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ORIGINAL ARTICLE

Image-guided catheter drainage of infected pleural effusions

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PURPOSE
To evaluate the safety and efficacy of image-guided drainage of infected pleural effusions.

MATERIALS AND METHODS
The clinical outcomes of 93 patients who underwent image-guided drainage of infected pleural effusions between 1998 and 2003 were retrospectively analyzed. Among the 93 patients, 31 (33.3%) were younger than 16 years of age. In all, 129 catheters (8F–14F pigtail catheters) were placed under ultrasonography (US) or computed tomography guidance. In 27 patients (29.0%) intracavitary fibrinolytic therapy with streptokinase was employed to improve drainage. The patients were followed up during daily rounds and, when drainage problems occurred, catheters were exchanged or repositioned. New catheters were placed for undrained loculations.

RESULTS
The success, failure, and recurrence rates were 92.5% (86/93), 7.5% (7/93), and 6.4% (6/93), respectively. In the pediatric age group the success rate was significantly higher. Intracavitary fibrinolytic therapy significantly improved daily output, but did not significantly reduce drainage duration or hospital stay. There was no significant difference between the successful and failed treatment cases in terms of US findings, gross appearance, or culture positivity. The only major complication was anaphylactic reaction due to intracavitary instillation of streptokinase (n = 1, 1.1%). The 30-day mortality rate was 2%.

CONCLUSION
Image-guided catheter drainage of infected pleural collections is a safe and effective method. Addition of intracavitary fibrinolytic instillation improves drainage, but early intervention prior to collections becoming more complicated remains an important factor in determining prognosis. Non-loculated anechoic collections without septa have a high probability of favorable outcome.

Key words: • *empyema* • *drainage* • *intracavitary fibrinolytic instillation*

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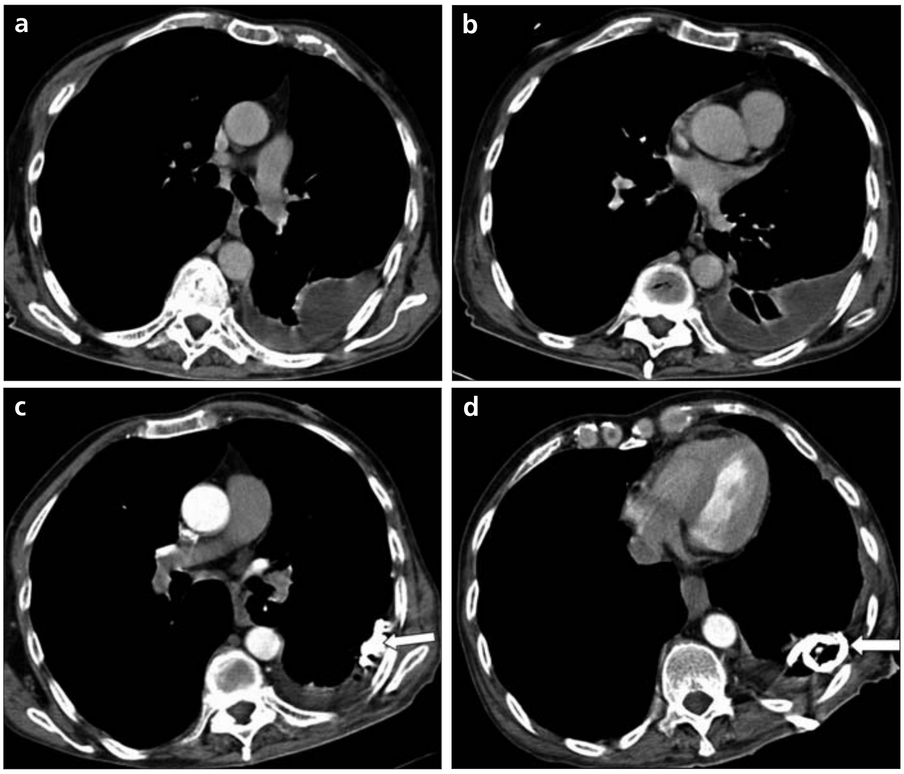
Parapneumonic effusion, which is a frequent complication of pneumonia, can progress to empyema if not properly treated at earlier stages. Prevention of the progression of disease is crucial since empyema has a 20% mortality rate, despite treatment (1). Treatment of parapneumonic effusion requires a multidisciplinary approach in most cases. Typically, percutaneous interventions have been sought when medical measures failed, which has led to surgery when percutaneous interventions have failed. With recent advances in minimally invasive surgical techniques, such as video-assisted thoracoscopic surgery (VATS), morbidity associated with surgical intervention has decreased. Recently, discussions have revolved around the timing (early versus late) and type (percutaneous versus surgical) of intervention to be used for the treatment of parapneumonic effusions. Herein, we present our experience with image-guided percutaneous catheter drainage (IGPCD) of empyemas at a tertiary center and discuss the results in light of the literature.

