

Prediction Model of Delayed Hemothorax in Patients with Traumatic Occult Hemothorax Using a Novel Nomogram

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Background: Delayed hemothorax (dHTX) can occur unexpectedly, even in patients who initially present without signs of hemothorax (HTX), potentially leading to death. We aimed to develop a predictive model for dHTX requiring intervention, specifically targeting those with no or occult HTX.

Methods: This retrospective study was conducted at a level 1 trauma center. The primary outcome was the occurrence of dHTX requiring intervention in patients who had no HTX or occult HTX and did not undergo closed thoracostomy post-injury. To minimize overfitting, we employed the least absolute shrinkage and selection operator (LASSO) logistic regression model for feature selection. Thereafter, we developed a multivariable logistic regression (MLR) model and a nomogram.

Results: In total, 688 patients were included in the study, with 64 cases of dHTX (9.3%). The LASSO and MLR analyses revealed that the depth of HTX (adjusted odds ratio [aOR], 3.79; 95% confidence interval [CI], 2.10–6.85; p<0.001) and the number of totally displaced rib fractures (RFX) (aOR, 1.90; 95% CI, 1.56–2.32; p<0.001) were significant predictors. Based on these parameters, we developed a nomogram to predict dHTX, with a sensitivity of 78.1%, a specificity of 76.0%, a positive predictive value of 25.0%, and a negative predictive value of 97.1% at the optimal cut-off value. The area under the receiver operating characteristic curve was 0.832.

Conclusion: The depth of HTX on initial chest computed tomography and the number of totally displaced RFX emerged as significant risk factors for dHTX. We propose a novel nomogram that is easily applicable in clinical settings.

Keywords: Delayed hemothorax, Occult hemothorax, Rib fractures, Least absolute shrinkage and selection operator, Nomograms

Introduction

Hemothorax (HTX) is a frequent complication in patients with blunt chest trauma, often resulting in adverse outcomes that range from hypovolemic shock due to blood loss to delayed complications such as empyema [1,2]. Consequently, it is essential to tailor treatment based on the patient's hemodynamic status and the severity of the injury [3].

The volume of HTX is critical in determining whether to opt for procedural interventions or conservative management [4]. In the past, the estimation of HTX volume primarily relied on plain chest radiographs [5,6]. However, the advent of widespread computed tomography (CT) scan usage in trauma care has enhanced the accuracy of these assessments. This technological progress now enables the detection of even minimal HTX amounts, which were previously undetectable on standard plain chest radiographs [3]. These small quantities of HTX, detectable only through CT scans, are known as occult HTX [7].

Although the initial volume of HTX is a critical factor in determining appropriate management, it is important to note that this volume is not static and may increase over time in some cases. Failure to detect such delayed onset of

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HTX (dHTX) can result in severe complications [8]. Numerous studies have aimed to predict the occurrence of dHTX in patients with occult HTX and to establish guidelines for effective treatment [4,9,10]. Recently, the Eastern Association for the Surgery of Trauma guidelines have recommended immediate drainage when the depth of HTX exceeds 1.5 cm on the initial CT scan [11].

However, applying these recommendations universally is complicated due to the varying degrees of injury among patients. For instance, recent research has highlighted that patterns of rib fractures (RFX) are significant risk factors for dHTX [12-14]. Furthermore, dHTX can develop in patients who initially show no signs of acute HTX on chest CT scans [15]. Additionally, even when the depth of the HTX on a CT scan exceeds 1.5 cm, drainage may not be necessary in every instance [4,9-11]. Thus, there is a lack of personalized admission and treatment guidelines that take into account both the degree of injury and the volume of HTX in patients with occult HTX.

Our study aimed to develop a personalized predictive model for the occurrence of dHTX, which necessitates closed thoracostomy or surgery in patients with either no HTX or occult HTX. Additionally, by representing the predictive model in a nomogram, we have made its application in actual clinical practice more straightforward.

