# Chemical Pleurodesis in Palliative Setting: A Brunei Experience

Muhammad Yusuf Shaharudin

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## Abstract

**Background**

Malignant pleural effusion is typically a sign of an aggressive and advanced disease, generally with a short life expectancy. This causes a lot of burdens symptomatically to patients with advanced malignancy. Hence, a lot of patients are made known early to palliative service to help optimize patients' quality of life. One of the procedures to help prevent the recurrence of symptomatic malignant pleural effusion is bedside chemical pleurodesis following thoracocentesis. The aim of this audit is to assess the efficacy and safety of carrying out the above procedure in a palliative setting.

**Method**

Retrospective electronic records of patients were reviewed from January 2020 until December 2021. Malignant pleural effusion was confirmed by cytological assessment of pleural fluid following chest tube drainage. Chemical pleurodesis was done by pleural fluid instillation of bleomycin.

**Results**

Eighteen patients were included, with 6 male cases and 12 female cases. The mean age was 69.4 years, with 61% of the patients suffering from lung malignancy. Complete response is seen in 44.4% and partial response is seen in 22.2%. The failure rate is 33.3%. The complications were minimal with only 5.6% of patients having fever and 11.1% having pleuritic pain.

**Conclusions**

The audit shows that bedside chemical pleurodesis performed by a palliative team is as efficacious and safe as when it is performed by other specialists. It helps improve the symptoms in 66% of our patients and thus improve their quality of life.

**Muhammad Yusuf Shaharudin**

*Palliative Unit RIPAS Hospital, Bandar Seri Begawan, Brunei Darussalam*

## Introduction

Malignant pleural effusion (MPE) is a common but distressing condition in patients with advanced malignancy. It affects up to 15% of patients with cancer and is most common in lung, breast, lymphoma, gynecological malignancies, and malignant mesothelioma[1]. It also indicates that the disease is now advanced and life expectancy is generally short with a median prognosis of 3-12 months[2]. Hence, a lot of patients are now known early to Palliative Services to help optimize patients' quality of life with treatment goals concerning relieving dyspnea, restoration of near-normal activity and function, and reducing the need for inpatient care.

Treatment options for MPE comprise repeated therapeutic thoracocentesis, chest tube drainage, chemical or surgical pleurodesis, thoracoscopy, and insertion of an indwelling pleural catheter (IPC). However, this is limited by the availability and resources available in each center. Pleurodesis is an intervention that's designed to get the two layers of the lung's lining (the pleura) to stick together with the aim to prevent the recurrence of pleural effusion. The procedure is traditionally performed by respiratory, cardiothoracic, and medical oncology colleagues. However, chemical pleurodesis can actually be done at the bedside with appropriate training and is thought to be the best palliative treatment for recurrent effusions of end-stage malignancies[3].

Palliative Care service is a relatively new specialty in Brunei which only started in 2009. Since then we have been developing both our in-patient, out-patient and community services. One of the services being offered as in-patient care would be that of bedside chemical pleurodesis for MPE as more and more advanced cancer patients are being referred early to our service to optimize their symptoms and optimizing their quality of life. The agent that we have been using in our practice is bleomycin. This study's aim is to audit our practice in doing chemical pleurodesis for malignant pleural effusion.

## Methods

Retrospective electronic records of patients with malignant pleural effusion who were referred to Palliative Service, RIPAS Hospital, the main tertiary center in Brunei Darussalam for chemical pleurodesis from January 2020 until December 2021 were reviewed. All of the patients had documented evidence of malignant pleural effusion from pleural cytology following thoracentesis. The level of pleural effusions was also documented to be at least moderate to severe before thoracentesis was done.