Materials and methods

Medical records and imaging findings of patients with empyemas who were treated in our department between 1998 and 2005 were retrospectively evaluated. The study included 93 patients with complete records and at least 3 months of follow-up. A retrospective review was conducted after institutional review board approval. Data were collected from patient medical records, and radiology and laboratory databases. Fifty-nine (63.4%) of the patients were male and 34 (36.6%) were female. Average age was 35.7 years (range, 1–80 years) and 31 patients (33%) were younger than 16 years.

In total, 129 locking pigtail catheters were used. In 26 patients (28.0%), more than one catheter was placed simultaneously or consecutively (in 20 patients, 2 catheters were placed, in 3 patients 3 catheters were placed, in 2 patients 4 catheters were placed, and in 1 patient 5 catheters were placed) (Figure). The indications for using multiple catheters were multiple collections in 12 patients, catheter exchange (for improving drainage or due to an occluded catheter) in 4, to replace a dislodged catheter in 4, and to treat recurrences in 6 patients. Catheter size ranged between 8F and 14F.

Intracavitary fibrinolytic instillation (ICFI) was used in 27 patients (29.0%). If satisfactory drainage was not obtained after catheterization, despite a patent catheter and good catheter position, the decision to use ICFI was made. The only agent that was used for ICFI was streptokinase. Intracavitary fibrinolysis was performed with 250,000 IU of streptokinase diluted in 50 ml of normal saline. After administering streptokinase the tube was clamped for 1–4 h, followed by aspiration of the contents. This was done daily for 3 days, but up to 7 times in some patients. Streptokinase was given daily for 3 days using 100,000–250,000 IU in 20–50



A 50-year-old man with multiloculated empyema. Contrast-enhanced CT scans show upper (**a**) and lower (**b**) parts of the empyema. After percutaneous catheter drainage and fibrinolytic instillation, resolution of the multiloculated empyema is observed (**c, d**). Two catheters are in place (*arrows in* **c** *and* **d**).

ml of physiologic saline for children, depending on the amount of pleural fluid.

All but 2 procedures were performed under ultrasonography (US) and/or fluoroscopic guidance. Computed tomography (CT) guidance was used for 2 patients with loculations and no safe access route under US. Monitored anesthesia care (MAC) was administered by an anesthesiologist for all procedures. Additionally, 2% prilocaine was used for local anesthesia. Using an 18 G Chiba needle, access to the pleural cavity was achieved under real-time US guidance. Indications for catheter placement were: 1) purulence of the aspirated fluid; 2) laboratory analysis from previously-aspirated fluid revealing a pH <7.2; 3) presence of microorganisms on Gram stain or positive culture; 4) pleural effusion unresponsive to appropriate antibiotic treatment, without any other source of infection, even in the absence of laboratory data supporting pleural infection. The most dependent portion of a collection was targeted for the catheter position. A 0.035″ Amplatz guide wire was advanced through the needle. After removing the needle, the tract was gradually dilated and a locking pigtail catheter was placed over the wire. The catheter was then connected to an underwater seal drainage system and samples were sent for laboratory analysis.

The outputs of the catheters were recorded. The patients were followed-up during daily rounds and with chest X-rays and chest CTs, when deemed necessary. The catheters were irrigated at least once daily. Patients were brought to the interventional radiology suite for US examination and catheter repositioning or exchange if there was a problem with the catheter.

