# An investigation on causes of delayed referral of patients with pleural empyema

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## Abstract

**Background:** In the treatment of pleural empyema, medical therapy is typically sufficient for the 1st or 2nd stage. However, surgical intervention becomes the optimal modality in the 3rd stage. A significant number of patients experience delayed diagnosis and treatment, leading to the conversion of non-surgical pleural empyema into complicated surgical empyema.

**Methods:** A cross-sectional study was conducted on patients with pleural empyema who were admitted to NRITLD in Tehran from 2015 to 2016. Initially, 66 patients were selected; however, after the exclusion of 12 patients, a total of 54 patients were included in the study.

**Results:** Delays were attributed to the medical system in 62% of cases and to the patient in 29% of cases. The median (IQR) of the total delay time attributed to the system was 38 (25) days. No significant difference was found in the median of delayed referrals between genders. A significant correlation was observed between the interval of the first and last visit and the interval between the onset of symptoms and chest x-ray (CXR), as well as the interval between the performance of CXR and the insertion of chest tube drainage (CTD).

**Conclusions:** The delay in referral and treatment can be attributed to the patient, practitioners, or both. In this study, it was found that the medical system is the primary cause of delay, primarily due to the long waiting times for admission and operation in hospitals. Patients who experience a delay in CXR and CTD insertion will face a significant delay in referral and their course of treatment. It is suggested that delayed referral could be prevented by providing patients with basic medical education, offering specialized training to general practitioners for early referral, and managing waiting lists effectively.

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**Keywords:** patient referral, delayed referral, self-treatment, pleural empyema

## Introduction

Nowadays, despite significant advancements in medical sciences and equipment, it appears that a majority of patients do not receive timely treatment. Often, patients dismiss their symptoms, attributing them to minor illnesses, which ultimately leads to a significant delay in diagnosis due to their self-diagnosis and self-treatment [1]. Furthermore, the absence of an organized referral system results in treatment delays concerning specialty and subspecialty healthcare services. However, general practitioners, who are trained on the necessity of early referral, are expected to play a pivotal role. A study on the delayed diagnosis of tuberculosis highlighted the importance of training medical staff to improve case detection [2]. Misdiagnosis and incorrect medical pathways by either the patient or the practitioner lead to delays in the treatment process, resulting in irreversible consequences.

Numerous surveys have been conducted regarding the delay in diagnosis of diseases such as lung cancer and breast cancer. A study revealed that patients with lung cancer experience extended delays in diagnosis and pre-surgical assessments [3]. Despite lung cancer being one of the most common

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types of cancer, delayed diagnosis still reduces the chances of early and effective treatment and patient survival [4]. The most crucial factor in the survival of lung carcinoma is associated with the time of diagnosis; thus, screening programs help reduce the mortality rate. Moreover, educating society about clinical symptoms and retraining those involved in first-line therapy are some effective and cost-benefit strategies in this regard [5]. A study demonstrated that a database system and an Integrated Electronic Health Record can assist with the early diagnosis of lung carcinoma and avoid numerous errors in paper-based medical systems, which cause delayed diagnosis [6].

Another study on breast cancer illustrated that the primary reason for delayed diagnosis was practitioners' lack of confidence about the malignant nature of the mass, even before biopsy. It was crucial to note that 6-16% of women with mammary cancer encountered practitioners' delay in diagnosis [7]. Also, it was reported that most of the patients were detected secondary to the incidence of symptoms, not in screening. A delay in diagnosis of 3 to 6 months is associated with a lower survival rate [8]. Another study stated that delayed referral of patients with primary breast cancer is associated with undesirable results [9].

