450 (5.0)
Tightening/squeezing pain	8,207 (12.0)
Bursting pain	821 (1.2)
Heaviness	8,278 (12.1)
Ripping pain	1,128 (1.6)
Other	3,737 (5.4)
Radiating Pain of Chest Pain	
Left arm	1,632 (2.4)
Right arm	794 (1.2)
Back	2,126 (3.1)
Neck	1,179 (1.7)
Other	1,007 (1.5)
Factors Exacerbating Chest Pain	
Exercise	2,317 (3.4)
Other	767 (1.1)
Factors Relieving Chest Pain	
Nitroglycerin	3,198 (4.7)
Rest	3,317 (4.8)

(Continue)

Table 6. The chest pain profile of the study subjects

Variables	Mean \pm SD ¹ or N(%)
Other	688 (1.0)
Pain score (0-10)	1.75 \pm 2.84
Duration of Chest Pain	
No chest pain	43,810 (63.8)
Less than 5 minutes	3,608 (5.3)
5-20 minutes	5,857 (8.5)
20 minutes or more	13,341 (19.4)
Unknown	2,007 (2.9)
Circumstances of cardiovascular disease occurrence	
Daily life	47,941 (69.9)
While sleeping/resting	10,066 (14.7)
Working	1,979 (2.9)
Sports/leisure	807 (1.2)
Education/training	170 (0.2)
On the move	3,414 (5.0)
Under treatment	734 (1.1)
Other	3,512 (5.1)

¹SD: Standard deviation;

Table 7. Advanced profile of the study subjects

Variables	Mean \pm SD ¹ or N(%)
3-lead electrocardiogram apply	25,752 (37.5)
12-lead electrocardiogram apply	5,311 (7.7)
Finding on 3-lead electrocardiogram	
Normal sinus rhythm	13,700 (20.0)
Sinus tachycardia	3,739 (5.4)
Regular wide QRS tachycardia	229 (0.3)
Irregular wide QRS tachycardia	63 (0.1)
Regular narrow QRS tachycardia	668 (1.0)
Irregular narrow QRS tachycardia	317 (0.5)
Sinus bradycardia	1,385 (2.0)
Second degree atrioventricular block	84 (0.1)
Third degree atrioventricular block	45 (0.1)
Other atrioventricular block	52 (0.1)
Unrecognizable	3,669 (5.3)
ST segment elevation on 12-lead electrocardiogram	1,056 (1.5)

(Continue)

Table 7. Advanced profile of the study subjects

Variables	Mean \pm SD ¹ or N(%)
Sildenafil citrate try in pre-hospital stage	50 (0.1)
Nitroglycerin try in pre-hospital stage	4,190 (6.21)
Transport time, minute	18.84 \pm 10.80
Thrombolysis in myocardial infarction risk score except cardiac enzyme (0-6)	1.67 \pm 1.71

¹SD: Standard deviation;

2. Patient class prediction

Figure 6 shows the performance of the first-step in our model that predicts 13 subclasses with information on the pre-hospital stage of all patients. The predictive performance of classes predicted to have undergone cardiopulmonary resuscitation for in-hospital arrest (Class 1) or intubation (Class 2), central catheterization (Class 3), and percutaneous coronary intervention after transport (Class 5) was relatively high, at 0.842, 0.865, 0.838 and 0.855, respectively.

