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Indwelling pleural catheter for malignant pleural effusions – our experience

Uporaba trajnega drenažnega plevralnega katetra pri malignih plevralnih izlivih – naše izkušnje

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Abstract

Background: An indwelling pleural catheter (IPC) is a definitive palliative treatment option for symptomatic malignant pleural effusion (MPE). The purpose of our study was to analyze the applicability and safety of IPC in our patients with recurrent MPE.

Methods: In this single-centre retrospective cohort study, we included 105 patients with MPE, in whom IPC was inserted between April 2009 and July 2017 at the University Clinic Golnik. We analyzed patients' characteristics, indications for IPC insertion, post-interventional complications, and the occurrence of pleurodesis.

Results: The most common aetiologies of MPE in our patients were lung cancer (59.0%), mesothelioma (9.5%), breast cancer (6.7%), and ovarian cancer (4.8%). The indications for choosing IPC over pleurodesis were lung entrapment in 50 (47.6%) cases, poor performance status, short life expectancy or comorbidities in 50 (47.6%) cases, and patients with prior talc pleurodesis failure in 5 (4.8%) cases. Complications occurred in 14 (13.3%) patients: catheter blockage in 7, dislodgement in 3, peri-catheter leakage in 2, and infection in 2 patients (empyema in one patient and cellulitis in one patient). Pleurodesis with subsequent catheter removal was achieved in 10 (9.5%) patients.

Conclusion: IPC is a safe and efficient option for a definitive palliative treatment of MPE.

Izvleček

Izhodišča: Vstavitev trajnega drenažnega plevralnega katetra (TDPK) nudi možnost trajnega paliativnega zdravljenja malignega plevralnega izliva (MPI). Namen naše raziskave je oceniti uporabnost in varnost zdravljenja naših bolnikov s TDPK pri ponavljajočih se MPI.

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Ključne besede: karcinomatoza plevre; dispneja; zapleti; paliativno zdravljenje; plevrodeza

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Metode: V retrospektivno kohortno raziskavo smo vključili 105 bolnikov z MPI, pri katerih smo med aprilom 2009 in julijem 2017 na Univerzitetni kliniki Golnik vstavili TDPK. Analizirali smo demografske podatke, indikacijo za vstavitev TDPK, zaplete in delež spontane plevrodeze.

Rezultati: Med pogostejšimi vzroki MPI pri vključenih bolnikih so bili pljučni rak (59,0 %), mezoteliom (9,5 %), rak dojke (6,7 %) in rak jajčnikov (4,8 %). Razlog za vstavitev TDPK namesto opravljene plevrodeze je bil nepopolno razpenjanje pljuč pri 50 (47,6 %) bolnikih, slaba splošna zmogljivost, kratko pričakovano preživetje ali pridružene bolezni pri 50 (47,6 %) in dotlej neuspešno opravljene torakoskopske plevrodeze pri 5 (4,8 %) bolnikih. Do zapletov je prišlo pri 14 (13,3 %) bolnikih: zamašitev katetra pri 7, izpad katetra pri 3, zatekanje ob katetru pri 2 in okužba pri 2 bolnikih (empiem pri enem bolniku in celulitis pri enem bolniku). Plevrodeza, ki je omogočila odstranitev katetra, je bila dosežena pri 10 (9,5 %) bolnikih.

Zaključek: Vstavitev TDPK je varna in učinkovita metoda trajnega paliativnega zdravljenja MPI.

1 Introduction

Malignant pleural effusion (MPE) is a common health problem and the second most common cause of exudative pleural effusion (1). It is most common in lung and breast cancer, lymphoma, mesothelioma, and ovarian, colon and kidney cancer (2). In Europe, more than 100,000 patients are hospitalized each year due to MPE, which also presents a major financial burden (3). Despite the fact that some MPEs are initially asymptomatic, most patients develop respiratory problems during their illness, which recur even after therapeutic thoracentesis and significantly reduce the quality of life (1). The prognosis of disease outcome in MPE patients is poor as the survival averages 4–12 months from diagnosis (4,5).