All patients were also subjected to the standard technique of chest tube insertions. This was done either by our radiologist colleagues or by respiratory physicians in the ward. The drainage pleural effusion was followed daily until it became less than 150cc in 24hrs. A subsequent chest X-ray was done to demonstrate complete pleural drainage with full lung expansion before chemical pleurodesis was performed. Following the above, 5-10cc of lidocaine was administered prior to the instillation of 45 units of bleomycin dissolved in 50cc of sterile normal saline solution into the pleural space via

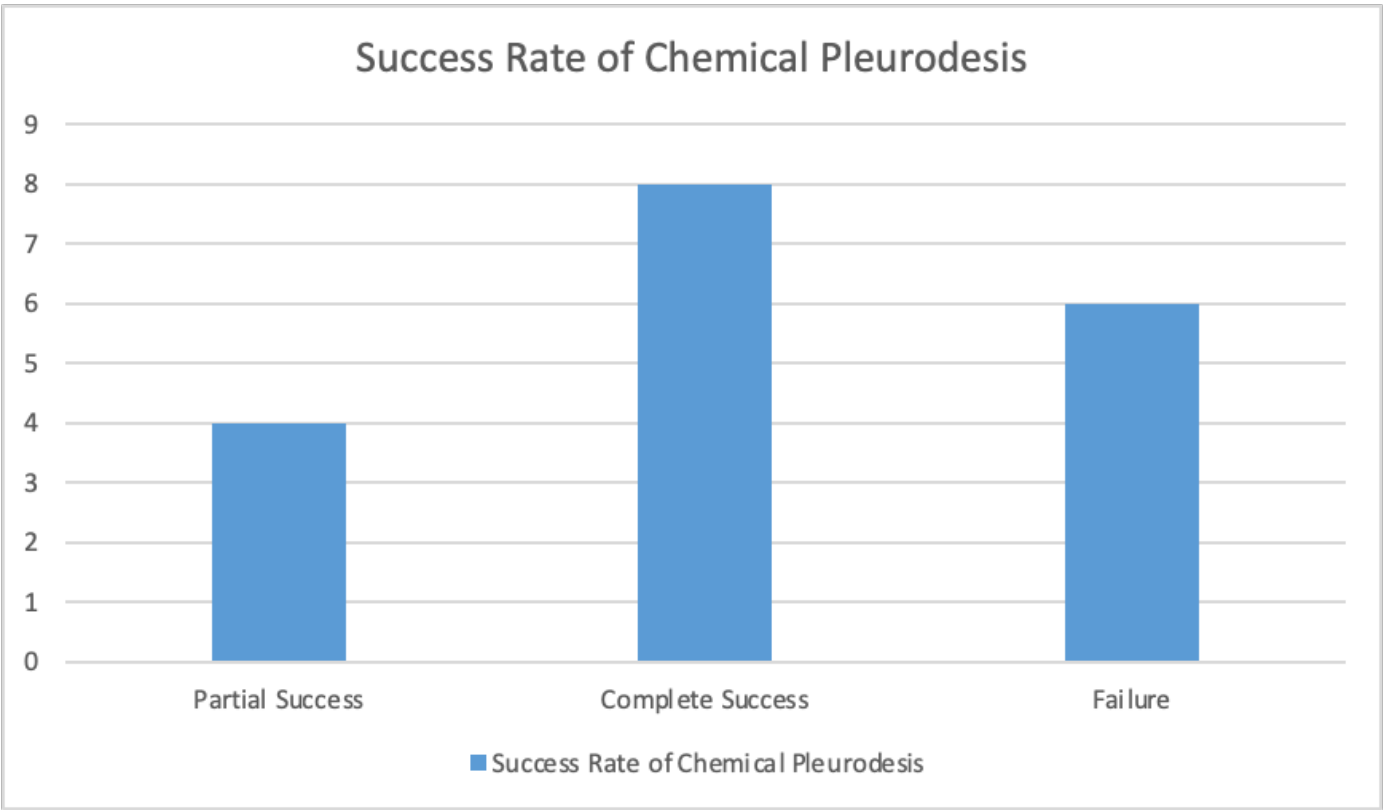
chest tube. The chest tube was then clamped for 4 hours and the patient's position was rotated to prone, supine, left lateral, and right lateral decubitus respectively for every 30 minutes. Thoracotomy tubes were removed when the daily drainage achieved less than 150cc. The patients were subsequently followed up in the outpatient clinics at 1, 3, or 6 months following the chemical pleurodesis or until patients were readmitted again.