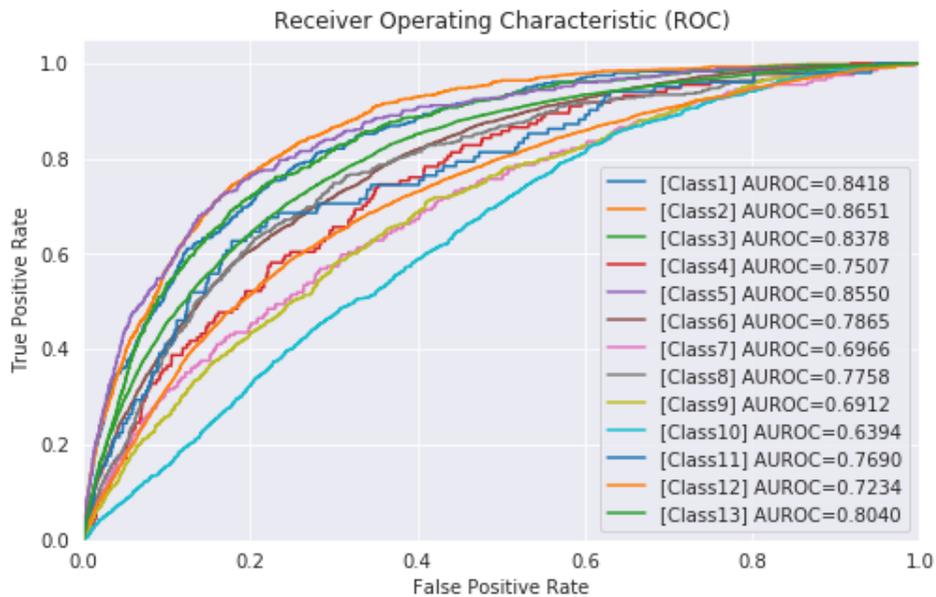


Figure 6. Performance of predictive model for patient class

Pre-hospital stage variables with high SHAP values to predict each patient class are presented in Figures 7 and, 8. Age was included in the top 10 features that predicted the classes of all patients except for one class (Class 8). When the transferred patient's age was lower, it was predicted that they would be discharged after ED treatment (Class 13) or receive psychiatric treatment in ED (Class 11). Patients with peripheral oxygen saturation of less than 94% and with 3-lead electrocardiogram monitoring at the pre-hospital stage were predicted to receive more intubation, central line catheterization and cardiopulmonary resuscitation in

ED. Patients with normal sinus rhythm on 3-lead electrocardiogram were more likely not to receive intubation and cardiopulmonary resuscitation. Patients with palpitation symptoms showed a high negative SHAP value, predicting Classes 1-6, whereas a high positive SHAP value was predictive of whether the patient has to receive psychiatric treatment or be discharged after ED treatment. Patients with dyspnea had high positive SHAP values, predicting Classes 1,2, and 3, but had a negative impact on being predicted to receive the percutaneous coronary intervention (Class 5). In the class predicted to receive percutaneous coronary intervention, the incidence of patients with cold sweating, chest pain, or upper pain core was high. The class predicted to receive magnetic resonance imaging (Class 9) had a high incidence of patients with syncope or dizziness; furthermore, patients with alertness had a negative SHAP value, predicting Class 9.