Methods

Study design and data source

This retrospective, observational, single-center study was conducted at a level 1 trauma center. We prospectively collected data from all patients presenting with blunt chest trauma from the time of their admission. This included recording the Injury Severity Score (ISS) [16] and the Abbreviated Injury Scale (AIS) [17]. We also tracked patients' progression, noting any occurrences of flail motion or pneumonia during their initial hospital stay. The patterns of RFX and the extent of pulmonary contusion (PC) were determined based on initial chest CT scans. Cases of HTX were assessed on chest CT by measuring the largest lamellar fluid stripe in the dependent pleural "gutter" on transverse axial cuts [4]. In our trauma center, comprehensive CT scans from the head to the pelvis were routinely performed for all patients, with additional scans of the extremities conducted as needed.

Primary outcome and definitions

Primary outcome

Even when dHTX is visible on plain chest radiographs, drainage procedures are not always required. Typically, a small volume of HTX, usually less than 260–300 mL, resolves on its own [15]. In our study, the primary outcome focused on instances of dHTX that required intervention or led to significant complications. This included cases requiring immediate drainage through closed thoracostomy and those involving massive bleeding or empyema that necessitated surgical intervention. We also included patients who declined treatment due to financial constraints, resulting in fibrothorax and subsequent permanent lesions.

Definition of occult HTX

We defined occult HTX as cases that were detectable only on chest CT and not visible on plain chest radiographs [7].

Definition of dHTX

We defined dHTX as cases in which patients initially presented with no HTX or only occult HTX, and subsequently demonstrated evidence of pleural effusion on plain chest radiography or follow-up chest CT 24 hours after admission.

Number of rib fractures and the degree of displacement

The number of ribs was calculated based on the degree of fracture displacement. Currently, there are 2 primary approaches to RFX classification [18-20]. One proposes dividing fractures into grade I and grade II based on a criterion of 50% displacement (grade I: RFX with a displacement of less than 50% of the rib width on axial CT; grade II: displacement between 50% and less than 100%), while fractures that are completely dislocated are classified as grade III. The other approach categorizes fractures as "undisplaced" or "offset," based on a criterion of 10% displacement (undisplaced: RFX with a displacement of less than 10% of the rib width on axial CT; offset: displacement between 10% and less than 100%), with completely dislocated fractures classified as "displaced." However, in our previous study, which applied both classification criteria, the only category that demonstrated a significant difference was totally displaced RFX [21]. In this study, we classified RFX based on a 50% threshold (grade 0, no RFX; grade 1, RFX with a displacement of less than 50% of the rib width on axial CT; grade 2, displacement between more than 50% and less than 100%; grade 3, complete displacement). Additionally, even if a single rib fractured into 2 or more pieces, only the fractures at the 2 most severely broken locations were recorded and evaluated [21,22]. In this study, as the analysis of risk factors was conducted for each individual hemithorax, a single hemithorax could have up to 12 RFX.

Rib fractures locations

The location of RFX was categorized into 3 sections using the anterior and posterior axillary lines. The upper first to second ribs and lower 11th–12th ribs were excluded from the definition of the flail segment. Equations were formulated using the remaining ribs (third to 10th) to determine the flail segment and primary fracture line locations [21].

The concept of the "primary fracture line," introduced in a previous study, was developed to more precisely represent the patterns of RFX [21]. Clinically, it is observed that multiple RFXs often align perpendicularly to the ribs. The orientation of these lines, whether anterior or lateral, influences clinical outcomes. The study highlighted that fracture lines located laterally significantly contributed to the occurrence of flail motion. We also recognized the primary fracture line as a critical parameter for predicting dHTX and incorporated it into our analysis. Patients with no RFX or only a single fracture, as well as those with multiple RFXs but no discernible pattern, were considered to lack a clear fracture line and were categorized separately in Table 1.

Flail segment and flail motion

A segmental RFX was diagnosed when a single rib had 2 or more fractures at different locations. Given that flail motion and flail segments present with entirely different clinical manifestations and require distinct differentiation [21,22], our study defined an anatomical flail segment as 3 or more consecutive segmental RFX confirmed radiologically, and flail motion as paradoxical movement of the chest wall clinically confirmed during the index hospitalization [20].

