A Propensity-Matched Comparison of Pleurodesis or Tunneled Pleural Catheter for Heart Failure Patients With Recurrent Pleural Effusion

Richard K. Freeman, MD, MBA, Anthony J. Ascioti, MD, Megan Dake, PA-C, and Raja S. Mahidhara, MD

Department of Thoracic and Cardiovascular Surgery, St. Vincent Hospital, Indianapolis, Indiana

Background. **Patients with severe heart failure often have recurrent pleural effusions that produce dyspnea and shortness of breath. It is unclear whether chemical pleurodesis or the placement of a tunneled pleural catheter that can be used for intermittent pleural drainage produces superior palliation, a shorter hospital stay, and less morbidity. This investigation compares these two treatments.**

Methods. **Patients with a recurrent, symptomatic, pleural effusion secondary to advanced heart failure who had undergone at least two unilateral thoracenteses were identified. Two patient groups were formed by propensity matching patients who received either talc pleurodesis or a tunneled pleural catheter. Patient demographics, length of stay, need for further intervention for the pleural effusion, and procedural morbidity and mortality were collected and compared. Patients who had undergone ventricular assist device placement or cardiac transplant were excluded.**

Results. **Over a 5-year period, 80 patients undergoing treatment were identified and propensity matched. All 80 patients were classified as having class III or IV heart failure. No significant differences in palliation from their effusion were identified. However, the group treated with a tunneled pleural catheter realized a significantly shorter hospital stay as well as a lower rate of operative morbidity and readmissions than patients undergoing talc pleurodesis.**

Conclusions. **This investigation found that a tunneled pleural catheter provided palliation of patients' pleural effusions and freedom from reintervention equal to that of talc pleurodesis using thoracoscopy while resulting in a shorter mean length of hospital stay. Lower rates of operative morbidity and readmission related to the pleural effusion were also seen in the tunneled catheter treatment group. This method of palliation of recurrent pleural effusion should be considered for symptomatic patients with advanced heart failure.**

(Ann Thorac Surg 2014;97:1872–7)
© 2014 by The Society of Thoracic Surgeons

Pleural effusion is commonly associated with congestive heart failure (CHF) with as many as 70% of patients having a significant unilateral, transudative effusion (Fig 1). The primary treatment for such pleural effusions, as in any nonmalignant pleural effusion, is directed at the underlying cause. However, a significant percentage of patients with advanced CHF have a symptomatic pleural effusion refractory to maximal medical management.

Several treatment options exist for a symptomatic pleural effusions caused by CHF. The optimal treatment requires individualization to each patient's performance status, prognosis, and comorbidities. This investigation compares the traditional treatment of thoracoscopic pleurodesis (TP) to the use of a tunneled pleural catheter (TPC) in patients with a symptomatic pleural effusion resulting from CHF.

Material and Methods

Institutional Review Board approval was obtained at the authors' institution, with individual patient consent not being required. This study was designed as a retrospective cohort analysis. The primary endpoint assessed in this study was palliation of the pleural effusion. The determination of adequacy of palliation was based on a lack of reintervention demonstrated during the follow-up period and the improvement in performance score after intervention.

All patients with class III or IV heart failure determined by the New York Heart Association functional classification undergoing TP of a unilateral pleural effusion during the study period who had undergone at least two previous thoracenteses and whose CHF therapy had been optimized were identified from the thoracic surgery service of the study institution. The same surgeons cared for all of the patients in both treatment groups. The

Accepted for publication Feb 4, 2014.

Presented at the Sixtieth Annual Meeting of the Southern Thoracic Surgical Association, Scottsdale, AZ, Oct 30–Nov 2, 2013.

Address correspondence to Dr Freeman, 8433 Harcourt Rd, Indianapolis, IN 46260; e-mail: richard.freeman@stvincent.org.

