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# Postoperative outcome after palliative treatment of malignant pleural effusion

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## Abstract

**Background:** The objective of this nationwide, registry-based study was to compare the two most frequently used procedures for the palliative treatment of a malignant pleural effusion (MPE) and to evaluate differentiated indications for these two procedures.

**Methods:** This was a retrospective observational study based on data of the "PLEURATUMOR" registry of the German Society for Thoracic Surgery. Patients who were documented in the period from January 2015 to November 2021 and had video-assisted thoracic surgery (VATS) talc pleurodesis or implantation of an indwelling pleural catheter (IPC) were included.

**Results:** A total of 543 patients were evaluated. The majority suffered from secondary pleural carcinomatosis ($n = 402$; 74%). VATS talc pleurodesis ($n = 361$; 66.5%) was performed about twice as often as IPC implantation ($n = 182$; 33.5%). The duration of surgery was significantly shorter in IPC-patients with 30 min compared to VATS talc pleurodesis (38 min; $p = 0.000$). Postoperative complication rate was 11.8% overall and slightly higher after VATS talc pleurodesis ($n = 49$; 13.6%) than after IPC implantation ($n = 15$; 8.2%). After VATS talc pleurodesis patients were hospitalized significantly longer compared to the IPC group (6 vs. 3.5 days; $p = 0.000$). There was no significant difference in postoperative wound infections between the groups ($p = 0.10$). The 30-day mortality was 7.9% ($n = 41$).

**Conclusion:** The implantation of an IPC can significantly shorten the duration of surgery and the hospital stay. For this reason, the procedure should be matched with the patient's expectations preoperatively and the use of an IPC should be considered not only in the case of a trapped lung.

KEYWORDS
indwelling pleural catheter, malignant pleural effusion, pleural carcinosis, pleurodesis, video-assisted thoracic surgery

## INTRODUCTION

About 15% of patients with malignant tumors develop an associated malignant pleural effusion (MPE).[1,2] Not only that, patients with MPE mostly have a very limited survival, and the significant influence of this condition on the quality of life (dyspnea) of patients has already been demonstrated in numerous studies.[3–7] While pleurocentesis may improve symptoms for some time, its repetitive practice is associated with well-known risks (e.g., infection, bleeding).[8] Therefore, several procedures are described which aim to permanently reduce the resulting dyspnea.[9,10]

Considering the usually advanced stage of the underlying disease and the often short remaining life span, the risk of complications and time of hospitalization should definitely be minimized. For this reason, particularly high

demands are placed on the indications for these procedures of the multimorbid patients in terms of the lowest possible invasiveness and a high level of safety. Video-assisted thoracic surgery (VATS) talc pleurodesis is a minimally invasive operation that is used as a standard procedure in thoracic surgery for the palliative treatment of MPE. Despite the best success rate in terms of MPE control, potential complications must also be taken into account in this surgery.[11,12] The implantation of an indwelling pleural catheter (IPC) has been established as an alternative treatment option for some years now, which also can be carried out under local anesthesia or during surgery under sedation or general anesthesia.[13] The decision whether to perform VATS talc pleurodesis or the implantation of an IPC mainly depends on morphological (e.g., trapped lung) and clinical criteria (e.g., general condition, performance status).[6]

Both procedures pursue palliative goals and are intended to alleviate the patient's symptoms.[14] A superiority of one procedure over the other is still unclear and subject of controversial discussions. Either intervention can be performed via VATS, but the IPC can also be implanted under local anesthesia if thoracoscopy/pleural biopsy is not required, while the application of talc slurry via a chest drain has shown significantly worse results when compared to VATS.[15,16] Another benefit of the IPC is that it can be also used in patients with a present trapped lung.[6] Chemical pleurodesis, on the other hand, and talc pleurodesis in particular have been reported to achieve excellent rates of MPE control up to over 90%.[12,17,18] Also, the psychological effect of a catheter that may remain in place for the rest of the patient's life is absent, as is the risk of infection associated with a tunneled catheter and regular nursing care. In a meta-analysis of 17 studies and 2515 patients, Savikumar et al. found no significant difference in quality of life between thoracoscopic talc pleurodesis and IPC.[19] There are already retrospective as well as prospective studies to compare VATS talc pleurodesis and the implantation of an IPC in the treatment of MPE. However, the conclusions of these studies differ and the cohorts studied are often small, despite the high incidence of this disease.[18,20–22]

The objective of this registry-based study was to evaluate treatment data and postoperative outcome after VATS talc pleurodesis compared to the implantation of an IPC in the treatment of MPE. The results should provide an overview of the surgical treatment situation for patients with MPE in Germany.

