Experience with indwelling pleural catheters in the treatment of recurrent pleural effusions

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***Abstract*:** Recurrent pleural effusions are frequently encountered in clinical practice. Whether malignant or nonmalignant, they often pose a challenge to the practicing clinician. When they recur, despite optimum medical therapy of the underlying condition and repeated thoracenteses, more invasive definitive approaches are usually required. Since its introduction in 1997, the PleurX catheter became the preferred method to treat recurrent malignant pleural effusions. Since then, a number of publications have documented its utility in managing recurrent nonmalignant pleural effusions. The purpose of this paper is to review the use of the PleurX catheter in recurrent pleural effusions.

Keywords: indwelling pleural catheter, recurrent pleural effusions, malignant pleural effusions, non-malignant pleural effusions

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Introduction

Recurrent pleural effusions (RPEs) are encountered fairly often in clinical practice. In general, these effusions could be divided into two categories: malignant pleural effusions (MPEs) and nonmalignant pleural effusions (NPEs) [Bhatnagar and Maskell, 2015]. In the US, breast and lung cancers are the most common etiologies for MPEs [Chetty, 1985; Bertolaccini *et al.* 2007], whereas congestive heart failure (CHF) and cirrhosis are responsible for most cases of recurrent NPEs [Thomas and Lee, 2013].

In general, treatment of the etiology with or without a therapeutic thoracentesis precipitates a significant relief of symptoms and prevents recurrences of most pleural effusions [Rahman *et al.* 2004; Tarn and Lapworth, 2004; Froudarakis, 2008]. In some instances, however, these effusions are refractory to medical therapy and recur despite optimal medical management of the underlying disease and repeated thoracenteses [Rahman *et al.* 2004; Roberts *et al.* 2010]. In those instances, more aggressive measures are needed to assure symptom control and to prevent frequent recurrences. Beside repeated thoracenteses, the main other therapeutic options to manage RPEs include chest-tube thoracostomy with chemical pleurodesis, surgical pleurodesis, or placement of an indwelling tunneled pleural catheter (IPC) or PleurX catheter (PC) [Brubacher and Gobel, 2003; Laws *et al.* 2003; Koegelenberg and Vorster, 2015].

Since its FDA approval in 1997, the IPC became the preferred method for managing recurrent MPEs on an outpatient basis [Brubacher and Gobel, 2003]. Different studies have shown that it is at least as effective as chest tube and chemical pleurodesis in controlling MPEs [Putnam *et al.* 1999, Blaukovitsch *et al.* 2011], and that it is the preferred method to treat MPEs associated with trapped lung [Efthymiou *et al.* 2009]. In addition, since our initial report on the use of the IPC in the management of recurrent NPEs [Chalhoub *et al.* 2006], other authors have reported on their experience with IPCs in managing recurrent NPEs [Davidoff *et al.* 1983; Mercky *et al.* 2010; Srour *et al.* 2013] the purpose of this review is to describe the experience with the IPC in the management of RPEs.

Technique and catheter characteristics

The IPC is a 15.5 Fr silicone catheter that is 66 cm long. Some of its characteristic features include: soft silicone shell, favoring more comfort than a stiff chest tube, one-way safety valve on the

outside end, allowing needless access, multiple-side beveled holes allowing fluid drainage, and a polyester cuff at the exit site allowing tissue ingrowth to keep the catheter in place and to decrease the incidence of infection. It is usually placed under local anesthesia with or without conscious sedation [Warren *et al.* 2008a; Bhatnagar and Maskell, 2015]. The basic procedure entails the subcutaneous tunneling of the catheter between two incisions and then placement of the catheter into the pleural cavity using a special introducer sheath. The pleural fluid is then drained daily, or every other day, using a special vacuum bottle that connects to the catheter [Putnam *et al.* 2000; Warren *et al.* 2008].

The indwelling pleural catheter and malignant pleural effusions

Introduction

Since its introduction into medical practice, the IPC has gained popularity in the management of recurrent MPEs. The first study to describe the experience with the IPC in the management of MPE was conducted by Putnam and colleagues [Putnam *et al.* 1999]. The study was published in 1999 and included a total of 144 patients, 96 of whom were treated with the IPC, whereas 48 patients were treated with chest tube and doxycycline pleurodesis. The median survival was similar in both groups, but the group treated with the IPC had a significantly shorter hospital stay; 1 day compared with 6.5 days. Successful pleurodesis occurred in 46% of the IPC group and in 56% of the chest tube and doxycycline sclerotherapy group. Recurrent significant pleural effusions developed in 13% in the IPC-treated group compared with 21% in the doxycycline sclerotherapy-treated group [Putnam *et al.* 1999]. Since that study, multiple studies were published that confirmed the utility of IPCs in the management of MPEs [Smart and Tung, 2000; Suzuki *et al.* 2011; Gilbert *et al.* 2015].