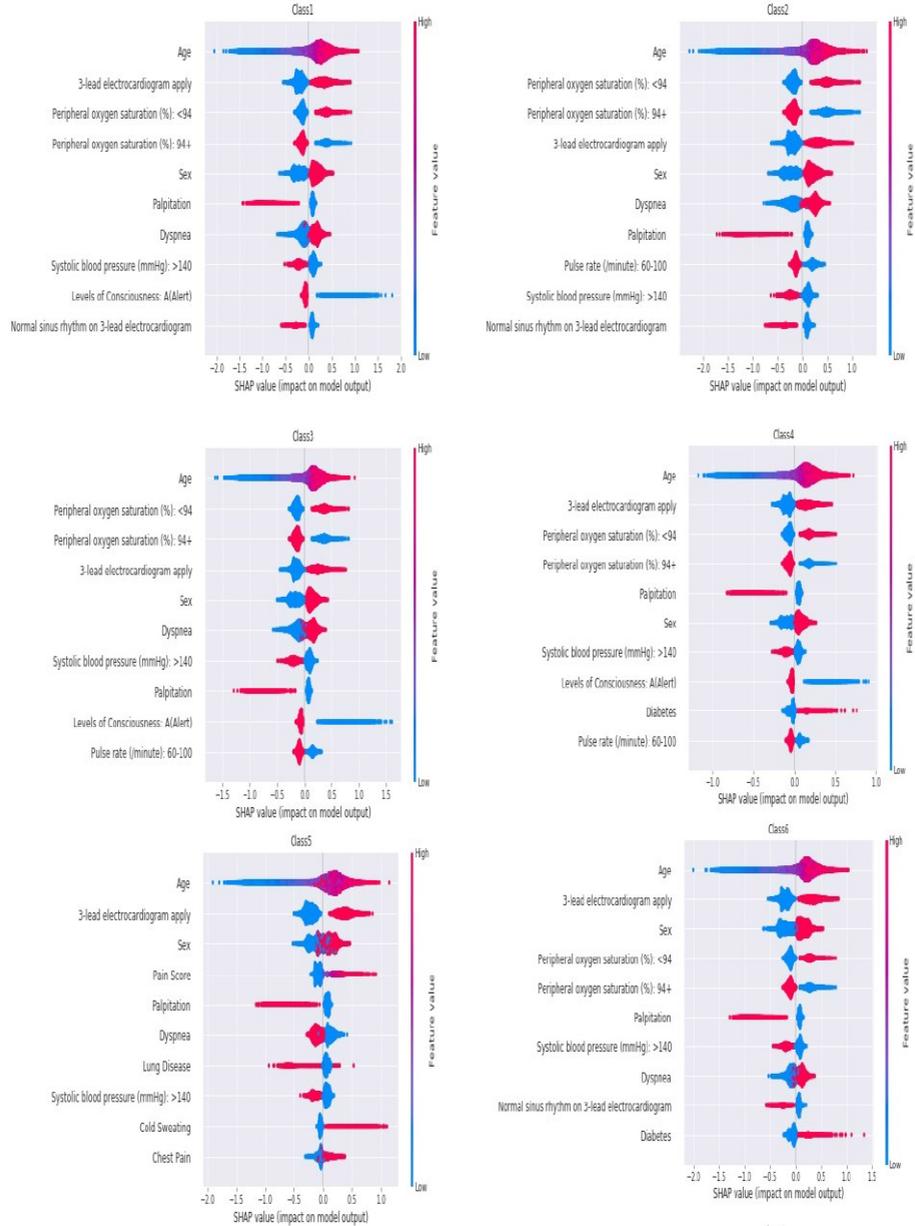


Figure 7. Pre-hospital stage variables with SHAP values to predict patient class 1-6