Degree of pulmonary contusion

The degree of PC was assessed using the blunt pulmonary contusion score (BPC18) [23]. This scoring system divides each lung field into upper, middle, and lower thirds, with each third receiving a score from 0 to 3, depending on the density of the affected lung. For the purposes of this study, the analysis of risk factors was conducted for each individual hemithorax; thus, the maximum possible score for the most severe degree of PC in a hemithorax was calculated to be 9 points.

Study population, as well as inclusion and exclusion criteria

This study enrolled 1,266 consecutive patients with blunt chest trauma who presented to the trauma center between January 2019 and December 2023. In our study, all plain chest radiographs and chest CT scans were jointly interpreted by a radiologist and thoracic surgeons. We excluded patients based on the following criteria: (1) patients with bilateral blunt chest trauma; (2) patients who underwent closed thoracostomy within 24 hours of admission; (3) patients with HTX not classified as occult HTX, such as those with costophrenic angle blunting identified on initial plain chest radiographs; (4) patients who were discharged or died within 24 hours of presentation; and (5) cases where the degree of PC could not be assessed, such as those with a totally collapsed lung due to tension pneumothorax or a single lung due to a previous pneumonectomy. Notably, we also excluded patients who developed pneumonia before the diagnosis of dHTX, due to the challenges in differentiating between parapneumonic pleural effusion and dHTX. As a result, 688 patients, either with no HTX or only occult HTX, were ultimately included in the study (Fig. 1).

Statistical analysis

The median and interquartile range were used to represent continuous data, while proportions were used for categorical data. We compared continuous data using either the Student t-test or the Mann-Whitney U test. For categorical data, comparisons were made using the chi-square test or Fisher's exact test, depending on what was most suitable. We set the threshold for statistical significance at p<0.05. All statistical analyses were performed using the R language ver. 4.2.1 (The R Foundation for Statistical Computing, Vienna, Austria). For data analysis and visualization, we utilized packages including "tidyverse," "autoReg," "moonBook," "glmnet," and "rms."

To minimize overfitting of the prediction model and increase the accuracy of the new dataset, we employed the **Table 1.** Comparisons of clinical characteristics and outcomes of patients with either no HTX or occult HTX

(Continued on next page)

Table 1. Continued

Values are presented as number (%), mean±standard deviation, or median (interquartile range).

HTX, hemothorax; LOS, length of stay; ICU, intensive care unit; MV, mechanical ventilator; ARDS, acute respiratory distress syndrome; BPC, blunt pulmonary contusion; PNX, pneumothorax; RFX, rib fractures; AIS, Abbreviated Injury Scale; ISS, Injury Severity Score; dHTX, delayed HTX.

Fig. 1. Flow chart for patient selection. HTX, hemothorax.

least absolute shrinkage and selection operator (LASSO) to reduce the regression coefficients to zero [24,25]. We conducted a tenfold cross-validation to determine the optimal hyperparameter (λ), selecting the most regularized model where the error was within 1 standard error of the minimum [24]. We incorporated various risk factors for dHTX into the LASSO regression model, including age, sex, body mass index (BMI), head AIS, face AIS, abdominal AIS, chest AIS, extremity AIS, external AIS, ISS, presence of flail motion, BPC18, and different RFX patterns.

After performing feature selection with the LASSO regression model, we constructed a multivariable logistic regression (MLR) model. Utilizing the MLR model, we developed a nomogram, a graphical tool that facilitates the approximation of probabilities [26].

Ethics statement

This study was approved by the institutional review

board (IRB) of Chungbuk National University Hospital (IRB no., CBNUH 2022-09-006). The requirement for informed consent was waived by the IRB of Chungbuk National University Hospital.