In a similar study, Davies and colleagues compared chest tube with talc pleurodesis to IPC for the treatment of MPEs [Davies *et al.* 2012]. A total of 106 patients were included in the final data analysis, 52 patients underwent IPCs, whereas 54 patients had a chest tube with talc pleurodesis. Dyspnea improved in both groups in a similar fashion at 42 days of the intervention. At 6 months, however, the IPC group experienced significantly more dyspnea improvement compared with the chest tube and talc pleurodesis group [Davies *et al.* 2012]. There was no difference in quality of life between both groups. In a similar fashion to Putnam's initial study, the length of stay was significantly shorter in the IPC group compared with the chest tube and talc pleurodesis group; a median of 0 days in the IPC group compared with 4 days in the talc group. There were more patients in the talc group who required further pleural intervention compared with the IPC group; 22% compared with 6%, respectively. In contrast, however, there were more adverse events in the IPC group compared with the talc group; 40% compared with 13%, respectively [Putnam *et al.* 1999; Davies *et al.* 2012].

Quality of life after indwelling pleural catheter placement

The main study that addressed quality of life after IPC placement was published in June 2014. In that study, Ost and colleagues evaluated quality-adjusted survival in 266 patients who received IPC for MPEs [Ost *et al.* 2014]. Quality of life, measured by SF-6D did not differ significantly after IPC placement. Patients who were given chemotherapy or radiation after IPC insertion and those who were more dyspneic at baseline, however, had greater improvement in utility at one month. Dyspnea, measured by the Borg Dyspnea Scale, improved significantly after IPC insertion at 1 month, and this improvement remained statistically significant at 12 months. 58.6 patients died at a median follow up of 3.5 months (range 0–14.5 months) [Ost *et al.* 2014]. Using multivariate analysis, factors that predicted longer survival included: older age, patients treated with chemotherapy or radiation after IPC insertion, patients with less shortness of breath, and patients with better quality of life.

Underlying malignancies

In the US, the most common underlying malignancies leading to IPC placement are breast and lung cancers [Johnston, 1985; Antony *et al.* 2001; Bhatnagar and Maskell, 2015]. In addition, the IPC has been placed for almost all kinds of malignancies leading to MPEs including gynecologic and hematologic malignancies, mesotheliomas, as well as different kinds of solid tumors [Warren *et al.* 2008; Gilbert *et al.* 2015].

Indwelling pleural catheter for hematologic malignancies

One paper reviewed the use of IPC for hematologic malignancies [Gilbert *et al.* 2015] 91 patients were included in the final analysis. Lymphoma represented the most common malignancy (62%), followed by leukemia (21%), and lastly multiple myeloma (13%). There was no predilection to either side of the chest, and 7% of the patients had bilateral IPCs. The mean time to IPC removal was 89.9 days (range 2–867 days). Death was the most common reason for IPC removal (58.2%), followed by spontaneous pleurodesis (23.1%). IPC was removed in three patients (3.3%) secondary to pain. Empyema occurred in 7.7% in that cohort, with *Staphylococcus aureus* growing in the majority of cultures (71.4%). A total of 57% (four out of seven) patients with empyema required additional interventions to treat the pleural infection in addition to the removal of the IPCs. There was no mortality reported when additional intervention was performed (thoracotomy, video-assisted thoracoscopy, and chest-tube thoracostomy). In contrast, 43% (three out of seven) patients did not undergo additional interventions and had a mortality of 66.6% (two out of three) [Gilbert *et al.* 2015].