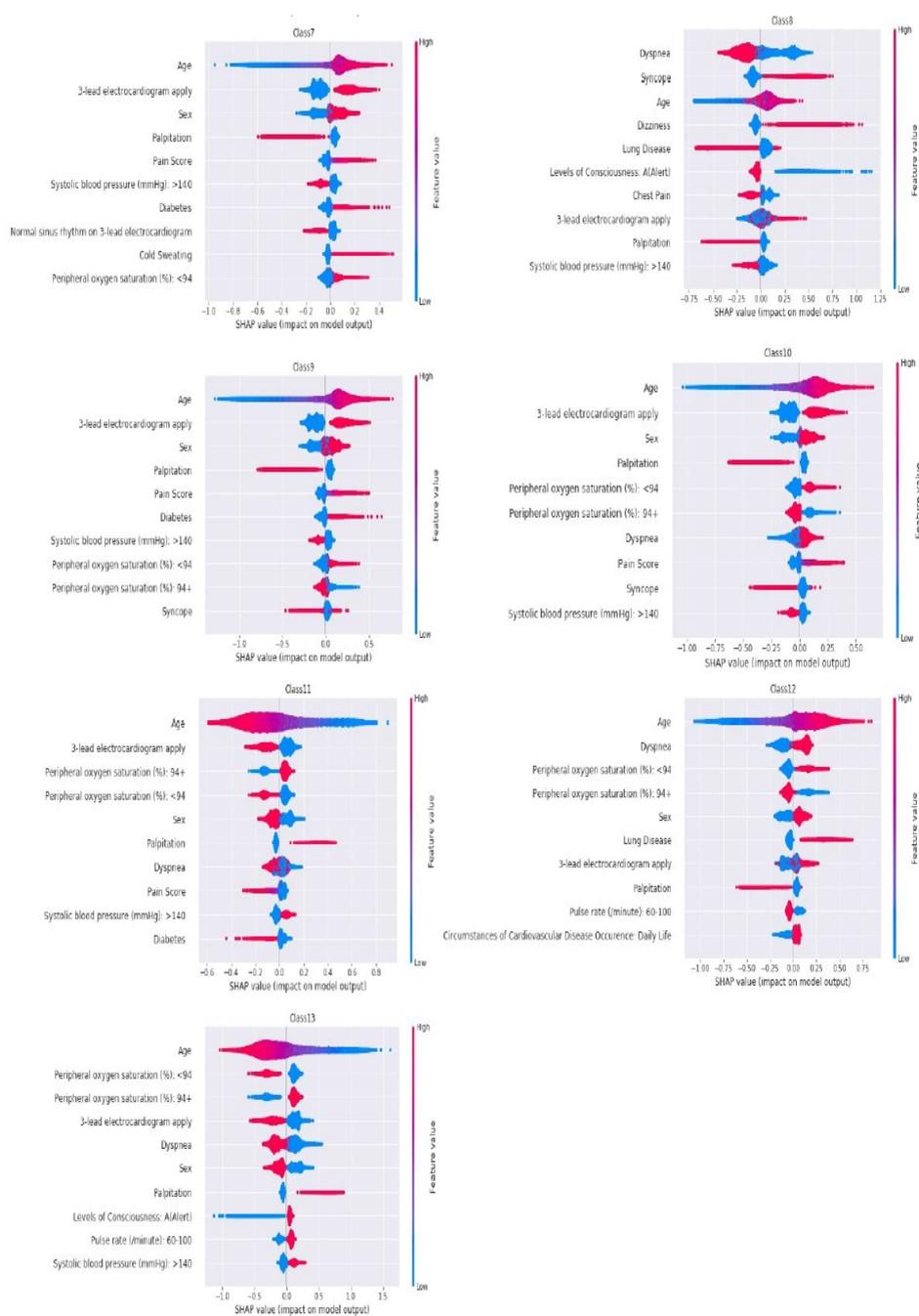


Figure 8. Pre-hospital stage variables with SHAP values to predict patient class

7-13

3. Prediction for inappropriate transfer

Figure 9 shows the top features in the predictive model for inappropriate transfer. It was found that the probability of inappropriate transfer was high for patients who were expected to receive intubation (Class 2), cardiopulmonary resuscitation (Class 1), central line catheterization (Class 3) and massive transfusion (Class 4). Patients who were predicted to be discharged after ED treatment (Class 13) and require psychiatric treatment (Class 11) were more likely have experienced appropriate transfers. It was found that the patient classes with a high probability of inappropriate transfer (Class 2, Class 3) increased the probability of the transfer to a capable hospital as they were transferred to a hospital with a high admission rate. The AUROC of the final model for predicting the transfer to an incapable hospital was 0.792 (95% confidence interval, 0.776-0.807).

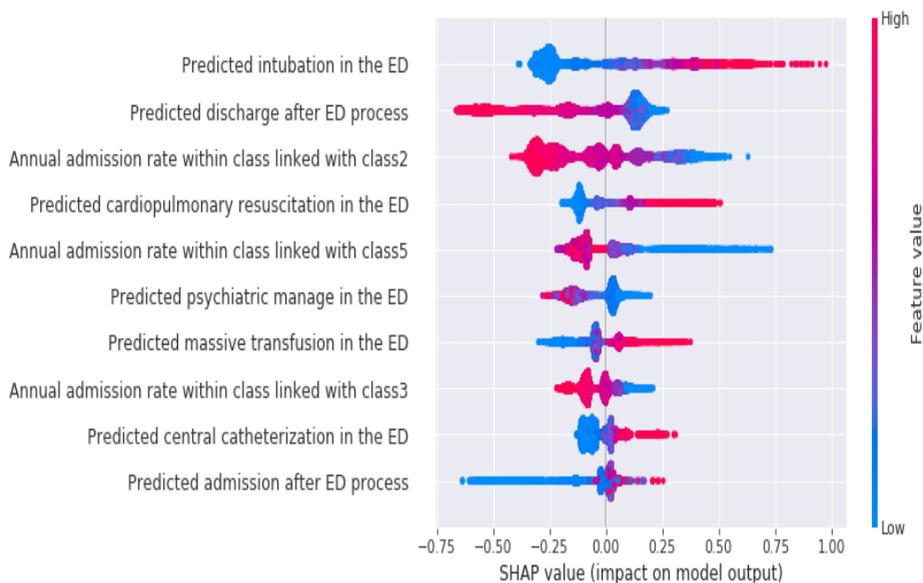


Figure 9. Top features in the predictive model for the inappropriate transfer

4. Estimation of productivity loss cost from avoidable deaths by using the predictive model

The inappropriate pre-hospital transfers were estimated by the performance of the present model. We defined avoidable cases in which our model's prediction of inappropriate pre-hospital transfers and the real world results was the same. Accordingly, the number of avoidable cases was 801 (Table 8).