Some malignancies respond well to systemic treatment (lymphoma, breast cancer), but despite the previously successful effect of treatment, much of the pleural effusion recurs later. Most MPEs need additional measures to achieve relief which significantly reduce the patient's problems. Palliative pleural effusion can be treated with repetitive therapeutic thoracenteses, pleurodesis, or insertion of an indwelling pleural catheter (IPC). The choice of permanent palliative care is based on the MPE phenotype (symptoms, response to systemic treatment, expandability of the lungs, comorbidity, general psychophysical state of the patient, expected survival), the patient's wishes and experiences of the centre (6-8). Repetitive therapeutic thoracenteses are chosen in patients with an expected survival of less than one month. However, if the expected survival is longer, pleurodesis or IPC insertion is most often used (6). Pleurodesis induces adhesion of the pleural layers, so no further intervention is required, which allows for a better quality of life and brings fewer further complications compared to IPC (9). Pleurodesis can be triggered mechanically or chemically. In the latter, talc can be injected into the pleural space during thoracoscopy or injected in its dissolved form through the chest drain, and has proven to be most effective. The success of chemical and mechanical pleurodesis is comparable (72–98%), with the incidence of complications (empyema, pneumonia, acute respiratory distress syndrome – ARDS, re-expansion pulmonary oedema) in the more common, chemical pleurodeses, being 2–17.2% (10,11).

IPC is a silicone catheter that is inserted subcutaneously into the pleural space under local anaesthesia. After training, relatives can empty the pleural effusion at the patient's home with the help of vacuum bottles connected to a catheter. The advantages of IPC over pleurodesis are mainly less invasive procedure, shorter hospitalization and the possibility of outpatient insertion of IPC (8). Complications associated with IPC insertion are divided into early and late. Early complications are related to the procedure itself; they are rare (2.8–6%), mostly minor, and usually do not require additional measures. These include pneumothorax, subcutaneous emphysema, bleeding, pain, and others (12,13). Possible late complications of IPC are septation of the pleural space, which prevents further emptying of the pleural effusion, infection, metastasis in the area of the inserted IPC, pain, IPC dislodgement from the pleural space, leakage of pleural effusion at the catheter, and catheter blockage. Serious complications are very rare (7).

The purpose of this retrospective study is to evaluate the safety and efficacy of using an indwelling pleural catheter for drainage in malignant pleural effusions in the population of patients treated at the University Clinic Golnik.

2 Methods

The retrospective analysis included 105 patients with MPE in whom IPC was inserted at the University Clinic

Golnik in the period from April 2009 to June 2017.

Before deciding on permanent palliative treatment of MPE, a thoracentesis was performed in all patients, in addition to the functional assessment, to assess the degree of improvement of dyspnoea (confirmation of symptomatic pleural effusion) and lung expandability. The expandability of lungs before IPC insertion was determined by thoracentesis (since January 2013 performed with manometry) and chest X-ray. The inability of the lungs to expand, determined by manometry, was defined as a rapid decrease in negative pleural pressure during thoracentesis (increased elestance of the lung in the last part of the procedure). The elastance curves in these patients follow the biphasic or monophasic curves with high elastance (14,15,16). In addition, the suspicion of inability to expand the lungs was confirmed by X-ray image after thoracentesis, with remaining pleural effusion and in some cases pneumothorax. The IPC insertion was opted when: pleurodesis was not indicated (inability of lungs to expand; aged over 80; poor performance status according to the ECOG PS (Eastern Cooperative Oncology Group Performance Status); significant associated diseases) and symptomatic MPE recurred within one week, or after a failed thoracoscopic talc pleurodesis. In most patients, IPC was inserted on an outpatient basis the day before discharge or on the day of discharge from hospital, where they had been hospitalized for diagnosing pleural effusion.

Following the insertion of the IPC, patients and relatives were trained in handling the IPC, received written instructions which included information on the frequency of drainage and intervention in case of complications or problems, and a contact telephone number. The calls were answered by a specialized graduate nurse, who, if necessary, activated an interventional pulmonologist or referred the patient for a follow-up examination. Regular outpatient follow-up after IPC insertion, during which we checked for possible problems, followed one month after insertion. Complications were identified and resolved at a subsequently arranged outpatient examination, and infection complications were dealt with in hospital treatment.