## METHODS

### Study design

This was a retrospective, observational, registry-based study with data from the "PLEURATUMOR-registry" of the German Society for Thoracic Surgery. The length of postoperative hospital stay after one of the above mentioned interventions was defined as the primary endpoint of the study. Secondary endpoints were the duration of surgery, the rate of postoperative complications according to the Clavien–Dindo classification, the rate of wound infections, the readmission rate in the first 30 days after surgery and the 30-day mortality.

### PLEURATUMOR-registry of the German Society for Thoracic Surgery

The nationwide PLEURATUMOR registry of the German Society for Thoracic Surgery was launched in January 2015 and is intended to improve the surgical treatment of malignant pleural tumors in Germany by serving as quality assurance. Therefore, the online database documents the most important parameters of surgically treated patients with malignant pleural tumors. This includes preoperative, surgical therapy and postoperative hospitalization data, histology, and 30-day mortality data. The registry allows, on the one hand, quality control (benchmarking), the evaluation of new therapy concepts and, on the other hand, provides a basis for possible studies. A requirement for participation in the registry is, in addition to prior registration of the clinic, the patient's informed consent as well as the presence of a malignant pleural mesothelioma, a thymoma/thymic carcinoma with pleural dissemination or a surgically treated pleural carcinomatosis.

### Study population

In December 2021 a structured evaluation of all patients entered into the database of the PLEURATUMOR-registry from January 2015 to November 2021 who received a VATS talc pleurodesis or the implantation of an IPC was performed. All patients were included in which the sections required for our research question were fully documented and in which at least 10 patients were entered into the registry by the respective clinic. The consent of the 10 participating clinics of this study was obtained in accordance with the guidelines of the registry. These departments included Department of Thoracic Surgery of the University Medical Center Regensburg (Regensburg), Hospital Barmherzige Brüder (Regensburg), Niels-Stensen-Kliniken (Ostercappeln), Thoraxzentrum Ruhrgebiet (Herne), Ibbenbueren General Hospital (Ibbenbueren), SRH Wald-Klinikum Gera (Gera), Lungclinic, Hospital of Cologne (Cologne), LungenClinic Grosshansdorf (Großhansdorf), Chemnitz Hospital (Chemnitz) and Waldburg-Zeil Clinic (Wangen im Allgäu). The consent of the local ethics committee of the University Regensburg was given (reference no.: 21–2668-104). Written informed consent was obtained from all patients before data collection.

### IPC implantation

The implantation of an IPC can be performed during thoracoscopy, as well as as a minor procedure under local anesthesia. Therefore, after localization of the puncture site in the region of the sixth or seventh intercostal space in the

**TABLE 1** Patient characteristics

| | All ($n = 543$) | VATS talc pleurodesis ($n = 361$) | IPC ($n = 182$) | $p$-value |
|---|---|---|---|---|
| Age (years) mean ± SD | 69.4 ± 11.5 | 69.5 ± 11.5 | 69.3 ± 11.7 | 0.84 |
| Female gender, *n* (%) | 269 (49.5) | 185 (51.2) | 84 (46.2) | 0.28 |
| Tumor entity, *n* (%) | | | | |
| MPM | 141 (26.0) | 97 (26.9) | 44 (24.2) | 0.54 |
| Pleural carcinosis | 402 (74.0) | 264 (73.1) | 138 (75.8) | |
| Manifestation, *n* (%) | | | | |
| Initial | 529 (97.4) | 351 (97.2) | 178 (97.8) | 0.76 |
| Recurrence | 13 (12.4) | 9 (2.5) | 4 (2.2) | |
| Data not available | 1 (0.2) | 1 (0.3) | 0 (0) | |
| Localization, *n* (%) | | | | |
| Left side | 188 (34.6) | 130 (36) | 58 (31.9) | |
| Right side | 324 (59.7) | 214 (59.3) | 110 (60.4) | 0.29 |
| Both sides | 31 (5.7) | 17 (4.7) | 14 (7.7) | |
| Karnofsky Index [%] mean ± SD | 77.6 ± 13.3 | 78.9 ± 13 | 74.9 ± 13.5 | 0.001* |

Abbreviations: IPC, indwelling pleural catheter; MPM, malignant pleural mesothelioma; SD, standard deviation; VATS, video-assisted thoracic surgery.
*Statistical significance.

anterior/middle axillary line by ultrasound and local anesthesia, a pleural puncture was performed using the Seldinger technique with insertion of a wire. After making a second incision (approximately 10 cm ventral to the first puncture site), subcutaneous tunneling was performed between the two incisions and the end of the catheter was inserted into the pleural cavity via the wire. The wire was then removed and the catheter secured with a suture. It took approximately 10–20 min to perform the procedure.