Table 8. Performance of predictive model for the inappropriate transfer in the test set (N=20,601)

Prediction of the model \ Real world	Appropriate transfer, N(%)	Inappropriate transfer, N(%)
Appropriate transfer, N(%)	14,424 (97.6)	5,023 (86.2)
Inappropriate transfer, N(%)	353 (2.4)	801 (13.8)

Table 9 shows the estimation of the number of avoidable deaths by the predictive model in the test set. In order to estimate the productivity loss costs, the deaths among transferred patients were calculated by the ED mortality of patients with suspected AMI (1.33%) and the risk ratio of death within 30 days (1.11 times) depending on transfer to other hospital. ¹⁷

Table 9. Estimation of the number of avoidable deaths by the predictive model in the test set (unit: person)

Age	Male		Female		Total	
	16 months	12 months*	16 months	12 months*	16 months	12 months*
15~19	0.03	0.02	0.00	0.00	0.03	0.02
20~24	1.00	0.75	0.01	0.01	1.01	0.76
25~29	0.00	0.00	0.00	0.00	0	0.00
30~34	0.01	0.01	0.01	0.01	0.02	0.02
35~39	0.01	0.01	0.01	0.01	0.02	0.02
40~44	2.10	1.58	0.03	0.02	2.13	1.60
45~49	4.27	3.20	1.04	0.78	5.31	3.98
50~54	6.38	4.79	2.10	1.58	8.48	6.37
55~59	10.41	7.81	1.15	0.86	11.56	8.67
60~64	17.56	13.17	2.27	1.70	19.83	14.87
Over 65	104.56	78.42	75.60	56.70	180.16	135.12
Total	146.34	109.76	82.23	61.67	228.57	171.43

* The number of avoidable deaths during the research period of 16 months (September 2017 to December 2018) was converted into 12 months.

Table 10 summarizes the results of estimating the productivity loss from avoidable deaths by the predictive model based on the population of Korea. For 16 months (research period), the productivity loss per 100,000 people was approximately 748,196,000 Korean won (KRW) in total, KRW 655,459,000 for males, and KRW 92,737,000 for females. When the results are converted to one year, the estimated productivity loss is KRW 491,594,000 for males and KRW 69,553,000 for females, for a total of KRW 561,147,000.

Table 10. Estimated productivity loss from avoidable deaths by predictive model based on the population of Korea (unit: person, 1,000 won (PL))

Age at death	Transfer with suspected AMI ¹	Population ²	Incidence of transfer	Avoidable Deaths per 100,000 population		Productivity Loss per 100,000 population	
				16 months	12 months ³	16 months	12 months ³
Male							
15~19	769	1,469,053	0.05%	0.002	0.002	3,389	2,542
20~24	820	1,856,658	0.04%	0.054	0.040	88,616	66,462
25~29	878	1,868,308	0.05%	0.000	0.000	-	-
30~34	899	1,766,587	0.05%	0.001	0.001	1,203	903
35~39	1,380	2,116,733	0.07%	0.001	0.001	867	650
40~44	1,739	2,023,646	0.09%	0.104	0.078	105,186	78,890
45~49	2,662	2,311,564	0.12%	0.185	0.138	138,414	103,810
50~54	3,039	2,076,615	0.15%	0.307	0.231	147,517	110,638
55~59	4,025	2,163,953	0.19%	0.481	0.361	111,075	83,306
60~64	4,097	1,669,024	0.25%	1.052	0.789	59,192	44,394
Over 65	18,752	3,674,902	0.51%	2.845	2.134		
Total	39,060	22,997,043	0.17%	5.032	3.774	655,459	491,594
Female							
15~19	985	1,348,192	0.07%	0.000	0.000	-	-
20~24	1,293	1,639,906	0.08%	0.001	0.001	1,481	1,111
25~29	981	1,629,072	0.06%	0.000	0.000	-	-
30~34	860	1,599,914	0.05%	0.001	0.001	1,299	974
35~39	1,103	1,983,849	0.06%	0.001	0.001	893	669
40~44	1,208	1,932,121	0.06%	0.002	0.001	1,463	1,097
45~49	1,618	2,245,193	0.07%	0.047	0.035	31,693	23,770
50~54	1,856	2,046,927	0.09%	0.103	0.077	42,700	32,025