The issues mentioned suggest that two periods of intervals should be considered in the delayed referral of patients with empyema to thoracic surgeons: the delay in the onset of symptoms until referral to a practitioner and the hospital delay [10]. The delayed diagnosis caused by the patient, the practitioner, or the hospital [1] in this study has been classified as follows: the interval between the onset of symptoms and the first referral, the interval between referral and CXR, the interval between the CXR and thoracosynthesis and insertion of the CTD, the interval between the insertion of the CTD and surgery, the interval between the first and the last visit of the practitioner (defined as the last practitioner; the thoracic surgeon of NRITLD who administers the final treatment), the delayed referral of other practitioners to the aforementioned medical service, and ultimately the delay in surgery which is commonplace in referral hospitals such as NRITLD due to a large number of patients on the admission waiting list on one hand and a shortage of medical staff and an inadequate number of operation rooms and ICU beds on the other hand.

Results of a study indicated that patients who followed the pathway of their general practitioners had a faster diagnostic and treatment process in comparison to those who took other ways of their own choice. Despite mild clinical symptoms, it seems reasonable to encourage patients to refer to a practitioner early in order to prevent delayed diagnosis and treatment [11]

Antibiotics are usually administered in patients with the acute stage of empyema, but the drainage catheter is not inserted successfully and timely which results in referral to a thoracic surgeon. Misdiagnosis, administration of unsuitable antibiotics, and unsuitable insertion of the CTD are among the most important survival factors and even progression of empyema. Suitable and early surgical drainage in patients with empyema associates with less morbidity, shorter hospital stay, and longer-term health results. Therefore, more invasive treatment and early referral to thoracic surgeons are advisable in the case of such patients [12].

If pleural empyema patients undergo surgery 4 weeks after the onset of their symptoms, the lung decortication should be carried out by thoracotomy, as an open surgery, instead of thoracoscopy, as a minimal invasive surgery [13].

Considering the relative frequency of delayed referrals and the absence of a comprehensive study in this regard, the aim was to evaluate the causes, latency, and its adverse effects on treatment in order to develop strategies or guidelines to prevent waste of time and money in the future.

## Materials and Methods

This study investigated 66 patients with pleural empyema who were prospectively admitted to the surgery ward from June 2015 to December 2016. Data were collected using a questionnaire. Subsequently, 12 patients were excluded due to their different histologies, leaving 54 patients for the analysis.

The Ethics Committee of NRITLD approved this study. No interventions were made in this study; "the protection code of human subjects in medical research" from Iran's Ministry of Health was considered. As patients' records were utilized, all information was kept confidential [14]. Furthermore, the professional reputation of physicians was protected in cases of both justified and unjustified delays. The extracted data were analyzed using SPSS software. Numbers and median (IQR) indicators were used to describe qualitative and quantitative variables, respectively. The Mann-Whitney U test was employed to compare medians of quantitative variables between two groups, and the Spearman test was used to determine their correlation. A regression model was used to investigate the effect of independent factors (such as length of diagnostic time) on delayed treatment. The level of significance was considered less than 0.05.

## Results

The study included 54 patients, comprising 45 males (83.3%) and 9 females (16.7%), with a mean age of 42.39±14.999. Regarding educational level, 53.7% had not completed high school, 25.9% held a high school diploma, and 20.4% possessed a university degree. A relative response to treatment, including self-treatment or medical treatment, was observed in half of the patients, with all symptoms being studied separately. The most common clinical symptoms were fever (22.2%), chills (18.3%), chest pain (16.1%), shortness of breath (16.1%), and cough (13.09%). A total of 55.6% of patients were referred by a practitioner, while 44.4% chose their own referral pathway and practitioners. More than one-third of patients had experienced self-treatment. Among them, 29.6% had been drug addicts, and 18.5% were diabetic; however, this information was self-reported by the patients and found in their medical files. Particularly in most cases of addiction, patients usually refuse to tell the truth.

Approximately 80% of patients first referred to general practitioners, and the rest referred to specialists, most commonly including general surgeons (27.27%), pulmonologists (26.8%), internists (21.4%), infection specialists (7.1%), and cardiologists (4.5%) before being examined by thoracic surgeons. Nineteen patients who had first referred to a general practitioner, and five others who had first referred to a specialist, continued their course of treatment according to their own individual decision.