The terms success, recurrence, and failure were defined as follows:

1. Success: The disappearance of all clinical and laboratory findings related to pleural infection during follow-up of at least 3 months, or at the time of death due to other causes.
2. Failure: The persistence or exacerbation of clinical and/or laboratory findings related to pleural infection that eventually required surgery.
3. Recurrence: The reappearance of clinical and/or laboratory findings of pleural infection on the same side following a temporary period of improvement after catheter removal.

Statistical methods

Fisher's exact test was used for comparing qualitative data. Paired samples t-test and independent samples t-test were used for comparing the means of paired and unpaired samples, respectively. Mann-Whitney U test was used for comparing medians. Statistical analysis was performed with SPSS for Windows, v.11.0.0 (SPSS Inc, Chicago, IL, USA).

Results

Pneumonia was the cause of empyema in 44 patients (47.3%). The etiologies and conditions associated with empyema are summarized in Table 1. The average duration of drainage was 13.6 days (range, 1–66 days).

The success, failure, and recurrence rates were 92.5% (86/93), 7.5% (7/93), and 6.4% (6/93), respectively. Among the recurrences, 3 were treated with recatheterization. Another 3 recurrent empyemas and 4 other patients, including a child with tuberculosis who failed to respond clinically, underwent surgery. The empyema cavities were surgically drained and decortication was performed. There was no statistically significant difference between the success rates of the pediatric and adult groups (P = 0.418, Fisher's exact test). The only failure in the pediatric age group was a 13-month-old patient that presented 2 months after her symptoms began. After 2 recurrences with IGPCD, she underwent surgery for a right middle lobectomy, lower lobe superior segmentectomy, and decortication. In 16 of the patients, image-guided percutaneous pigtail catheter placement was performed due to failed tube thoracostomies. In 15 of these patients success was obtained with IGPCD, but in one patient, image-guided drainage failed as well. This patient had tuberculous pleurisy, and despite IGPCD and anti-tuberculosis medications, required decortication.

When we compared the success and failure groups in terms of US characteristics, gross appearance, and culture positivity of the effusion, we did not find any significant differences between the 2 groups. The presence of loculations, septa, internal echoes, a purulent appearance, or a positive culture result had low positive predictive values, but they all had high negative predictive values for failure in the range of 94.1%–100% (Table 2).

ICFI with streptokinase was used in 27 patients. To evaluate the efficiency of ICFI in improving drainage, we compared the volume of daily drainage on the day before the treatment to that of the day after treatment. The day before treatment, mean daily drainage was 135.0 ml (range, 0–500 ml; SD, 175.3), which increased to 422.6 ml (range, 0–1,800 ml; SD, 439.5). This was a statistically significant increase (P = 0.002, paired samples t test). The median duration of catheterization (after the first dose of intracavitary streptokinase for the group treated with ICFI) was 8 days for both groups of patients, and the difference was not statistically significant (P = 0.439, Mann-Whitney U test). When the overall length of catheterization (from the start of catheterization, not instillation of streptokinase) was compared, the length of catheterization was longer in the ICFI group (13 days vs. 8 days), but again there was no statistically significant difference (P = 0.122, Mann-Whitney U test). When the 2 groups were compared in terms of gender, mean age, proportion of pediatric patients, loculation, septa, internal echoes, and recurrence and success rates, there was a significant difference between the 2 groups only in the proportion of patients who had septa in their collections, which was higher in the ICFI group (Table 3).

There was one treatment failure in the group treated with ICFI. This was a patient who had a failed attempt at drainage without image-guidance prior to being referred to interventional radiology. We initially placed a 14 F catheter and then removed the catheter when drainage fell below 20 ml/day, but the collection recurred. After 2 other recurrences and drainages, the patient eventually underwent decortication.