Procedure success and complete response to treatment were defined as absence of fluid accumulation that requires repeated thoracocentesis/chest tube drainage in the follow-up imaging (chest x-ray or CT thorax). Partial response is defined as a small amount of fluid re-accumulation (less than 50% of initial radiograph) but not requiring repeated thoracocentesis/chest tube drainage. Failure to respond is defined as fluid re-accumulation causing clinical symptoms and/or requiring repeated thoracocentesis/chest tube drainage[4].

Data were entered into Excel and analyzed using descriptive statistics.

## Results

There were 18 patients identified. The median age was 69.4 and the majority was female making up about 67% of them. All the patients had documented at least moderate to severe pleural effusion prior to thoracocentesis being performed. Upon admission, 94.4% of patients presented with shortness of breath, 38.8% complains of chest pain or heaviness, and 22.2% suffered from dry cough prior to diagnosis. The mean duration of time from diagnosis of effusion to thoracocentesis was 5.8 days while the mean duration of time from thoracocentesis to chemical pleurodesis was 9.7 days. The average length of stay for these patients was 18 days.



The most common site of the primary tumor is lung adenocarcinoma with about 61% of them followed by ovarian carcinoma at 16.6%. Complete response towards chemical pleurodesis was seen in 44.4% of patients and partial response in 22.2%. Treatment failure is at the rate of 33.3%. 5.5% died shortly after pleurodesis.

In terms of complications, 77.7% of patients did not report any issue, while 1 out of 18 patients reported fever, and 2 of them had chest pain following chemical pleurodesis. After 6 months of follow-up, 6-months survival was 44.4%. None of those with failed pleurodesis survive after 6-months. Among those who did respond to pleurodesis, either be partial or complete response, 2/3 alive after 6 months.

## Demographic

| | |
|---|---|
| **Mean Age:**<br>**Male**<br>**Female** | 69.4<br>72.6<br>67.8 |
| **Gender:**<br>**Male**<br>**Female** | <br>33.3%<br>66.6% |
| **Average Length of Stay** | 18.0 (range from 5 to 51) in days |
| **Mean of time from thoracocentesis to pleurodesis** | 9.7 (range from 3 to 15) in days |
| **Mean of time from pleural effusion diagnosis to thoracocentesis** | 5.8 (range from 1 to 17) in days |

| Type of Primary Cancer | Partial Response | Complete Response | Failure | Total |
|---|---|---|---|---|
| **Lung:**<br>**Adenocarcinoma**<br>**Mesothelioma** | 3 | 4<br>1 | 3 | 10<br>1 |
| **Breast** | | | 1 | 1 |
| **Ovarian** | | 2 | 1 | 3 |
| **Renal** | 1 | 1 | | 2 |
| **Chronic Lymphocytic Leukemia** | | | 1 | 1 |
| **Total** | 4 (22.2%) | 8 (44.4%) | 6 (33.3%) | 18 (100%) |

| | Partial Response | Complete Response | Failure | Total |
|---|---|---|---|---|
| **Death within 6 months** | 2 | 2 | 6 (100%) | 10 (55.5%) |
| **Alive after 6 months** | 2 | 6 | 0 | 8 (44.4%) |

## Discussions

MPE causes a lot of distress for patients suffering with advance malignancy hence affecting patient function and

quality of life. There are a few treatment options that can be offered to the patient to relieve the symptoms and burden however not all center is equipped with the expertise to do VATS procedure or IPC insertion for example. Chemical pleurodesis is a relatively simple procedure that can be offered bedside to prevent the recurrence of pleural effusion. Pleurodesis is traditionally performed by the respiratory or cardiothoracic teams. However, as MPE is an indicator of advanced and aggressive disease, many patients are being referred early to Palliative services for holistic care. Hence, it is increasingly important now for the palliative team to be able to offer such a procedure bedside as technically it is not a difficult procedure and it may help achieve a better quality of life in patients suffering with advance malignancy. This study aims to review our practice in doing bedside chemical pleurodesis with bleomycin.