## Statistical analysis

The data were extracted from the database in tabular form using Excel, version 15.0 (Microsoft Corporation). The data was already present in an anonymous format. The statistical analysis was performed using IBM SPSS Statistics, version 26 (IBM Corporation). Demographic data were summarized as numbers and percentages. The normal distribution was examined using the Shapiro-Wilk test. The *t*-test was used for group comparisons of normally distributed variables and the Mann–Whitney U test was used for group comparisons with non-normally distributed data. The Chi-square test was used for group comparisons on categorical variables. If the minimum expected cell size assumption for application of Chi-square test did not hold, Fisher's exact test was used. A $p$-value <0.05 was considered statistically significant.

# RESULTS

## Demographic data

A total of 543 patients were included in the study (Table 1). The mean age of the patients was 69.4 ± 11.5 years and the gender distribution was balanced. With about three quarters of all patients, the majority of the study population suffered from secondary pleural carcinomatosis while the remaining quarter had malignant pleural mesothelioma. Nearly all patients (97.4%) suffered from an initial manifestation of an pleural disease. In statistical analysis, patients who received IPC were slightly worse overall in terms of the preoperative performance status (74.9 ± 13.5 vs. 78.9 ± 13; $p = 0.001$).

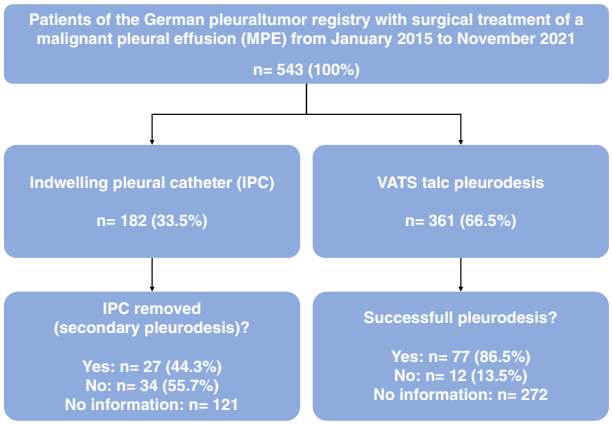


**FIGURE 1** Flow-chart of the study population

## Surgical therapy and hospitalization

Of the 543 patients in the cohort, 361 patients were treated with VATS talc pleurodesis, whereas 182 patients received an IPC (Figure 1). The mean duration of surgery was significantly shorter in IPC-patients with

**TABLE 2** Perioperative outcomes of both procedures

| | All ($n = 543$) | VATS talc pleurodesis ($n = 361$) | IPC ($n = 182$) | $p$-value |
|---|---|---|---|---|
| Duration of intervention (minutes) median; IQR | 35; 19 | 38; 18 | 30; 22 | 0.000* |
| Surgical revision, $n$ (%) | 13 (2.4) | 10 (2.8) | 3 (1.6) | 0.56 |
| Postoperative complications, $n$ (%) | 64 (11.8) | 49 (13.6) | 15 (8.2) | |
| Grade 1 | 29 (5.3) | 21 (5.8) | 8 (4.4) | |
| Grade 2 | 6 (1.1) | 6 (1.7) | 0 (0) | |
| Grade 3a | 10 (1.8) | 6 (1.7) | 4 (2.2) | 0.08 |
| Grade 3b | 10 (1.8) | 10 (2.8) | 0 (0) | |
| Grade 4a | 2 (0.4) | 2 (0.6) | 0 (0) | |
| Grade 4b | 0 (0) | 0 (0) | 0 (0) | |
| Grade 5 | 7 (1.3) | 4 (1.1) | 3 (1.6) | |
| Wound infection, $n$ (%) | 10 (1.9) | 4 (1.2) | 6 (3.4) | 0.10 |
| Postoperative stay [days] median; IQR | 5; 3 | 6; 3 | 3.5; 3 | 0.000* |

Abbreviations: IPC, indwelling pleural catheter; IQR, interquartile range; VATS, video-assisted thoracic surgery.
*Statistical significance.