Indwelling pleural catheter-related complications

Commonly described complications related to IPC placement for MPEs can be divided into two main categories: the first includes those complications that occur during the placement of the catheter, such as pneumothorax, misplacement, and bleeding [Wachsman *et al.* 2007], and the second category includes those related to the presence of a pleural catheter for a prolonged period of time [Cases *et al.* 2009; Van Meter *et al.* 2011]. These complications include infection at the site of placement, empyema, prolonged leak at the entry site, catheter blockage, kinked catheter, dislodged catheter, persistent pain or discomfort, suboptimal drainage secondary to malposition of the catheter or loculation formation, and incomplete re-expansion of the lung [Nasim *et al.* 2012]. There are no patient-related factors that can predict a particular kind of complication resulting from pleural catheter placement. In a retrospective chart review analysis of patients who developed symptomatic pleural loculations after IPC placement, 66 patients were treated with intra-pleural fibrinolytic therapy (urokinase, streptokinase, or tissue-plasminogen activator) [Thomas *et al.* 2015]. Successful intervention occurred in 93% of patients defined by increased fluid drainage. Dyspnea improved in 83% of patients. Two patients developed significant pleural hemorrhage (3%). No mortality was reported secondary to intra-pleural fibrinolytic therapy [Thomas *et al.* 2015].

Factors predicting successful pleurodesis

One study investigated factors that can predict successful pleurodesis and catheter removal in MPEs [Warren *et al.* 2008b]. In that study, Warren and colleagues looked at primary tumor site, presence of trapped lung, results of cytological examination of the pleural fluid, and prior chest irradiation as potential factors to predict catheter removal and spontaneous pleurodesis. The study included a total of 295 IPCs placed for 263 patients. A total of 58.6% of the catheters were removed with an average indwelling time of 29.4 days. Patients with breast cancer and gynecologic malignancies were more likely to have the catheter removed compared with patients whose catheters were placed for other types of malignancies. Positive cytological examination of the pleural fluid was associated with increased likelihood of catheter removal, as well as complete re-expansion of the lung after the catheter placement. In addition, patients with no history of chest wall irradiation were more likely to have their catheter removed compared with patients with chest wall irradiation [Warren *et al.* 2008b].

Indwelling pleural catheter and trapped lung

IPCs have also been used successfully in the management of MPEs associated with trapped lung. In a study that evaluated the use of IPCs in radiologically or surgically proven trapped lung, 116 patients underwent IPC placement. The authors reported on symptomatic relief, mobility, and ease of management following placement of the catheter [Efthymiou *et al.* 2009]. Patients who completed the questionnaires reported 'moderately' and 'very satisfied' in improved mobility and symptomatic relief, and 'slightly' and 'moderately satisfied' in ease of management after catheter placement [Efthymiou *et al.* 2009]. Complications reported in the setting of trapped lung were usually mild and self-limited. Pain developed in 35% of instances and it was commonly mild and transient (resolving in less than 3 days, on average). No catheter was removed as a consequence of pain. Pericatheter leakage was

Table 1. PleurX catheter and benign pleural effusions.

	Number catheters (Patients)	Complications *n* (%)	Time to pleurodesis mean/ median(IQR)	Satisfaction n (%)	Improvement *n* (%)	Absence of recurrence *n* (%)
Murthy (39)	11 (11)	4 (7)	– (5–330)	–	50 (86)	(95)
Herlihy (40)	5 (5)	3 (60)	– (30–450)	5 (100)	5 (100)	2 (40)
Vakil *et al*. [2010]	12 (9)	2 (16)	– (35–190)	–	11(91.6)	11 (91.6)
Chalhoub *et al*. [2011]	23 (23)	1 (4.3)	110.8 (–)	23 (100)	23 (100)	23 (100)
Parsaei *et al*. [2006]	45 (42)	9 (20)	– (1–429)	–	38 (84)	39 (87)
Borgeson *et al*. [2009]	23 (22)	4 (16)	109 (–)	–	–	23 (100)
Srour *et al*. [2013]	43 (38)	13 (34)	66 (34–242)		37 (97)	

N, number; IQR, interquartile range.

reported in 13% of cases and it was self-limited, with no patients requiring intervention to stop the leak. Catheter occlusion and displacement, requiring replacement, occurred in 4% of patients only [Efthymiou *et al.* 2009].

The indwelling pleural catheter and nonmalignant pleural effusions

Introduction

Recurrent NPEs are frequently encountered in clinical practice. These effusions can sometimes recur despite optimum and aggressive medical therapy for the underlying etiology. In the US, the two most common etiologies for recurrent NPEs are CHF and cirrhosis causing hepatic hydrothorax (HHT) [Alberts *et al.* 1991; Hunt *et al.* 2009]. Since its introduction as a therapeutic modality for malignant pleural effusions, the IPC quickly became the preferred choice among physicians treating these effusions [Suzuki *et al.* 2011]. Soon after, the IPC was also investigated and tried for the management of recurrent NPEs, and different papers and case series emerged describing its use and utility in managing recurrent NPEs [Parsaei *et al.* 2006].