Complications were seen in 11 patients (11.9%). Catheter dislodgement was seen in 4 patients (4.3%). While catheters were replaced in 3 of these patients, a new catheter placement was not considered for one patient that showed no evidence of residual fluid on US. One patient (1.1%) had a kinked catheter and 3 others (3.2%) had occluded catheters that were replaced with new ones. Two patients (2.2%) who had empyema as a result of infected malignant pleural effusion had pneumothorax due to trapped lung during follow-up. After the infection cleared, the catheters were removed and the patients did not have

Table 1. Etiologies and associated conditions of the patients

	n	%
Pneumonia	44	47.3
Malignancy/malignant effusion	15	16.0
Secondary infection of pleural effusion	14	15.1
Primary empyema	6	6.5
Infected hemothorax	5	5.4
Tuberculosis	5	5.4
Lung abscess	4	4.3
Total	93	100.0

Table 2. Distribution of ultrasonographic, macroscopic, and microbiologic characteristics of pleural fluid in the success and failure groups

	Failure (n = 7)	Success (n = 86)	P value	PPV for failure	NPV for failure	Sensitivity	Specificity
Loculation	3	22	0.381	12.0%	94.1%	42.9%	74.4%
Septa	6	59	0.670	9.2%	96.4%	85.7%	31.3%
Internal echoes	7	77	1.000	8.3%	100%	100%	10.4%
Purulent appearance	6	60	0.669	9.1%	96.2%	85.7%	30.2%
Positive culture	4	38	0.697	10%	94.1%	57.1%	55.8%

PPV: positive predictive value
NPV: negative predictive value

Table 3. Comparison of patient demographics, ultrasonographic features of pleural fluid, and procedure success rates between the intracavitary fibrinolytic instillation (ICFI) and non-ICFI groups. Numbers in parantheses denote total number in the subgroup.

	ICFI	Non-ICFI	P value
Male	18 (27)	41 (66)	0.814
Mean age (years)	36.35	35.39	0.867
Pediatric patients (<16 years of age)	8 (27)	23 (66)	0.809
Loculation	8 (27)	17 (66)	0.798
Septa	25 (27)	40 (66)	0.002
Internal echoes	25 (27)	59 (66)	1.000
Median duration of catheterization (days)	8	8	0.439
Median overall duration of catheterization (days)	13	8	0.122
Recurrence	1 (27)	5 (61)	0.668
Success	26 (27)	60 (66)	0.669

recurrence of empyema. One patient (1.1%) had a severe allergic reaction with fever, tremors, and bronchospasm due to ICFI with streptokinase, but he responded to pharmacological treatment and did not require intubation.

The 30-day mortality rate was 2%, but these deaths were not related to empyema. One patient who had laryngeal carcinoma died of probable aortic rupture and the other died due to cardiopulmonary arrest 1 day after surgery to repair a bronchopleural fistula.

Discussion

The cause of a significant proportion of pleural infections is pneumonia, but infection can develop in the pleural space without an underlying pneumonia (primary empyema) (1) or as a result of secondary infection of pleural fluid that develops due to other causes, such as heart or kidney failure, malignancy, or hemothorax. Treatment of infected pleural fluid collections is not always straightforward and usually requires a multidisciplinary approach. Treatment options include a conservative approach with antibiotic therapy, use of chest drains, ICFI, and VATS, and more aggressive surgical intervention with thoracotomy and decortication (2).

Parapneumonic effusions are the accumulation of pleural fluid associated with ipsilateral pneumonia. They are referred to as uncomplicated parapneumonic effusions when they are not infected and as complicated parapneumonic effusions when invaded by an infectious agent. At this stage, treatment involves drainage or sometimes decortication. The term empyema is used when the macroscopic appearance of the fluid is consistent with pus (3). The later the stage of the parapneumonic effusion, the more complicated the treatment.

Fibrin plays an important role in the pathophysiology of parapneumonic effusions. In later stages, surgical treatment may be required as a result of inefficient drainage due to fibrin deposits and the gelatinous nature of the fluid. Streptokinase was the first fibrinolytic used in the treatment of pleural effusions (4). Disadvantages of streptokinase are febrile allergic reactions and antibody-mediated deactivation (5). We had to use streptokinase mainly due to economic reasons, despite its side effects. The patient who had a severe allergic reaction responded to pharmacological therapy and did not require intubation. Newer agents, such as urokinase and tissue plasminogen activator (Alteplase®), are not associated with such allergic complications (6, 7).