Results

Patient characteristics

Table 1 presents the baseline characteristics of the study population and the results of univariate analysis for dHTX. During the study period, 688 patients were included after applying the exclusion criteria. These patients were categorized into 2 groups: those with dHTX and those without. Of these, 64 patients (9.3%) exhibited clinically significant dHTX, while 624 (90.7%) did not. The onset of dHTX occurred an average of 3.0 days after admission, with a range of 2.0 to 6.0 days. There were no significant differences in sex, age, or BMI between the 2 groups. In comparison to the non-dHTX group, the dHTX group experienced a longer hospital stay. The median hospital length of stay (LOS) was 19.0 days (interquartile range [IQR], 10.0–35.0 days) for the dHTX group versus 13.0 days (IQR, 6.0–26.3 days) for the non-dHTX group. Similarly, the median intensive care unit LOS was significantly longer for the dHTX group, at 3,335.0 minutes (IQR, 0.0–7,636.5 minutes) compared to 1,182.5 minutes (IQR, 0.0–4,290.0 minutes) for the nondHTX group (p<0.05 for both comparisons). There were no significant differences in the incidence of prolonged mechanical ventilation over 48 hours, pneumonia, acute respiratory distress syndrome, or mortality rates between the groups.

The occurrence rate of dHTX did not differ significantly between the left and right chest (53.1% versus 46.9%, p=0.404). However, in the dHTX group, PC was observed more frequently, and the BPC18 score was higher (43.4% versus 59.4% and 0.0 [0.0–1.0] versus 1.0 [0.0–3.0], respectively; all p<0.05). The incidence of pneumothorax and occult HTX was also higher in the dHTX group (25.8% versus 50.0%; 22.8% versus 76.6%, p<0.001, respectively). The depth of pneumothorax and HTX measured on initial chest CT also showed significant differences between the 2 groups (0.1±0.2 versus 0.2±0.4; 0.1±0.3 versus 0.5±0.6, p<0.05, respectively).

While the presence of RFX showed no significant difference between the groups with and without dHTX (96.9% versus 91.7%, p=0.218), there were significant differences in both the number and severity of RFX. Specifically, the dHTX group exhibited significantly higher counts of total, grade II, and grade III RFX (3.0 [2.0–5.0] versus 5.5 [4.0– 7.0]; 0.0 [0.0–1.0] versus 0.5 [0.0–1.0]; 0.0 [0.0–1.0] versus 2.0 [0.5–3.0], p<0.05, respectively). Additionally, segmented RFX, including those with at least 1 grade II or III fracture, were significantly different (0.0 [0.0–0.0] versus 1.0 [0.0–

4.0]; 0.0 [0.0–0.0] versus 0.0 [0.0–0.5]; 0.0 [0.0–0.0] versus 0.0 [0.0–1.5], p<0.001, respectively).

Additionally, the incidence of flail segments was significantly higher in the dHTX group compared to the control, with rates of 31.2% versus 9.5% (p<0.001). Additionally, a greater number of patients in the dHTX group exhibited RFX in the lateral portion, with percentages of 48.4% versus 31.9% (p=0.011). In terms of the AIS scoring, only the chest AIS scores and the ISS demonstrated statistical differences, with values of 3.0 (2.0–3.0) versus 3.0 (3.0–3.0) and 14.0 (10.0–22.0) versus 18.0 (13.5–26.5), respectively $(p<0.05)$.

Among the 64 patients diagnosed with dHTX, the majority (n=55, 85.9%) were treated with closed thoracostomy. However, 3 patients (4.7%) underwent exploratory thoracotomy due to massive bleeding, 2 (3.1%) required empyemectomy and decortication surgeries, and 4 (6.2%) opted out of drainage procedures because of financial constraints, which resulted in the development of fibrothorax from chronic empyema.

Risk factor analysis using the LASSO regression model

In our study, we performed a multivariable analysis to investigate the occurrence of dHTX, employing LASSO regression to prevent overfitting of parameters that demonstrated statistical significance in the univariate analysis (Fig. 2). Fig. 2A illustrates how the coefficients were shrunk by the hyperparameter (λ), while Fig. 2B shows the model's accuracy through cross-validation. During the cross-validation, the optimal log (λ) was determined to be −3.078. At this level, only 2 risk factors were identified as significant: the number of grade III RFX and the depth of occult HTX. The LASSO regression reduced the coefficient estimates of

Fig. 2. Clinical variables were selected using a least absolute shrinkage and selection operator (LASSO) logistic regression model alongside the rib fracture grade I–III scoring system. (A) Shrinkage of coefficients by hyperparameter (λ). (B) Hyperparameter selection (λ) using cross-validation. The dotted line indicates the value of the harmonic log (λ) when the model error is minimized. In the LASSO logistic regression model, 3 variables were selected when log (λ) was −3.078.

cOR, crude odds ratio; CI, confidence interval; aOR, adjusted odds ratio; HTX, hemothorax; RFX, rib fracture.