© 2014 by The Society of Thoracic Surgeons
Published by Elsevier Inc

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2014.02.027

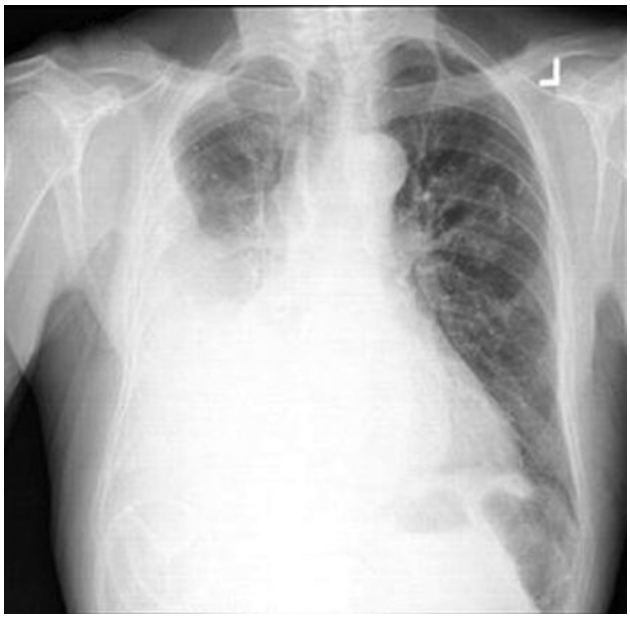

Fig 1. Chest roentgenogram of a patient with congestive heart failure and a pleural effusion.

propensity score method was used to control for potentially confounding variables and minimize the effect of selection bias in the allocation of patients to two cohorts: TP or TPC [1, 2]. Propensity scores were computed after multivariable regression analysis assessing a set of preoperative risk factors that included age, sex, heart failure severity score, and their Charlson comorbidity score. Patients who underwent TPC were matched nearest neighbor in a 1:1 fashion to those who had TP on the basis of the propensity score so that only patients with similar scores were compared.

Excluded from eligibility were patients who had undergone prior ipsilateral intrathoracic surgery or attempted pleurodesis, patients who required procedures other than pleurodesis at the time of surgery, had bilateral pleural effusions or ascites, or were a candidate for or had undergone cardiac transplantation. Also excluded were patients whose hospital stay was extended because of factors not related to the procedure, such as pneumonia, stroke, myocardial infarction, or acute renal failure. A minimum of 6 months of follow-up was required for inclusion.

Operative Technique

THORACOSCOPIC PLEURODESIS. Utilizing contralateral single-lung ventilation under general anesthesia, a single 5 mm or 10 mm video-assisted thoracic surgery port was placed most often in the anterior axillary line of the seventh intercostal space. Any pleural fluid was aspirated and sent for cytologic examination. Thoracoscopy was performed and the visceral and parietal pleural surfaces inspected. Talc pleurodesis was performed by insufflating 3 g sterile talc powder (Bryan Corporation, Woburn, MA) into the pleural space with the patient in the Trendelenburg position so that it would subsequently disseminate over the entire pleural surface. This dose is our standard in an attempt to reduce the incidence of what has been shown to be dose-dependent acute respiratory distress syndrome [3]. A tube thoracostomy was used to drain the pleural space exiting through the port incision. The chest tube was place to suction for 48 hours after surgery except when the patient was ambulating. The chest tube was removed when the drainage was recorded as being less than 250 mL over a 24-hour period with the intention to discharge the patient that day.

TUNNELED PLEURAL CATHETER. The TPC (Pleurx catheter; CareFusion, San Diego, CA) was placed by tunneling the catheter in the subcutaneous tissues laterally from a skin insertion site approximately 8 cm, at which point it was placed into the pleural space using a modified Seldinger technique. Once in place, the TPC was used to remove all of the pleural fluid present. All catheters were inserted in the operating room. Fluoroscopy was utilized selectively in the minority of patients. All of the catheters were placed using local anesthesia with or without intravenous sedation as required. Patients were discharged home the same day unless there was another cause for admission. Drainage of the TPC was typically carried out twice a week. If a patient's pleural effusion resolved during follow-up, the catheter was removed using local anesthesia.

The use of TPC or TP was at the discretion of the operating surgeon and was based primarily on the preference of each patient as expressed in preoperative counseling and consideration for preferences expressed by the referring physician with regard to other treatment modalities that were in process or planned. During such counseling, both treatment alternatives were presented along with the expected hospital length of stay, associated potential morbidities, and aftercare requirements. A decision was then made with the patient taking into account their unique circumstances, treatment goals, and performance status.

Bivariate analysis of data was performed using GraphPad Prism software 4.02 (San Diego, CA) for Windows (Microsoft, Redmond, WA). Differences between categorical variables were evaluated by Fisher's exact test. Differences between continuous variables were measured by the two-tailed Student t test or the Mann-Whitney U test for nonnormally distributed data. Multivariate analysis was performed using Stata version 11 (StataCorp, College Station, TX). A value of p less than 0.05 was considered significant.