In other words, it can be interpreted that 24 patients (44.4%) chose their next practitioner by themselves, regardless of the referral pathway defined by the first practitioner. Additionally, 24 patients who had been first visited by a general practitioner, and six who first referred to a specialist, making a total of 30 patients (55.6%), continued the referral pathway defined by their first practitioners. However, statistical analysis of Chi Square did not show a significant relationship (P-value < 0.001), so only raw data is provided.

Table 1 shows different intervals in the trend of referrals of patients with pleural empyema. It is notable that the median means 50% of patients have experienced that certain interval. For example, 50% of patients referred to a practitioner in less than 2 days after the onset of symptoms. The interval between the first and the last visit refers to the period of time between the first referral to a practitioner and the thoracic surgeon in NRITLD, which is the last visit in this study. Total waiting time refers to the total period of patients' waiting time out of the hospital to be admitted (due to the lack of hospital beds in the surgical ward) and inside the hospital (for pre-op measures and waiting on the overcrowded list of operating rooms).

No special result was obtained regarding patients' jobs, and the only point to mention is that six patients were housewives. A total of 7.4% of patients were discharged with Heimlich and 14.8% with an empyemal catheter. Overall, four patients had non-loculated and 50 had loculated empyema. The latter group is expected to refer to thoracic surgeons more than the former one.

According to Chung et al., if 28 days is considered as delay, patients with a four-week interval between the onset of their symptoms and surgery have a chance to undergo thoracoscopy. In this study, 75% of the patients had a delayed referral (13).

There was no significant difference between

**Table 1:** Description of variables attributed to time intervals using Mean (±Standard deviation) and Median (Interquartile range)

| | N | Mean(±SD) | Median (IQR) |
|---|---|---|---|
| **Interval between the onset of symptoms and the physician visit** | 42 | 9.62(±20.91) | 3 (9) |
| **Interval between the onset of symptoms and CXR** | 43 | 16.58(±22.67) | 10 (15) |
| **Interval between CXR and insertion of CTD** | 35 | 13.51(±21.88) | 5 (7) |
| **Interval between CXR and thoracentesis** | 24 | 6.75(±20.05) | 2 (5) |
| **Interval between insertion of CTD and surgery** | 35 | 21.34(±20.68) | 16 (13) |
| **Interval between the first and the last physician visits** | 42 | 34.81(±36.46) | 20 (28) |
| **Interval between the onset of symptoms and main treatment for insertion of CTD** | 36 | 28.94(±29.75) | 16 (27) |
| **Total main interval** | 43 | 48.05(±33.54) | 38 (25) |
| **Waiting time for hospitalization in the surgical ward (waiting time at home, ER[1] or non-surgical wards)** | 43 | 9.05(±7.80) | 7 (12) |
| **Interval between hospitalization in the surgery ward and the operation** | 28 | 6.43(±5.98) | 6 (7) |
| **Total waiting time in NRITLD for the operation** | 42 | 13.50(±8.15) | 13 (9) |
| **Total delay time** | 43 | 47.65(±32.98) | 38 (25) |
| **Delay time attributed to the patient** | 42 | 9.62(±20.91) | 3 (9) |
| **Delay time attributed to the physician** | 42 | 31.86(±29.98) | 22.50 (12) |

**Table 2:** Comparison of the median intervals between both referral types (practitioner referral & self-treatment) using the Mann-Whitney U test, significance level of 0.05