Fig. 3. Nomogram predicting the risk of delayed hemothorax. Each variable is assigned a score on each axis. The sum of all points for all variables is computed and denoted as the total points. The predicted probability can be obtained on the lowest row corresponding to the sum of total points.

other risk factors to zero.

Prediction model, nomogram, and model performance

The MLR model, which incorporates 2 risk factors identified by the LASSO model, is detailed in Table 2. In this MLR analysis, significant predictors included the depth of HTX, with an adjusted odds ratio (aOR) of 3.79 (95% confidence interval [CI], $2.10-6.85$; $p<0.001$), and the number of grade III RFX, with an aOR of 1.90 (95% CI, 1.56–2.32; p<0.001). A nomogram was developed to estimate the individual probability of dHTX, as shown in Fig. 3. The area under the receiver operating characteristic curve (AUROC) for the proposed model was 0.832, as depicted in Fig. 4.

The optimal cut-off values for these 2 variables were as follows: HTX depth at 0.5 cm and the number of grade III RFX in the hemithorax at 0. Utilizing these cut-off values, our model demonstrated a sensitivity of 78.1%, a specificity of 76.0%, a positive predictive value of 25.0%, and a negative predictive value of 97.1%.

Discussion

In this retrospective study, our objective was to identify risk factors for dHTX in patients who have experienced

Fig. 4. The accuracy of a multivariable logistic regression model for predicting delayed hemothorax. PPV, positive predictive value; NPV, negative predictive value; AUC, area under the receiver operating characteristic curve; CI, confidence interval.

blunt thoracic trauma and either have no HTX or only occult HTX. Additionally, we aimed to develop a personalized model to predict the necessity for closed thoracostomy or surgical intervention, thereby enabling quicker decision-making regarding hospital admission. To our knowledge, this is the first study to propose a prediction model for dHTX by analyzing RFX patterns, pneumothorax (PC) degree, and HTX depth, based on initial CT scans. We specifically combined these factors to address the limitations noted in previous studies.

In 2005, Bilello et al. [4] conducted a study involving 99 HTXs in 78 patients. They found that when the HTX exceeded 1.5 cm on chest CT, patients were more likely to require interventions like closed thoracostomy. Conversely, if the HTX depth was less than 1.5 cm, many patients could be managed conservatively. However, the study did not distinguish in detail between RFX patterns and PC severity, categorizing them merely as present or absent. These factors were not identified as significant risk factors for the occurrence of dHTX.

A prospective observational study by Mahmood et al. [10] included 81 patients with occult HTX, as confirmed by chest CT. Of these, 67 were managed expectantly, while 12 underwent closed thoracostomy within 48 hours. The authors clearly defined occult HTX and found no significant differences in the number of RFX, ISS, or age between the group that underwent drainage procedures and the group that did not. They also suggested that patients with an HTX greater than 1.5 cm on CT are more likely to require drainage. In our study, the number of RFX was not a significant risk factor for the development of dHTX. However, our analysis of RFX severity indicated that grade III RFX was a strong risk factor, consistent with findings from several recent studies [12-14].

Another study by Gonzalez et al. [12] analyzed detailed RFX patterns, similar to our analysis, but their definition of dHTX was ambiguous. Additionally, they did not report the HTX depth on the initial CT scan, which is a critical criterion for deciding on drainage procedures [12]. A recent study by Ahn et al. [14] identified displaced RFX as risk factors for dHTX, but they did not specify the initial volume of HTX. They defined dHTX as either a new occurrence in a previously HTX-free state or an increase in the amount of an existing HTX. The AUROC derived solely from displaced RFX was 0.681, indicating it is not sufficiently reliable for practical clinical use. Moreover, the absence of precise criteria for the amount of HTX limits the creation of effective guidelines. Although both studies demonstrated an association between displaced RFX and dHTX, similar to our findings, the definition of displaced RFX varies significantly. Both studies defined displaced RFX as a displacement distance of half the rib width [27]; however, the definition of RFX severity has been extensively debated, and various approaches for external validation have been conducted [18,20-22]. Therefore, the decision to define RFX with more than 50% displacement as "displaced" warrants further review and consideration.