55~59	2,267	2,175,966	0.10%	0.053	0.040	9,037	6,778
60~64	2,351	1,721,804	0.14%	0.132	0.099	4,171	3,128
Over 65	15,041	5,334,372	0.28%	1.417	1.063		
Total	29,563	23,657,316	0.12%	1.755	1.316	92,737	69,553

¹ AMI, Acute Myocardial Infarction

² Population by age in Korea at the end of 2018

³ The number of avoidable deaths during the research period of 16 months (September 2017 to December 2018) was converted into 12 months.

IV. DISCUSSION

Since AMI is a life-threatening disease that causes a poor prognosis if not treated in a timely manner, a patient with suspected AMI at the prehospital stage should be transferred to a hospital with availability of prompt definite care.¹⁸⁻²⁰ In particular, for ST elevation myocardial infarction patients, the guidelines recommend emergency percutaneous coronary intervention to be performed within 60 minutes of patient arrival.¹⁰ Since it is practically impossible to continuously build qualified hospitals in all communities,^{21,22} it is important to develop a system that can cover AMI treatment capabilities in as wide a range as possible in the community.²³ Therefore, it is necessary to accurately select a hospital suitable for the patient's condition at the pre-hospital stage. If an AMI patient is transferred to a hospital with insufficient capacity, it can have a fatal outcome. In contrast, if the patients without life-threatening conditions are transferred to a higher-level hospital, emergency resources could be saturated. Saturation of emergency resources can prevent immediate resuscitation of critical patients and increase the possibility of transfer to other hospitals for definite care.^{24,25} Various studies have been performed to predict emergency conditions such as AMI with the initial patient information acquired at the pre-hospital stage, but studies predicting inappropriate pre-hospital transfer are rare.²⁶⁻³⁰ In order to assess appropriate pre-hospital transfer, information on individual hospitals should be shared in addition to the patient's features. Thus, our study developed a model that can predict the appropriateness of pre-hospital transfer for the patient's condition by considering the real-time crowding status of hospitals and EDs, distance from the scene, and capacity including percutaneous coronary intervention of the hospital. In particular, the appropriateness can change depending on the real-time capacity or hospital quality even for patients with the same features, and our model was developed by considering these variable factors. For example, our final model demonstrated that even in the class of patients with a high rate of inappropriate transfer, the

incidence of death or transfer to other hospitals could be reduced if the patients were transferred to a hospital with a high admission rate on these patients over the past year. In addition, the appropriateness of pre-hospital transfer was increased when the patient was transferred to a hospital where real-time percutaneous coronary intervention was possible. Although it is a natural result, inappropriate pre-hospital transfers are bound to occur because the hospital information is not shared in real-time with paramedics who need to make a transfer decision immediately at the scene. Therefore, the final model developed by the present study can provide a practical guide in deciding which hospital to transfer the patient to in the pre-hospital stage, beyond simply predicting the patient's severity.

In our study, patient classes were classified based on the procedure or treatment to be received after the patient was transported to the hospital, rather than based on a simple severity index or final diagnosis. Moreover, the present study confirmed the significant pre-hospital stage features associated with patient class with a high probability of inappropriate transfer. These were the features that were typically present when the patient was unstable or had a life-threatening disease such as AMI.^{31, 32} In particular, patients with 3-lead electrocardiogram monitoring were predicted to be classes with a high probability of inappropriate transfer. Since these classes comprised patients who were unstable or had life-threatening conditions, it is presumed that paramedics transferred them while monitoring 3-lead electrocardiogram. Considering patients with normal sinus rhythm on 3-lead electrocardiogram did not require cardiopulmonary resuscitation, intubation, or intensive care unit admission in our model, it can be interpreted that electrocardiogram monitoring at the pre-hospital stage plays an important role in predicting the patient class. The usefulness of electrocardiogram performed at the pre-hospital stage has been reported in current guidelines.³³ It was reported that modified History, Electrocardiogram, Age, Risk Factors, and Troponin (HEART) scores in the pre-

hospital setting had high negative predictive values for 30-day major adverse cardiac events.²⁷ Correspondingly, the results of our study suggest that electrocardiogram monitoring could also aid in the selection of appropriate hospitals linked to patient severity prediction.