Demographic data, aetiology of MPE, date and reason for IPC insertion, complications, and time of IPC insertion were obtained from existing medical records. Statistical analysis of the data was performed using the Excel software program. Numerical variables are presented with median and interquartile ranges, and descriptive variables with frequencies or shares and 95% confidence intervals. Survival is defined as the time from IPC insertion to death and is presented by median and interquartile ranges. At the time of the analysis, all patients involved died.

The research was approved by the Medical Ethics Committee of the Republic of Slovenia (decision no. 0120-540/2020/3, dated 16 December 2020).

3 Results

Among the 105 patients with MPE in whom IPC was inserted, 59 (56.2%) were men and 46 (43.8%) were women. The median age was 71 years, the interquartile range (IQR) was 62–80 and the performance status according to the ECOG PS 2 scale (IQR: 1–3). The most common cause of MPE was lung cancer, which was demonstrated in 62 patients (59.0%, CI-confidence interval: 49–68.5%), and other causes are shown in Table 1. In 103 patients (98.1%), MPE was confirmed cytologically, and in two (1.9%) radiologically (significant pleural changes, visible during computed tomography examination of thoracic organs).

In 50 patients (47.6%, CI: 37.8–57.6%), unexpandable lung was an indication for IPC insertion. In 50 patients

Table 1: Aetiology of malignant pleural effusions - presentation of the proportion of individual types of cancer in malignant pleural effusions.

Aetiology of MPE	No. of patients (%)
Lung cancer	62 (59.0)
Mesothelioma	10 (9.5)
Breast cancer	7 (6.7)
Ovarian cancer	5 (4.8)
Endometrial cancer	2 (1.9)
Stomach cancer	2 (1.9)
Kidney cancer	2 (1.9)
Lymphoma	2 (1.9)
Prostate cancer	1 (0.9)
Throat cancer	1 (0.9)
Lung carcinoid	1 (0.9)
Malignant melanoma	1 (0.9)
Urothelial carcinoma	1 (0.9)
Soft tissue cancer	1 (0.9)
Unspecified	7 (6.7)

Legend: MPE – malignant pleural effusions; No – number.