In our study, the mean age of patients was 69.4 years old of which 33.3% were male and 66.6% were female. This is similar to most of the studies of chemical pleurodesis being performed largely by the respiratory or cardiothoracic team in other studies. The median age in their studies was more than 60 years old and female was in higher proportion than male. Zimmer et al's study has patients (14 with bleomycin and 19 with talc) a with male to female ratio of 4 to 10, Ong et al collected data for 38 patients (20 with bleomycin and 18 with talc) while Nikbaksh et al 50 patients where 62% were female in their study[5][6][7]. The main limitation of our study would be the number of cases studied as we managed to collect our data over 2 years. Nikbaksh et al collected their data for around 5 years while Zimmer et al collected around 3 years of data. Pleurodesis for malignant pleural effusion is not a frequently performed procedure and this is apparent in the number of patients accrued in different studies.

In terms of types of cancer, 61% of patients in our study suffer from lung cancer with lung adenocarcinoma constituting the predominant number with 10 out of 11 patients suffering from it. In both Ong's and Zimmer's studies, lung cancer also constitutes a large portion of their cases with 9 cases in Ong's study bleomycin group and 8 cases in Zimmer's study bleomycin group. Nikbaksh et al's study however has breast carcinoma as their predominant cancer at 40% while lung adenocarcinoma at 22%.

In our study, complete responses to treatment were seen in 44.4% while 22.2% had a partial response. Failure to respond is at a rate of 33.3%. This gives a total response to treatment (complete and partial response) of about 66%. This is comparable to Ong's study in which 70% of patients in the bleomycin group have treatment success, 79% success rate in Zimmer's study, and 88% in Nikbaksh's study. Other older studies in the literature gave almost similar success rates with bleomycin around 64% in Moores et al, 66% in Hamed et al and 62% in Kessinger et al studies. This showed that our success rate is comparable with other studies of chemical pleurodesis being performed by respiratory or cardiothoracic teams.

In terms of complications, the majority of our patients did not report any immediate issues, with only 5.6% of patients having fever and 11.1% having pleuritic pain. This is almost similar to Nikbaksh's study with only 4% of patients having fever and 14% of patients having pleuritic pain. In Ong's study, 4 out of 20 patients had a fever and only 2 cases had pleuritic pain. This showed that bedside chemical pleurodesis is a generally safe procedure with minimal complications.

MPE generally is indicative of advanced disease and life expectancy is generally short with a median prognosis of 3-12 months[2]. In our study, 55.5% of patients did not survive the past 6 months with all patients that failed to respond to chemical pleurodesis being in this category. In Nikbaksh's study, 36% of patients died within the first 6 months while median survival in Ong's study was 5 months.

Many studies have described the benefit of pleurodesis to patients suffering from malignant pleural effusion. Parthipan et al in their study have described that pleurodesis did improve quality of life in 4-12 weeks although insufficient long-term data is needed[8]. Steffano et al in their study also reported of improvement in quality of life with the improvement of Karnofsky performance score from 62.1 to 71.3 and an improvement of MRC dyspnea score from 4.2 to 2.7[9]. Hence, it is proved that aiming for pleurodesis patients with MPE does help optimize and improve the quality of life which is one of the main palliative goals in this setting.

For future improvement, other alternative and newer ways to achieve pleurodesis in managing patients with malignant pleural effusion may be considered. This included strategies such as IPC insertion as well as the usage of another pleurodesis agent such as talc slurry which is cheaper and effective too. Further training may be needed to equip our Palliative team to offer more services to help improve patients' quality of life.

## Conclusions

Bedside chemical pleurodesis service is a relatively simple procedure that can also be safely offered by the Palliative team as a part of holistic care in patients with malignant pleural effusion. The outcome is comparable to those being performed traditionally by respiratory, cardiothoracic, or medical oncology colleagues with minimal complications. In a center that did not offer VATS pleurodesis or IPC insertion, bedside chemical pleurodesis can be offered safely and relatively easily by the Palliative team so as to achieve an overall improvement in quality of life. Further studies may need to look into other comparable agents such as talc slurry which is cheaper compared to bleomycin, and thus will further reduce the patients and their families' financial burden in long run.

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