| | referral type | | | | | | P-VALUE |
|---|---|---|---|---|---|---|---|
| | self-treatment | | | previous practitioner | | | |
| | N | Median | IQR | N | Median | IQR | |
| **interval between the onset of symptoms and the physician visit** | 23 | 2 | 7 | 30 | 3 | 9 | 0.297 |
| **interval between the onset of symptoms and CXR** | 24 | 10 | 15 | 30 | 11 | 17 | 0.814 |
| **interval between CXR and insertion of CTD** | 20 | 7 | 14 | 25 | 4 | 8 | 0.088 |
| **interval between CXR and insertion of thoracentesis** | 13 | 3 | 3 | 16 | 3 | 6 | 0.877 |
| **interval between insertion of CTD and surgery** | 14 | 19 | 12 | 22 | 15 | 8 | 0.205 |
| **interval between the first and the last physician visits** | 24 | 26 | 38 | 29 | 19 | 31 | 0.124 |
| **interval between the onset of symptoms and main treatment for insertion of CTD** | 21 | 20 | 27 | 25 | 17 | 25 | 0.453 |
| **interval between the onset of symptoms and main treatment for operation** | 18 | 42 | 24 | 26 | 35 | 23 | 0.424 |
| **interval between hospitalization in the surgery ward and the operation** | 11 | 8 | 5 | 20 | 5 | 5 | 0.071 |
| **delay** | 17 | 45 | 17 | 25 | 34 | 23 | 0.299 |
| **total waiting time in NRITLD for the operation** | 17 | 13 | 11 | 26 | 13 | 9 | 0.404 |

the median of delayed referrals in men and women (p-value=0.169). To compare the median delayed referrals between educational levels, the Kruskal-Wallis test was performed, and no significant difference was observed (p-value=0.559). Furthermore, when comparing the median of delayed referrals between two types of referrals (self-treatment and whether the first visit was carried out by a general practitioner or a specialist), no significant difference was found (Table 2).

To assess the correlation among time intervals between the first and the last visit of the practitioner, the Spearman correlation coefficient was used. A significant correlation was found in the interval between the onset of symptoms and CXR, and another interval between the performance of CXR and the insertion of the CTD. Moreover, results of the Spearman Correlation test showed a significant association between the interval of CTD insertion and the surgery, considering the waiting time for admission or surgery. The relationship between clinical symptoms and the interval of their onset until referral (to a practitioner) was studied to figure out if types of symptoms played a role in the early referral of patients. Results of the Mann-Whitney U test showed no significant relationship in two steps, with and without the presence of irrelevant data.

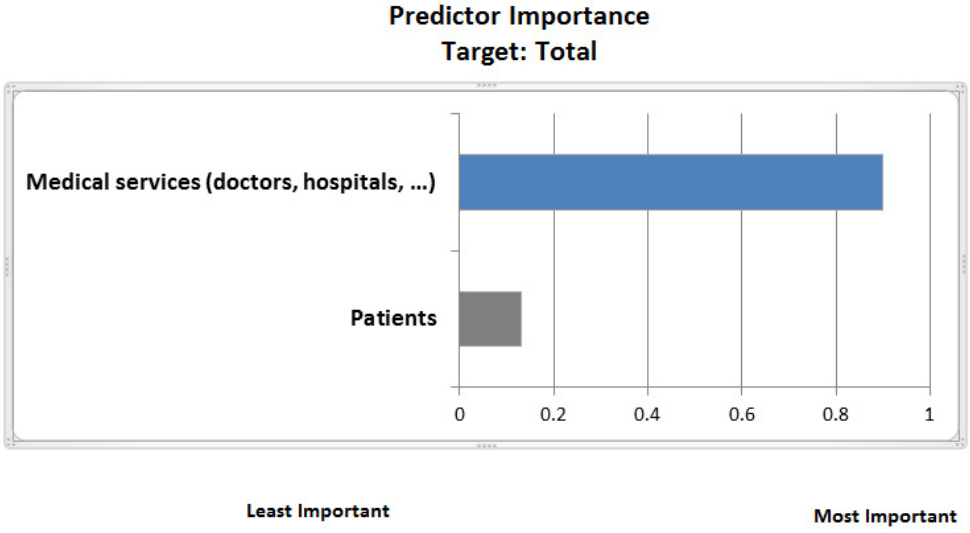
It was challenging to separately identify in which part of the treatment course the patient or the medical system was the contributing factor for delay, since these two factors overlapped each other at some points in the referral trend (from the onset of symptoms to thoracotomy, which is defined as an overall delay in this study). The patient seems to cause a delay from the onset of symptoms to the first visit by a practitioner, which is followed by another delay caused by the medical system from CXR to surgery. Therefore, the intervals between the first visit and CXR overlap each other. Analysis of data by regression revealed a strong correlation between the overall delay and the two variables of delay caused by the patient and the medical system (R=0.70). Analysis of variance was significant (P-value < 0.001), and regression coefficients showed 62% of the whole delay was caused by the medical system and only 29% by the patient (Graph 1).