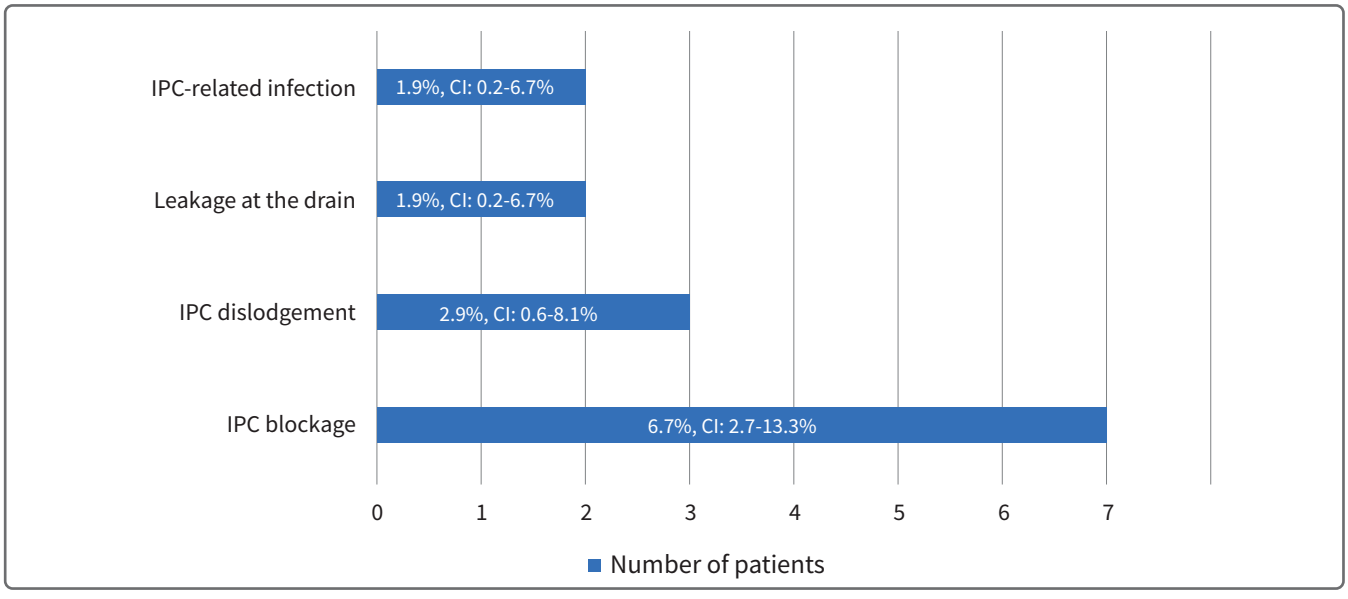

Figure 1: Late complications of indwelling pleural catheter (IPC) - display of the number and proportion of patients with individual late IPC complications.
Legend: IPC – indwelling pleural catheter

(47.6%, CI: 37.8–57.6%), IPC was chosen due to poor performance status, short expected survival, or comorbidities, making these patients unsuitable candidates for invasive procedures such as thoracoscopic pleurodesis. In 5 patients (4.8%, CI: 1.6–10.8%), IPC was inserted due to a previous failure of thoracoscopic pleurodesis.

No early complications arose during insertion and during the observation period, i.e. one hour after procedure, except for pain, which was well controlled with oral analgesics. Late complications occurred in 14 patients (13.3%, CI: 7.5–21.4%), of which only two patients had infection. One patient developed cellulitis 50 days after insertion and another had empyema 224 days after IPC insertion. In the latter, *S. epidermidis* was isolated from the effusion. Other late complications were minor and are presented in Figure 1. Spontaneous pleurodesis, which enabled the removal of IPC, occurred in ten patients (9.5%, CI: 4.7–16.8%), most of whom were in good general condition (ECOG PS 2), 78 years of age (median), 70% were female, most had lung cancer (60%) or breast cancer (20%), and had good expected survival (median 265 days, IQR: 239–463). Spontaneous

Table 2: Survival of patients by type of cancer, age and performance status, expressed by median and interquartile range.

		Median survival (days)	Interquartile range (days)
Type of cancer	Lung cancer (N[b]=62)	38.5	18.8–113.3
	Mesothelioma (N=10)	123	48.5–194.5
	Breast cancer (N=7)	175	54.5–519
Age	≤80 (N=81)	44	21.5–129.3
	>80 (N=24)	63	20.3–220
ECOG PS[a]	≤2 (N=69)	78	78
	>2 (N=36)	20	20
Total	(N=105)	54	20.5–152

Legend:
[a] Overall performance is defined by the ECOG PS scale (Eastern Cooperative Oncology Group Performance Status).
[b] N = No. of patients in a particular subgroup

pleurodesis occurred in our patients within 62.5 days (median, IQR: 44–86.5) after IPC insertion.

The use of IPC was assessed as effective in 91 patients (86.7%, CI: 78.6–92.5%), who had no problems with regular drainage of the effusion through IPC until death or the occurrence of pleurodesis, and who did not require additional consultations or measures due to effusion.

The median survival in the entire study group was 54 days (IQR: 20.5–152). Survival by cancer type, age, and performance status according to the ECOG scale is shown in Table 2.

4 Discussion

The study, which included 105 patients who had IPC inserted at the University Clinic Golnik in the period between 2009 and 2017, confirmed that IPC is a safe and effective option for permanent palliative treatment of MPE. The frequency of complications in our patients is comparable to previous studies, while spontaneous pleurodesis was achieved in a smaller proportion of patients compared to previous reports.

In most patients, the cause of MPE was lung cancer. The most common indications for insertion of IPC instead of pleurodesis were unexpandable lung and poor patient performance status, which are contraindications for more invasive procedures and it is a result of our MPE treatment strategy. At the University Clinic Golnik, we usually decide on thoracoscopic pleurodesis at the time of diagnosis in most of the patients who achieve lung expansion and have a good prognosis and performance status, as pleurodesis is more successful in the early stages of pleural disease. In those with unexpandable lung, with poor performance status, or in those over 80 years of age, IPC insertion is opted for in the case of recurrent MPE with symptoms.