A randomized, double-blind study by Bouros et al. demonstrated the efficacy of urokinase in the treatment of loculated pleural effusions (8). This study showed a significantly higher drainage volume during intracavitary fibrinolytic treatment compared to the group of patients that received intracavitary normal saline instillation. When urokinase was compared to streptokinase by the same group in another study, both agents were found to be effective, but urokinase was associated with fewer complications (9). They concluded that with fewer complications and only slightly higher cost, urokinase could be the drug of choice. Various other researchers reported improved drainage after intracavitary fibrinolytic instillation, both in adults and children (7, 10–15). There are recent controlled studies reporting positive results with fibrinolytic treatment, in terms of radiological improvement, shorter drainage period, shorter hospital stay, reduced need for invasive treatment, or higher success rate (8, 16–19). On the other hand, one recent multicenter, randomized prospective study compared ICFI with normal saline and did not find any significant difference in mortality, surgery rate, radiographic result, or hospital stay (20). However, imaging guidance was not used in that study, and all stages of empyema were included in the study, which may have affected the response to treatment. Tokuda et al., in their recent meta-analysis, reviewed series that compared drainage and fibrinolytic treatment (21). They concluded that although the data provided no evidence of the benefit of intrapleural fibrinolytic therapy, selected patients could still benefit from the treatment.

In our series, there was significant improvement in the daily drainage volume after ICFI; however, we did not find any significant difference in the duration of catheter placement between the group that was treated with ICFI and the group that was not. Although it did not reach significance, when the overall catheter placement duration was considered, the group that received ICFI had longer median catheter placement. This was probably due to selection bias as a result of administering ICFI treatment only to more complicated effusion cases. The significantly higher proportion of septated effusions in the ICFI group supports this conclusion. This bias probably also prevented the occurrence of a significant difference between the 2 groups in success rates. Currently, we prefer using ICFI earlier in the course of treatment.

When large-bore chest tubes are placed without imaging guidance, success rates of less than 50%, sometimes as low as 6%, have been reported (22–26). Higher success rates have been reported when imaging guidance (US or CT) was used for pigtail catheters (27–30). Obviously, imaging guidance has advantages, such as the ability to direct a catheter in a loculation and to place as many catheters as required, depending on the number of loculations. It has been emphasized in the literature that correct positioning of the chest tube is more important than size (31). Furthermore, pigtail catheters have the advantage of larger fenestrations, despite their smaller diameter, and do not occlude completely when kinked, unlike a conventional, stiff large-bore tube, resulting in better patient mobilization (32). In our series, 15 of 16 patients with a previously unsuccessful treatment attempt with non-image-guided chest tube placement had favorable outcomes with IGPCD. The only patient with an unsuccessful response was a patient with tuberculous pleurisy. The value of aspiration (33) or drainage in tuberculous pleurisy is controversial, but 4 of our 5 patients with this entity had a good outcome with drainage, together with anti-tuberculous treatment. Frequent irrigation, checking residual fluid with chest X-rays, CT, or US, and repositioning the catheter under fluoroscopy (with or without breaking the septa) are some of the measures that can decrease the incidence of occlusion, especially in fibrinopurulent and empyema stages. When ICFI is added to the drainage, success rates as high as 100% have been reported for image-guided chest tube drainage, both in adults and children (7, 34). Improved success rates in the range of 56%–63% have been reported when ICFI is added to non-image-guided drainage (11, 35, 36). Both methods are less effective in empyemas.

The mean catheter placement duration in our series was 13.6 days. The reason for this relatively long time period might have stemmed from the fact that the patients referred to us were mostly late cases. Another contributing factor may have been that the threshold for seeking a minimally-invasive or aggressive surgical approach was not very low at our institution, especially for adult patients. Therefore, catheter drainage is given a chance to work before proceeding to a more invasive approach. This strategy may increase the duration of catheter placement and hospitalization, but on the other hand, it may help to avoid unnecessary surgery in patients who can be treated by drainage only. Evidently, close follow-up of patients and the quick correction of problems (as catheter occlusion) are mandatory for minimizing drainage duration. We did not evaluate the length of hospital stay as an outcome measure, which was long, mostly due to comorbidities, but with little correlation with the duration of drainage.