Congestive heart failure and cirrhosis

The largest four series describing the experience with the PleurX catheter for the management of recurrent NPEs are included in Table 1. The most common diagnoses leading to placement of IPC in NPEs were CHF and cirrhosis. In the three studies that documented the mean time to pleurodesis [Efthymiou *et al.* 2009; Chalhoub *et al.* 2011; Srour *et al.* 2013], the average mean time was 95 days. The mean incidence of complications was 18.5%, ranging from 4.5% in Chalhoub's series, to 34% in Srour's. Commonly described complications included site infection (one patient), empyema (two patients), symptomatic loculations (two patients), catheter-valve leak (one patient), and catheter occlusion (two patients). Other reported complications included intractable pain, pneumothorax, and seroma. In Srour's report there were five moderate-to-large pneumothoraces but those were thought to be related to trapped lung (pneumothorax *ex vacuo*) [Srour *et al.* 2013]. In the series that described symptom relief, dyspnea significantly improved in 84–100% of patients. The rate of successful spontaneous pleurodesis ranged 29–100%.

Electrolyte imbalance

In NPEs, IPCs are usually placed for large and refractory transudative pleural effusions and are usually left in place for a long period of time, where they are drained on a regular basis [Parsaei *et al.* 2006; Borgesen *et al.* 2009; Chalhoub *et al.* 2011; Srour *et al.* 2013]. With repetitive transudative fluid drainage, there is theoretical risk of electrolyte or fluid imbalances. This potential complication was reported in two patients with HHTs that were treated with chest tubes [Runyon *et al.* 1986]. In the report by Chalhoub, however, where the electrolytes were examined in 23 patients with NPEs who received IPCs, no significant electrolyte imbalances were found [Chalhoub *et al.* 2011]. Five patients required adjustment in their potassium supplementation, but the diuretic dosage was not altered. There was no incidence of hypotension related to repetitive drainage [Chalhoub *et al.* 2011].

Indwelling pleural catheter and pleural effusions after lung transplantation

Another potential area in which IPC proved effective is in the management of chronic pleural effusions occurring after lung transplantation [Vakil *et al.* 2010]. In nine lung-transplant recipients, 12 IPCs were placed. In 11 out of the 12 IPCs, the desired outcome was achieved, defined as resolution of the pleural effusion and adequate palliation of lung entrapment. In the setting of lung entrapment after lung transplantation, the median time to removal of the catheter was 86 days. Catheter-related complications included one hemothorax and one empyema [Vakil *et al.* 2010].

Indwelling pleural catheter in chronic pleural infection

Davies and colleagues reported the successful use of IPC in two patients with chronic pleural infection, where other therapeutic modalities failed [Davies *et al.* 2008]. In that report, both patients achieved pleurodesis, and the catheters were eventually removed, without evidence of recurrence of the pleural infection.

Mechanism of pleurodesis

The exact mechanism by which IPC achieves pleurodesis is neither well understood nor studied. The mechanism is thought to be related to an inflammatory reaction and adhesion formation in response to the presence of the catheter inside the pleural cavity. With repetitive drainage, an inflammatory reaction to a foreign object inside the pleural cavity occurs, leading to pleural symphysis [Chalhoub *et al.* 2011]. One advantage of the pleural catheter over a chest tube is the fact that it is less stiff, allowing for increased free movement inside the pleural cavity, and thus, direct contact with more pleural surface as the catheter sweeps inside the pleural cavity [Chalhoub *et al.* 2011].

Conclusion

IPC is proven to be the preferred choice for treating MPEs, and offers a successful and well tolerated outpatient therapeutic option. In addition, after multiple case series describing its successful use in NPEs, it seems that IPC is also a reasonable alternative in managing recurrent NPEs, especially those secondary to CHF, when optimum medical therapy fails. In this setting, it assures pleurodesis on an outpatient basis, with what appears to be a low complication rate and good patient satisfaction. Prospective studies are needed, however, to compare the IPC with other therapeutic modalities in NPEs.

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