The median survival in our case was 54 days, with survival being best in breast cancer patients (Me = 175 days) and worst in lung cancer (Me = 38.5 days). The results of overall survival and survival by type of cancer are comparable to the study by Frost et al., which had the highest number of ovarian cancer patients, with a median survival of all patients included being 60 days, 120 days in the case of breast cancer and 48 days in the case of lung cancer (17). A study by Demmy et al. attributes the much longer survival of patients, median survival being 147 days, to the inclusion of patients in a much better general condition. In 65% of patients, performance status was rated 0 or 1 on the ECOG PS scale, while only 15% of our patients were included in the ECOG PS 1 group (18). Longer survival in patients with better performance status was also confirmed by the results of our study. Patients with ECOG PS 1 or 2 had almost four times longer survival than those in poor general condition (PS > 2). Better survival was also observed in patients over 80 years of age, which is attributed to the fact that thoracoscopic pleurodesis is generally not performed in these patients, regardless of psychophysical condition and associated diseases. In contrast to the group of younger people, in the case of people over the age of 80, IPC is also inserted to those with expandable lungs, good performance status, and less advanced disease.

The use of IPC has been increasing in recent years, as it is equally effective in reducing dyspnoea and improving quality of life compared to pleurodesis (19). The number of complications is slightly higher than in pleurodesis and amounts to 10–20%, but the vast majority of complications are mild and manageable with minor measures (13). No early complications were recorded except for occasional pain (which was managed with analgesics) which we attribute to the fact that the procedure is safe if it is well planned and performed by an experienced pulmonologist. Early complications such as pneumothorax, subcutaneous emphysema, pain, and bleeding are rare in the literature as well (2.8–6%) and mostly do not require additional measures (7,20). Late complications are more common and occasionally require removal of the IPC. The most common late complication in our patients was catheter blockage, which occurred in 7 patients (6.7%). Catheter blockage occurs mainly due to fibrin accumulation, which can be resolved by flushing the catheter with saline (12), but in the case of more extensive fibrin sheath formation, this method is sometimes unsuccessful. In the literature, flushing with fibrinolysis agents is also described as a successful method, but these were not used in our cases (21). Catheter removal was required in all seven patients with a blocked catheter. Recurrence of symptomatic effusion was found in only one of these patients, to whom a new IPC was inserted on an outpatient basis one week later. In six patients, re-insertion of IPC was not necessary, as the appearance of pronounced septation of the pleural space was also observed, which prevented additional accumulation of effusion and successful drainage. In the literature, the incidence of catheter blockage is similar to our results and is 4.8–19% (22,23). In three (2.9%) patients, IPC fell out of its original position, leading to removal in all three cases. Re-insertion was not performed in any patient, as all were in poor general condition at the time of removal, and survival after removal was less than one month in all of them. Data on movement or dislodgement of the catheter vary

widely in the literature. The incidence is 0.9–18%, and is thought to be mainly related to cachexia and loss of subcutaneous fat where the catheter was placed (7). We also observed less subcutaneous fat in our three patients, all of whom were over 75 years of age, but we did not objectively define this. In two patients (1.9%) there was leakage of effusion at the drain. Leakage of pleural fluid is associated with higher intrapleural pressure, is usually self-limiting, and occurs in up to 13% of patients (7). In our case, a patient who had swelling of the subcutaneous tissue as a result of effusion leakage at the drain was advised more frequent draining, which was effective and therefore no further action was required. Another patient sought help with effusion leakage at the district hospital (the complication is not entirely clear due to lack of event documentation), where IPC was removed and a thoracic drain (24F) was inserted and connected to a drainage system due to hydropneumothorax being visible on X-ray. The patient was later transferred to us, where talc pleurodesis was performed through an already inserted drain due to prolonged air leakage at bronchopleural fistula. Due to the success of the mentioned pleurodesis, the insertion of IPC was no longer necessary. It is unclear whether the fistula was a complication of IPC or subsequent active drainage. We have also not found any similar examples in the literature that could explain this situation. IPC-related infections occur in 0–12% of patients and are caused by bacteria that colonize the skin, most commonly *Staphylococcus spp.*, *Pseudomonas aeruginosa*, and *Enterobacteriaceae*. Infection occurs approximately 6–8 weeks after insertion. Antibiotic treatment is usually sufficient (12). In our case, IPC-related infection occurred in two patients (1–1.9%) after 7 and 32 weeks. Empyema caused by *Staphylococcus epidermidis* was found in one patient, resulting in removal of IPC and control of infection with antibiotics. In another patient with cellulitis, the causative agent could not be proved. Spontaneous pleurodesis also occurred in this patient, so IPC was removed and cellulitis was controlled with antibiotic therapy. No deaths related to insertion or complication of IPC were recorded.