The timing and indications of surgical intervention for parapneumonic effusion have been the subject of active debates, which are based on the comparison of non-surgical measures, including chest tube drainage and antibiotic treatment, and surgical interventions. However, the comparisons are usually made with series in which imaging guidance was not used in the chest tube groups. Kalfa et al. retrospectively compared the results of children that underwent early thoracoscopic decortication (latest was 4 days after diagnosis) to those of late thoracoscopic surgery cases (37). They found shorter operative time and postoperative hospital stay, as well as fewer technical difficulties and complications, in the early VATS group. They concluded that VATS should not be delayed for more than 4 days in cases unresponsive to drainage. A randomized study also compared immediate VATS to 3 days of fibrinolytic therapy (38). The authors found shorter drainage times and hospital stays in the immediate VATS group. In both of these studies the sample sizes were small and imaging guidance was not used for chest tube placement. Immediate use of VATS can be justified in small children if general anesthesia is required for chest tube placement to prevent another procedure in case of failure; however, we think, especially in adults, that an initial trial of chest tube drainage with fibrinolytic instillation for a week should be attempted until proven unwise by a well-designed study comparing image-guided catheter drainage (and early ICFI) with early VATS. The cut-off for defining failure in chest tube drainage and fibrinolytic therapy varies, but is generally accepted that either thoracoscopic or open surgery is indicated in cases of persistent fever and sepsis beyond 5–8 days of treatment (1, 39).

Two patients in our series died within 30 days of the procedure due to comorbidities. There was no mortality related to sepsis.

While analyzing parapneumonic effusions in children, one should be aware of the differences between adult and pediatric cases. In contrast to adults, children rarely have underlying lung disease or co-morbidity, factors that worsen the prognosis in adults. Therefore, the final outcome is usually excellent (39). The British Thoracic Surgery (BTC) guidelines emphasize that there is no place for routine biochemical analysis of pleural fluid in guiding therapy in children (39). Epaud et al. reported that chest-tube insertion (with VATS) should be restricted to the most voluminous and loculated pleural empyema causing mediastinal shift, respiratory distress, and/or uncontrolled septic situations (40). The only failed drainage case in our pediatric age group was a patient that presented 2 months after her symptoms began.

All 5 patients with tuberculosis in our series received anti-tuberculosis medications along with IGPCD and 4 of them had a successful outcome. The overall success rates of IGPCD were 96.7% and 90.3% in children and adults, respectively, but the difference between the 2 age groups was not statistically significant.

We investigated the value of radiological findings (loculation, septa, and internal echoes), gross appearance, and culture positivity of aspirated pleural fluid in predicting failure of IGPCD. When we compared the proportions of patients that had collections with loculation, septa, internal echoes, grossly purulent and culture-positive fluid between the successfully-treated patients and the patients with failed drainage, we did not find any statistically significant difference. These parameters had low positive predictive values, but high negative predictive values for failure. Although Shankar et al. found US to be useful in predicting the likelihood of image-guided drainage of empyema (without ICFI) in their series of 85 patients with pleural infection, other results conflict with theirs (41). Kearney et al. reported that CT and US findings were not able to predict failure of chest tube drainage and ICFI (42). In light of the current knowledge, we can conclude that we currently do not have a good method for predicting which patients will have failed drainage based on radiological or microbiologic characteristics of pleural fluid, as some seemingly very complicated effusions can respond well to image-guided percutaneous drainage, especially with the addition of ICFI. However, in cases of simple collection without a purulent appearance, one can expect a higher likelihood of successful drainage.

In conclusion, image-guided catheter drainage of infected pleural collections is a safe and effective method. A failed attempt with a large-bore chest tube should not preclude another attempt with IGPCD, since successful treatment of infected pleural fluid collections can be achieved with percutaneous treatment following unsuccessful large-bore tube thoracostomies. The addition of ICFI improves drainage, but early intervention before collections become more complicated is an important factor in determining prognosis. Anticipating drainage failures based on the US or macroscopic appearance of pleural fluid is not possible; however, non-loculated, anechoic collections without septa have a high probability of favorable outcome.

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