We developed a clear nomogram that predicts the likelihood of developing dHTX based on the number of grade III RFX and the initial volume of occult HTX. We determined that the optimal cut-off for our predictive model is an initial occult HTX depth of 0.5 cm in the absence of grade III RFX. In these instances, the positive predictive value is 25.0%, and the negative predictive value is 97.1%, suggesting a minimal risk of dHTX development in these scenarios.

Occult HTX, which is only detectable through chest CT, typically does not necessitate immediate interventions such as closed thoracostomy. In contrast, grade III RFX can be detected using plain chest radiography. Our study revealed that the risk of dHTX increases with the number of grade III RFX, even in patients who do not initially have HTX. For instance, the nomogram from our study indicates that patients without HTX but with 3 or more grade III RFX, or patients without grade III RFX but with an initial HTX depth of 1.5 cm or more, have a greater than 50% chance of developing dHTX that requires intervention within approximately 6 days of admission. The study included patients hospitalized for more than 24 hours, with intervention-requiring dHTX occurring in 64 cases (9.3%). The majority (n=55, 85.9%) were managed with closed thoracostomy, but 2 of the 3 patients who underwent emergency exploratory thoracotomy died. Given that dHTX can occur suddenly and without warning [14], careful monitoring is recommended for these high-risk groups. We believe our study provides a valuable guideline for the hospitalization of patients with RFX, especially in emergency department settings where chest CT is not available.

Additionally, the nomogram could also be used as a criterion for deciding whether to admit RFX patients who present to the emergency department. Our study results could also inform the design of future prospective studies. Given that numerous studies have already identified the degree and number of RFX, along with the PC degree, as significant risk factors for adverse outcomes [21,23,27], further research involving larger sample sizes is necessary to develop a more reliable predictive model. Nonetheless, our study has several limitations. First, the retrospective design may have inadvertently induced selection bias. This is particularly relevant because our study was based on data collected from a level 1 trauma center where most patients had chest trauma along with other injuries. For this reason, induced sedation, including general anesthesia, is common, and we actively perform closed thoracostomy to preemptively prevent tension HTX or pneumothorax. Patients who underwent closed thoracostomy early in their admission were excluded from the study; however, they might have had more severe injury patterns. This is a major limitation of our study. Although our study focused on patients commonly encountered in the emergency department who have relatively minor injuries—specifically targeting those without HTX on initial CT scans and those with a small amount of occult HTX—and the LASSO regression did not select external thoracic injuries other than chest injuries as risk factors for dHTX, we believe that future meta-analyses of multiple prospective studies will be necessary to address this limitation. Second, RFX patterns were recorded only once based on the initial chest CT scan. Because the degree of RFX displacement changes over time [28], follow-up examinations with a repeat chest CT were necessary; however, we could not perform chest CT scans owing to its cost and safety concerns. Third, to assess model performance, we employed the receiver operating characteristic (ROC) curve and area under the curve (AUC) metrics despite their known limitations [29]. Notably, the ROC-AUC framework did not show meaningful results in terms of either positive or negative predictive value [30]. Nonetheless, to adhere to standard analytical practices for binary classifiers, we utilized the conventional AUC metric because it continues to be the preferred evaluative standard [29]. Finally, we did not conduct external validation. Overall, future multicenter trials and external validations are warranted.

The depth of HTX on initial chest CT and the number of grade III RFX significantly influence the risk of developing dHTX. Based on these findings, we propose a novel nomogram designed for easy application in clinical settings. We believe this nomogram will enable more proactive monitoring of patients at slight risk of developing dHTX. Additionally, it should help in identifying high-risk patients, informing both patients and caregivers, and guiding the development of protocols for future prospective studies. To accurately determine the effect sizes, future large-scale prospective studies are necessary.

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Conflict of interest

No potential conflict of interest relevant to this article was reported.

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