## Discussion

A total of 54 patients, including 45 males (83.3%) and 9 females (16.7%), participated in the study. Half of these patients responded to treatment, either self-treatment or medical treatment, through the referral trend. Self-treatment, carried out by 29.6% of

**Table 3:** Investigating the correlation of delay (patient, practitioner and total) and the intervals using Spearman's correlation test, significance level of 0.05

| | Patient's delay | | | Physician's delay | | | Total Delay | | |
|---|---|---|---|---|---|---|---|---|---|
| | **N** | **R** | **p-value** | **N** | **R** | **p-value** | **N** | **R** | **p-value** |
| **Interval between the onset of symptoms and the physician visit** | 42 | 1.000 | - | 41 | .032 | 0.844 | 42 | .414 | .006 |
| **Interval between the onset of symptoms and CXR** | 42 | .655 | <.001 | 42 | -.311 | .045 | 43 | .457 | .002 |
| **Interval between CXR and insertion of CTD** | 34 | .066 | .710 | 34 | .579 | <.001 | 35 | .419 | .012 |
| **Interval between CXR and thoracentesis** | 24 | .335 | .109 | 23 | -.098 | .656 | 24 | .173 | .419 |
| **Interval between insertion of CTD and surgery** | 34 | -.023 | .897 | 35 | .665 | <.001 | 35 | .434 | .009 |
| **Interval between the first and the last physician visits** | 41 | .056 | .730 | 41 | .400 | .010 | 42 | .765 | <.001 |
| **Interval between the onset of symptoms and main treatment for insertion of CTD** | 35 | .555 | .001 | 35 | .205 | .237 | 36 | .765 | <.001 |
| **Total main interval** | 42 | .414 | .006 | 42 | .434 | .004 | 43 | 1.000 | - |
| **Waiting time for hospitalization in the surgical ward (waiting time at home, ER or non-surgery wards)** | 42 | p-.101 | .526 | 42 | .341 | .027 | 43 | .171 | .273 |
| **Interval between hospitalization in the surgical ward and the operation** | 28 | .200 | .307 | 28 | .193 | .326 | 28 | .324 | .092 |
| **Total waiting time in NRITLD for the operation** | 41 | -.038 | .815 | 42 | .422 | .005 | 42 | .180 | .254 |




**Graph 1:** the effect of delay caused by the patient and the medical system on the overall delay in the treatment course of pleural empyema

patients in this study, led to the masking of symptoms (e.g., pain relief) and a false sense of recovery. This resulted in delayed referrals at a more advanced stage of the disease, increasing the rate of morbidity and mortality.

Patients with empyema usually refer to general surgeons, internists, pulmonologists, and infection specialists before thoracic surgeons, accounting for more than 83% of first referrals. This indicates that the majority of patients are usually visited by specialists relevant to their diseases. Cardiologists are the next group of specialists to whom 4.5% of such patients refer, which seems justifiable due to the similarity of symptoms to those of cardiac diseases, including shortness of breath and chest pain.

The relationship between the clinical symptoms and the interval of their onset until referral to a practitioner was studied. It is clear that patients themselves play an important role in delayed referral during this period. However, the relationship between types of symptoms and early referral to the medical system was studied in two steps, with and without irrelevant data, which was not significant.

A total of 24 patients (44.4%), (19 first referred to a general practitioner and 5 to a specialist), decided about their next step practitioner individually and without attention to the referral trend. This could be due to patients' overall distrust in the medical system and practitioners. However, it should be noted that the other 30 patients (55.6%) (24 visited by a general practitioner and 6 by a specialist) continued the referral trend defined by their first practitioner.