**TABLE 3** Thirty day follow-up

| | All ($n = 521$) | VATS talc pleurodesis ($n = 342$) | IPC ($n = 179$) | $p$-value |
|---|---|---|---|---|
| Readmission, $n$ (%) | 51 (9.8) | 33 (9.6) | 18 (10) | 0.88 |
| Thirty day mortality, $n$ (%) | 41 (7.9) | 20 (5.8) | 21 (11.7) | |
| Due to primary disease | 32 (6.1) | 15 (4.4) | 17 (9.5) | |
| Surgical complication | 0 (0) | 0 (0) | 0 (0) | 0.007* |
| Nonsurgical complication | 3 (0.6) | 0 (0) | 3 (1.7) | |
| Unknown | 6 (1.2) | 5 (1.5) | 1 (0.6) | |

Abbreviations: IPC, indwelling pleural catheter; VATS, video-assisted thoracic surgery.
*Statistical significance.

32.8 ± 19.1 min compared to patients with talc pleurodesis with 40.7 ± 17.5 min ($p = 0.000$). Resulting postoperative complications were classified according the Clavien–Dindo classification and are demonstrated in Table 2.[23] Overall, postoperative complications occurred with a rate of 11.8%. Considering only those complications that required at least interventional therapy (grade 3 or higher), 5.3% of patients were affected ($n = 29$). Postoperative complications were slightly more frequent after VATS talc pleurodesis ($n = 49$; 13.6%) compared to IPC implantation ($n = 15$; 8.2%; $p = 0.14$). Surgical revisions were performed in 2.4% ($n = 13$) of patients. Reasons for surgical revision included postoperative hematothorax ($n = 4$), recurrent effusion ($n = 2$), persistent bronchopleural fistula ($n = 1$), wound infection ($n = 1$), pleural empyema ($n = 1$), chylothorax ($n = 1$), pneumothorax ($n = 1$), catheter dysfunction ($n = 1$), and emphysema of the skin ($n = 1$). Patients after VATS talc pleurodesis had a significantly longer hospital stay than patients after implantation of an IPC (8.8 ± 15.8 vs. 4.5 ± 7.5 days, $p = 0.000$). We did not find a significant difference between the two groups with regard to the occurrence of postoperative wound infections in the first 30-days after surgery ($p = 0.10$).

## Thirty day mortality and follow-up

Overall, the mortality rate was relatively high with 7.9% ($n = 41$) in total (Table 3). In the majority of these patients (6.1%, $n = 32$), the primary disease was reported as the cause of death. The 30-day mortality rate was significantly higher in patients after IPC implantation at 11.7% ($n = 21$) than after VATS talc pleurodesis with 5.8% ($n = 20$; $p = 0.007$). Differences in rates of necessary hospital readmissions were not significant ($p = 0.88$). In 150 patients (27.6%), the opportunity to enter a follow-up for the patients in the registry was used. Among those patients after implantation of an IPC with documented follow-up, the catheter was removed in 27 cases due to pleurodesis. In patients after VATS talc pleurodesis, successful pleurodesis was documented in 77 cases (Figure 1).

## DISCUSSION

Several procedures can be performed in the symptomatic management of dyspnea due to MPE.[6,24] The present study shows that VATS talc pleurodesis as well as the implantation of an IPC are safe procedures and expected to successfully

relieve dyspnea. The indications for these two procedure should be chosen depending on the anatomy (trapped lung), general condition and associated prognosis of the patient and patient request.[14]

The Karnofsky index of our patients ranged mostly between 70% and 80%. Approximately 66% of patients presented with only mild symptoms and a corresponding Karnofsky index of ≥80% at the time of the procedure. Before surgery, both groups differed in the Karnofsky index ($p = 0.001$). This could lead to a bias in the outcome of the following postoperative analyses. However, the mean value showed only a difference 4% between both groups, so that the difference was judged to be clinically of minor relevance. Here, it should certainly be noted that the Karnofsky index of the patients was of course not only determined by dyspnea but also by fatigue of the patient, etc., which probably also influences the lower index of the IPC patients.[25]