Unlike previous studies, our study not only developed a predictive model, but also attempted to quantitatively analyze the productivity loss cost calculated by avoidable death from this model. In order for authorities to decide on the application of the developed system in the field, the economic effectiveness should be quantitatively measured along with scientifically verified evidence.³⁴ Furthermore, for the present model to be used in the field, paramedics should be able to input patient information promptly at the scene, and real-time hospital information from NEDIS should be shared with them. In addition, a computerized system that can decide the capable hospital by integrating this information should be additionally provided. We derived the avoidable productivity loss cost on patients with suspected AMI at the pre-hospital stage using the present model. Therefore, our model allows governments to evaluate the feasibility of budgeting for improving EMS systems. In addition, if the target population of this system is not limited to patients with suspected AMI but extended to other severe emergency patients such as cardiac arrest, acute stroke, and major trauma, more cost can be saved than the productivity loss cost derived from our study.

The limitations of our study include the following. First, there is a possibility of bias due to the study's retrospective design. In particular, the final model has not been validated in a real scenario; therefore, our final model should be prospectively verified in the real world. Secondly, NEDIS and EMS registry could not be merged completely because matching keys do not exist between the datasets to protect the anonymity of the registry. Lastly, since the present study was performed on fire-department-based EMS in South Korea, it is difficult to generalize the results of this study.

V. CONCLUSION

We investigated the potential clinical usefulness from the prediction of inappropriate pre-hospital transfers of suspected AMI patients. In order for this study results to be linked to changes in EMS systems, communication facilities that enable real-time collection of information should be established in the EMS field. It is believed that the clinical benefit quantitatively estimated by the present study could guide government's decision-making.

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ABSTRACT (IN KOREAN)

급성 심근경색이 의심되는 환자의 부적절한 구급 이송 예측:
국가 응급실 정보 시스템과 소방청 데이터를 이용한 기계 학습
분석

< 지도교수 김현창 >

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김 지 훈

급성 심근경색이 의심되는 환자의 치료에서 병원 전 단계의 중요성이 널리 알려지면서 병원 전 단계에서 수용 가능한 병원을 예측하는 것이 중요하다. 그러나 우리 나라에서는 여전히 부적절한 구급 이송이 발생하고 있다. 따라서 우리 연구는 통합된 전국 데이터 세트에서 얻은 변수들을 사용하여 병원 전 단계에서 급성 심근경색이 의심되는 환자의 부적절한 이송에 대한 예측 모델을 개발하고 이 모델의 효과를 분석하고자 했다.

본 연구는 2017년 9월부터 2018년 12월까지 119 구급차를 통한 이송 환자 중 병원 전 단계에서 심혈관 레지스트리가 작성된 환자 중 국가 응급실 정보 시스템 데이터와 일치하는 68,742명을 대상으로 하였다. 우리는 기계 학습 알고리즘을 이용하여 2단계의 예측 모델을 개발했다. 환자 분류 예측은 3층의 다층 퍼셉트론 모델로 수행하였고, 이 모델에 특정 병원 요인을 추가한 최종 예측은 익스트림 그레이던트 부스팅 모델로 수행되었다. 최종 예측 모델의 수신기 동작 특성 곡선 아래 면적은 0.793 (95% 신뢰구간, 0.776-0.807) 이었다. 우리는 연구에서 개발된 모델로 예측할 수 있는 부적절한 구급 이송 건수를 토대로 피할 수 있는 사망을 추정하였으며, 이 수치는

연간 172건이었다.

본 연구는 급성 심근경색증이 의심되는 환자의 부적절한 구급 이송 예측을 통해 임상적으로 얻을 수 있는 잠재적인 유용성을 조사하였다. 우리 연구의 결과가 응급 의료 시스템 개선으로 이어지기 위해서는 실시간 정보 수집을 위한 통신 설비가 구축되어야 한다. 피할 수 있는 사망을 통해 추정된 생산성 손실 비용은 응급 의료 정책에 대한 근거로 사용될 수 있다.

핵심 되는 말: 급성 심근 경색, 구급 이송, 생산성 손실 비용