Considering addiction and diabetes, 29.6% of patients were drug addicts and 18.5% were diabetic according to patients themselves and their medical records. As it is probable that patients avoid telling the truth, more samples are needed to prove the significance of the relationship between addiction, diabetes, and pleural empyema.

A significant correlation was found between the interval of the first and the last visit and the interval between the onset of symptoms and CXR and another interval between the performance of CXR and insertion of the CTD. It can be concluded that when patients have a delay in CXR and CTD insertion, they will face a significant delay in referral and their course of treatment. The interval between CTD insertion and surgery is estimated to be a mean of 21.17 days. However, according to its median, which is 16 days, it can be said that 50% of patients undergo surgery after CTD insertion in less than 16 days, which is a considerable amount of time. The golden time for thoracoscopic treatment of patients with pleural empyema is 28 days (13), but unfortunately, most of this time is wasted as there are always a large number of patients on the waiting list for admission and operation. The interval of CTD insertion and surgery was significantly correlated with patients' waiting time for admission and surgery. This implies that a longer inner-hospital waiting time will lead to a wider interval between CTD insertion and surgery. However, the insufficient number of hospital beds, personnel, and operation rooms add to the problem.

The study re-analyzed data from 39 patients, including 45 males (83.3%) and 9 females (16.7%), with pleural empyema who had undergone thoracotomy. Of these, 43 (79.6%) first referred to a general practitioner, while 11 patients (20.4%) were visited by a specialist at their first referral. Out of the total number of 39 patients, 24 made their own individual decision to refer (44.4%), and 30 were referred by their previous practitioner (55.6%). A history of CTD insertion during the course of treatment was found in 45 patients (83.3%), but not in 9 patients (16.7%). Considering the 28-day delay, it was found that 11 patients (25.0%) had no delay, while 33 patients (75.0%) did. Eight patients (14.8%) were discharged with an empyema catheter and four with a Heimlich catheter (7.4%). Sixteen patients (29.6%) had a positive history of addiction, and 10 (18.5%) were diabetic. Thirty patients (55.6%) had a history of hospital admission in another center, while 24 patients (44.4%) did not.

Statistical analyses revealed that approximately 22% of patients were discharged with an empyema or Heimlich tube to shorten their hospital stay. Most of the patients were treated with muscle relaxants or nutritional supplements, as they had been diagnosed with muscle spasm or fatigue during their referral trend, and 55.6% of them had a history of hospital admission before referring to NRITLD. Therefore, it can be inferred that a lack of adequate awareness among practitioners towards signs of empyema plays a destructive role in the referral and treatment of such patients.

Nine patients had no history of CTD insertion, and 25 had no history of thoracosynthesis. Ten patients did not undergo surgery, 43 underwent thoracotomy, one patient underwent an Eloesser flap, and no patient underwent thoracoscopy. Overall, it can be concluded that due to the delayed referral of patients with empyema, the tendency of the thoracic surgeons at this center, the lack of facilities, and inadequate insurance coverage for thoracoscopy, thoracotomy is considered the surgical choice of treatment for the purpose of performing decortication in such patients.

## Conclusion

In summary, according to the regression coefficients presented in the results, delays in referral and treatment, whether caused by the patient, practitioners, or both, contribute 29% and 62%

respectively to changes in response variables (overall delay). It is evident that long admission waiting lists and prolonged pre-operative waiting times in university hospitals are among the most significant causes of delay. It appears that delayed referral and treatment could be largely prevented by implementing certain measures. These include providing patients with accessible and easy-to-understand medical education, changing the public's incorrect attitude towards self-treatment, offering specialized early referral training to general practitioners working in clinics or non-referral centers, defining a proper referral pyramid for each disease, increasing the number of tertiary referral centers, and managing waiting lists appropriately.

Finally, a more comprehensive, multi-centered study with a larger sample size is recommended to investigate the role of financial issues in the referral trend and treatment course of patients with empyema.

## Conflict of Interests

The authors declare that they have no conflicts of interest.

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