The mean duration of surgery was significantly shorter in IPC patients compared to patients after VATS talc pleurodesis ($p = 0.000$). The clinical impact of the duration of surgery on the postoperative outcome and the effort to keep it as short as possible are well known.[26] Additionally, it must be considered that VATS talc pleurodesis is commonly performed in general anesthesia with corresponding pre- and postoperative time in addition to the duration of surgery, whereas the implantation of an IPC can be performed under local anesthesia even in an ambulatory setting if thoracoscopy or pleural biopsy is not required.[11] The difference in duration of surgery can thus may be explained by the fact that a proportion of patients received IPC implantation under local anesthesia. Even though local procedures are increasingly available for talc pleurodesis with the more recent developments of NI-VATS (nonintubated VATS), this option still represents an advantage of the IPC.[27] In addition to a faster surgery, we observed a significantly shorter postoperative length of hospital stay in the IPC patients (4.5 vs. 8.8 days; $p = 0.000$). In the meta-analysis by Iyer et al., hospital stay was also found to be shorter after IPC implantation compared with chemical pleurodesis.[28]

The length of hospitalization is of particular importance when considering the prognosis of these patients. The median survival of patients with breast (6.0 months, range 1.0–58.0 months) and lung cancer (4.0 months, range 1.0–96.0 months) with associated MPE surveyed by Zamboni and colleagues can certainly illustrate the relevance of halving the length of postoperative hospital stay.[29] In terms of patient-centered care, reducing the length of inpatient stay should be a primary goal to meet the desire to spend what is likely to be short remaining time of life at home.[30]

The incidence of postoperative complications in this study was slightly lower in the IPC patients than in those after VATS talc pleurodesis, although it did not reach statistical significance ($p = 0.14$). However, especially those complications that required invasive treatments (Clavien–Dindo grade ≥3) were considerably less frequent in the IPC group. These complications also determine the length of hospital stay. The rate of necessary reoperations (Clavien–Dindo grade 3a) after VATS talc pleurodesis was 2.8%, whereas it was 0% in the IPC patients. A common concern about permanent tunneled catheters is the risk of associated infection. The incidences of IPC-related pleural infection ranged from 0% to 12% in the literature.[31] Also, in our study, we observed more wound infections in the first 30 days after surgery in the IPC group (3.4%) than after VATS talc pleurodesis (1.2%). However, both rates were low without a statistically significant difference ($p = 0.10$) (Table 2).

With regard to the rate of necessary hospital readmissions, there were no relevant differences between the two groups, each with approximately 10% ($p = 0.88$). In contrast, 30-day mortality was significantly higher in patients of the IPC group with 11.7% compared to 5.8% in patients after VATS talc pleurodesis ($p = 0.007$). The fact that in the majority of deceased patients the primary disease was documented as the cause of death confirms that there were probably other reasons involved than simply the choice of surgical procedure. Considering the higher 30-day mortality of the IPC patients, it can be assumed that the lower life expectancy was perhaps a factor to tend towards IPC for the treating physician. However, due to the retrospective approach, it is unfortunately not possible to make a final assessment in this regard.

Not only with regard to catheter-associated infections, but also in terms of successful pleurodesis, long-term follow-up in particular is decisive. Unfortunately, due to our registry-based approach, long-term follow-up was inconsistent in our study, resulting in a lack of long-term data longer than 30 days postoperatively in about 70% of our patients. Nevertheless, among patients in whom follow-up was documented by the respective hospital, VATS talc pleurodesis was successful in 86.5% of patients, whereas secondary pleurodesis was achieved in 44.3% of patients after IPC implantation. Pleurodesis rates after IPC implantation are usually reported to be lower in the literature than after chemical pleurodesis procedures, but also depend, to some extent, on regular drainage of pleural fluid.[32] The influence of the regular loss of pleural effusion on the patient's nutritional status after IPC implantation may also warrant further investigation.

In conclusion, both VATS talc pleurodesis and implantation of an IPC offer individual advantages and disadvantages, which should be matched with the patient's expectations already preoperatively. Finally, the procedure should be chosen depending on the anatomy (full expansion of the lung), the general condition and associated prognosis of the patient and the need for tissue biopsy. If the patient agrees to a visible IPC, which may last until the end of life, its application can serve to significantly shorten the duration of surgery and also the hospital stay. For this reason, the use of an IPC should be considered not only in the case of a trapped lung.

## LIMITATIONS

First, the retrospective, registry-based approach of the study must be mentioned. This led to high rates of undocumented

patients, especially with regard to long-term follow-up. The high rate of mesothelioma patients must also be considered, which was certainly due to the fact that only patients from thoracic surgery clinics were examined. Also, both groups differed in the Karnofsky index, which may have led to a potential bias in the analyses. However, only a 4% difference was shown in comparing the mean of both groups, and we judged the difference to be clinically of minor relevance.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data presented in this study are available on request from the corresponding author.

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