Results

Between 2007 and 2012, 40 patients who met the study's inclusion criteria underwent TPC for the treatment of a unilateral pleural effusion despite optimal medical management of their CHF at the study institution. These patients were propensity matched with 40 of the 144 patients who underwent TP for a heart failure related effusion during the same period. Table 1 compares their

Table 1. Demographic Comparison of Patients Undergoing Thoracoscopic Pleurodesis or Tunneled Pleural Catheter

Variable	TP	TPC	*p* Value[a]
Number	144/40	40	
Female	23 (58%)	23	1
Age, years, mean ± SD	66 ± 13	69 ± 11	0.3
Inpatient status	21 (53%)	23 (58%)	0.8
Heart failure, NYHA class	3.3	3.4	0.6
Charlson index, mean	7.1	7.3	0.4

[a] After matching.

NYHA = New York Heart Association; TP = thoracoscopic pleurodesis; TPC = tunneled pleural catheter.

demographic data, which imply they are comparable based on the results of the matching process.

Table 2 displays the outcomes reviewed for the cohort analysis. The determination of adequacy of palliation was based on a lack of reintervention demonstrated during the follow-up period and the improvement in performance scores for each treatment group. Neither of these metrics varied significantly between the two cohorts. Reinterventions included ipsilateral ultrasound-guided thoracentesis or image-guided pleural drainage catheter placement. No patient in either group required further surgical intervention including reinsertion of a tunneled pleural catheter. One TPC was associated with a superficial infection that did not require removal during the follow-up period.

Significantly more patients undergoing TP experienced a complication related to the procedure. That was primarily influenced by the higher rate of respiratory insufficiency, defined by persistent hypoxemia requiring high flow supplemental oxygen or mechanical ventilation or both observed in the TP group but also included patients who had a pulmonary embolism or atrial fibrillation. Although operative mortality did not differ between the treatment cohorts, the only deaths in either cohort occurred in the TP group and were attributed to talc-induced respiratory failure.

Table 2. Comparison of Outcomes After Thoracoscopic Pleurodesis and Tunneled Pleural Catheter

Variable	TP	TPC	*p* Value
Number	40	40	
Follow-up, months, mean ± SD	7 ± 3	6 ± 2	0.08
Reintervention for PE	2 (5%)	1 (2.5%)	1
Hospital LOS, days, mean (range)	6 ± 4 (4–13)	2 ± 2 (1–6)	<0.0001
HF score change, mean	−0.7	−0.9	0.1
Readmission	9 (23%)	2 (5%)	0.048
Morbidity	8 (20%)	1 (2.5%)	0.03
Respiratory insufficiency	5	1	
Pulmonary embolism	1	0	
Atrial fibrillation	2	1	
Operative mortality	2 (5%)	0	0.5
TPC removal	…	14 (35%)	

HF = heart failure; LOS = length of stay; PE = pleural effusion; TP = thoracoscopic pleurodesis; TPC = tunneled pleural catheter.

The TPC patients had a significantly shorter hospital stay than TP patients. The longer length of stay in TP patients was related to two factors. The first was the need for continued chest tube drainage in the TP group, with a mean of 5 ± 4 days. Length of stay was also extended by the higher rate of morbidity in the TP group, as previously described. Patients receiving TPC also had a lower incidence of readmission to the hospital than TP patients.

Mean follow-up was comparable between the two patient groups (Table 2). At last available follow-up, mean survival of the two groups was also comparable. Fourteen patients (35%) had their TPC removed because of resolution of the effusion during the follow-up period at a mean of 5 months after insertion (Fig 2). None of these patients required further intervention for an ipsilateral pleural effusion.

Comment

Approximately 5.7 million people in the United States have been diagnosed with heart failure, of whom nearly one half will die within 5 years [4, 5]. Despite significant advances in the treatment strategies for patients with CHF, as many as 70% will experience a symptomatic, unilateral pleural effusion during some phase of their care [6]. A smaller subset of patients will have a persistent, symptomatic pleural effusion despite optimal medical management of their CHF.