Although pleurodesis is not the primary goal of IPC insertion, it is reported in approximately 45–68% of patients in the literature (18,24,25). The mechanism of occurrence is not entirely clear. Most likely, septation of the pleural space occurs with the inflammatory response due to mechanical irritation of the pleura, which leads to stabilisation of the pleural space and prevents additional accumulation of pleural effusion (9). Spontaneous pleurodesis, which was found in our study one to five months after IPC insertion, occurred in ten patients (9.5%). These were mostly in good general condition (ECOG PS 2) and had good expected survival (median 265 days, IQR: 239–463). A lower proportion of pleurodesis compared to other studies is mainly due to the differences between the included patients. In our case, the highest proportion of patients with lung cancer was 71 years of age, and unexpandable lung was present in 48% of cases, which is more than in previous studies, where the proportions were 3 and 12% (17,23). All of the above are unfavourable factors for the development of pleurodesis. In previous studies a higher proportion of spontaneous pleurodesis was observed in ovarian and breast cancer, patients who had expandable lungs, and were younger than 60 years (17,23). Pleurodesis usually develops within 29–59 days (in our case, a median of 62.5 days), so the possibility of pleurodesis has been further limited by the short survival of our patients, with a median survival of 54 days (19). The study, which included patients with similar survival, also reported a lower proportion of spontaneous pleurodesis, in 28%, but they did not report a proportion of patients with unexpandable lungs. In recent years, they have additionally determined the beneficial effect on the development of pleurodesis in those who had talc injected into the pleural space via IPC, which was not performed in our patients (17). The formation of pleurodesis is also influenced by the drainage regime, pleurodesis is achieved in a larger proportion with more aggressive or daily drainage (26,27). In most cases, such a drainage regime was not used by our patients, as researches in the last five years have shown the advantage of a more aggressive way of achieving spontaneous pleurodesis.

The limitation of our analysis is mainly that the patients were systematically monitored only at a single check-up, one month after insertion, and subsequent check-ups were foreseen only in case of problems. Patients were given written instructions explaining possible complications and were told to call our endoscopy unit if any occurred. Nevertheless, the proportion of complications may be underestimated, as they have been reported by relatives and patients without actively being asked about them. The impact of the lack of data could be reduced by conducting a prospective survey and regular monitoring after the insertion of the IPC. Our patients were with slightly poorer performance status and more associated diseases, as pleurodesis is performed in most patients capable of thoracoscopy. Therefore, the patients included had a shorter life expectancy and thus a lower probability of spontaneous pleurodesis.

5 Conclusion

Palliative treatment of MPE significantly improves quality of life and includes different methods, which differ in the invasiveness of the procedure, the duration of hospitalisation, and the number of re-visits to the hospital. According to the above characteristics, treatment should be tailored to each patient according to their performance status, expected survival, and their wishes. IPC insertion is chosen mainly in patients in whom thoracoscopy is contraindicated, but their expected survival is long enough and frequent therapeutic thoracentesis would impair quality of life and increase the chances of complications. By performing an analysis on our patient population, IPC insertion was confirmed to be an effective and safe method of permanent palliative treatment of symptomatic MPE. Due to the low risk of complications, good efficacy, the possibility of spontaneous pleurodesis, and outpatient treatment, it should be used in patients who have reservations about thoracoscopic pleurodesis and those who want as few days in hospital as possible or less invasive procedure. Unlike in the case of thoracoscopic pleurodesis, patients and their relatives need to be taught to handle IPC and at the same time be made aware that a foreign body is constantly present in the pleural space.

Conflict of interest

None declared.

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