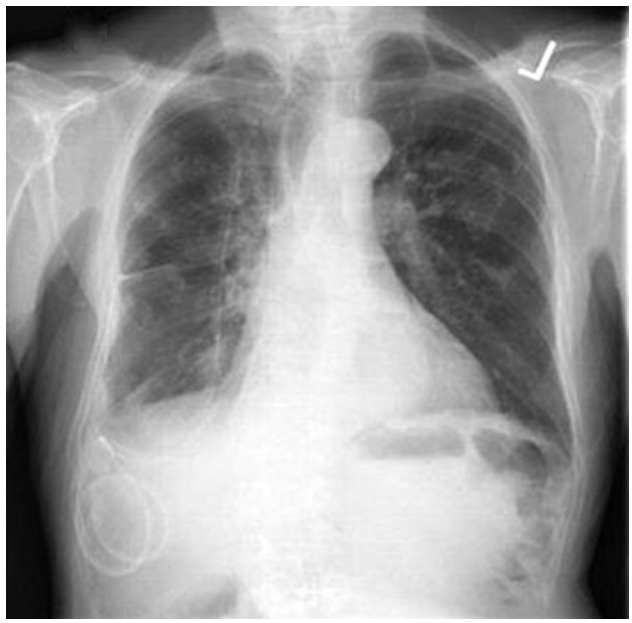

Fig 2. Chest roentgenogram of a patient whose pleural effusion from congestive heart failure has been controlled with a tunneled pleural catheter.

The optimal treatment for a patient with CHF and a symptomatic pleural effusion depends on the patient's prognosis, functional status, and personal preferences. Traditional options for therapy have included intermittent thoracenteses, "bedside" chemical pleurodesis, thoracoscopic pleurodesis, and various forms of indwelling pleural catheters. Intermittent thoracentesis is useful for the patient with a significant latency period between accumulations of the effusion. However, it is not optimal for patients with a rapidly accumulating effusion, patients maintained on systemic anticoagulation therapy, or patients who do not reside in proximity to centers offering such services. Despite the movement toward image-guided thoracentesis, the procedure is also not without some degree of risk.

Pleurodesis is an effective treatment for patients with a pleural effusion related to CHF. Nonoperative, or bedside, pleurodesis involves the installation of a sclerosant through a tube thoracostomy. Many centers have abandoned this practice in favor of the more effective thoracoscopic pleurodesis [7]. Thoracoscopic pleurodesis offers the advantages of better distribution of the sclerosant and the ability to assess the lung and pleural space, often with a single port incision. The TP can also be performed without general anesthesia [8]. However, either form of chemical pleurodesis is associated with an extended hospital stay because of the need for pleural drainage and the risk of respiratory complications associated with the sclerosants [9, 10].

Indwelling pleural catheters of various forms have been utilized for patients with benign and malignant pleural effusions. Catheters that create a shunt of pleural fluid to the peritoneal cavity or venous system have been well described but are used infrequently today because of their complexity of placement and unreliability [11]. Tunneled pleural catheters have been widely embraced for the palliation of malignant pleural effusions with reports of decreased hospital stay, cost, rates of reintervention, and morbidity when compared with TP [12–14].

Some tunneled pleural catheters, such as the one used in this investigation, have been approved for the treatment of symptomatic, benign pleural effusions. Two published reports were discovered in which TPC placement was performed in patients for palliation of benign pleural effusion. Chalhoub and coworkers [15] in 2011 reported a series in which 23 patients received a TPC for a symptomatic pleural effusion resulting from various etiologies. This cohort included 13 patients with CHF. The investigators found that a TPC achieved a high rate of palliation of the effusion without the need for reintervention in their patients. They also found that the majority of these patients eventually realized resolution of their pleural effusion and had their TPC removed at a mean of 111 $\pm$ 41 days. No comparison between other forms of therapy was made.

In a similar review published in abstract form, Parsaei and colleagues [16] in 2006 reported a series of 42 patients with benign pleural effusions of various causes treated with a TPC. Nine of these patients had effusions related to CHF. The researchers reported that 38 patients (84%) had significant palliation without a complication related to the TPC. Mean duration of catheter use was 95 days, with 26 catheters (58%) removed after the effusion resolved. Nine catheters (20%) were removed because of infection, bleeding, or failure.

This investigation found that a TPC achieved rates of palliation and improvement in mean heart failure scores similar to those for patients who underwent TP. However, the TPC patient cohort realized a significantly shorter mean hospital stay, reduced incidence of procedural morbidity, and reduced rate of readmission. Although cost data were not available for this study, the significant difference in the two cohorts' mean lengths of stay would imply a lower cost for the TPC group. Furthermore, no TPC failures and only one catheter-associated infection was identified.

No significant difference was identified in the reintervention rate between the two patient groups. That is, in part, likely due to a relatively low rate of reintervention in our TP patients that we attribute to a conservative protocol for chest tube removal. The rate of respiratory insufficiency in this investigation is similar to previously reported series of patients undergoing talc pleurodesis. However, the overall rate of morbidity was significantly less in the TPC cohort. This was an important clinical finding as it certainly affected the length of stay in the TP group and could be a contributing factor to readmission rates, as well.

While the results of this investigation are compelling, some limitations exist in the comparison of the two patient groups. A retrospective analysis was performed and, despite using propensity analysis to generate two similar patient cohorts, a prospective, randomized design would have been preferable. However, as has been pointed out in previous discussions regarding the TPC, patient and referring physician expectations and preferences would pose difficulties for administering such a protocol. In fact, a recent cooperative group trial attempting to randomize patients between TPC and TP was closed because of insufficient patient accrual [9].

Further criticisms of this review are that a relatively small absolute number of patients was involved in this comparison and that all the patients received their treatment at a single institution. Although a weakness of this review, small sample size is inherent in evaluating a very select subset of patients with a pleural effusion resulting from CHF. The inclusion and exclusion criteria that were believed necessary to allow a valid comparison such as a 6-month follow-up and the optimization of medical therapy further narrowed the available number of patients. However, these criteria were considered essential when comparing complex patients for a single treatment effect.

In conclusion, this investigation found that a TPC provided palliation and an improvement in heart failure classification equal to that of TP. However, patients receiving a TPC realized a significantly shorter mean hospital length of stay, reduced rate of readmission, and a lower incidence of operative morbidity. Tunneled pleural

catheters should be considered a safe and effective form of palliation of a symptomatic pleural effusion associated with CHF.

References

1. Pearl J. Causality: models, reasoning, and inference. 2nd ed. Cambridge, UK: Cambridge University Press; 2009.
2. Parsons L. Reducing bias in a propensity score matched-pair sample using greedy matching techniques. Cary, NC: SAS Institute. Proc 26th Annual SAS Users Group Int Conf, 2001:214–26.
3. Montes JF, Ferrer J, Villarino MA, Baeza B, Crespo M, Garcia-Valero J. Influence of talc dose on extrapleural talc dissemination after talc pleurodesis. Am J Respir Crit Care Med 2003;128:348–55.
4. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. Circulation 2012;125:e2–220.
5. Kochanek KD, Xu JQ, Murphy SL, Miniño AM, Kung HC. Deaths: final data for 2009. Natl Vital Stat Rep 2011;60(3).
6. Porcel JM, Light RW. Diagnostic approach to pleural effusion in adults. Am Fam Phys 2006;73:1211–20.
7. Dresler CM, Olak J, Herndon JE, et al. Phase III intergroup study of talc poudrage vs talc slurry sclerosis for malignant pleural effusion. Chest 2005;127:909–15.
8. Katlic MR, Facktor MA. Video-assisted thoracic surgery utilizing local anesthesia and sedation: 384 consecutive cases. Ann Thorac Surg 2010;90:240–5.
9. Hunt BM, Farivar AS, Vallières E, et al. Thoracoscopic talc versus tunneled pleural catheters for palliation of malignant pleural effusions. Ann Thorac Surg 2012;94:1053–9.
10. Freeman RK, Ascioti AJ, Mahiidhara RS. A propensity-matched comparison of pleurodesis or tunneled pleural catheter in patients undergoing diagnostic thoracoscopy for malignancy. Ann Thorac Surg 2013;96:259–64.
11. Light RW. Pleural diseases. Philadelphia: Lippincott, Williams & Wilkins; 2007:154–5.
12. Putnam JB, Walsh GL, Swisher SG, et al. Outpatient management of malignant pleural effusion by a chronic indwelling pleural catheter. Ann Thorac Surg 2000;69:369–75.
13. Warren WH, Kim AW, Liptay MJ. Identification of clinical factors predicting Pleurx catheter removal in patients treated for malignant pleural effusion. Eur J Cardiothorac Surg 2008;33:89–94.
14. Puri V, Pyrdeck TL, Crabtree TD, et al. Treatment of malignant pleural effusion: a cost-effectiveness analysis. Ann Thorac Surg 2012;94:374–80.
15. Chalhoub M, Harris K, Castellano M, Maroun R, Bourjeily G. The use of the Pleurx catheter in the management of non-malignant pleural effusions. Chron Respir Dis 2011;8:185–91.
16. Parsaei N, Khodaverdian R, McKelvey AA, Federico JA, Fabian T. Use of a long-term indwelling tunneled pleural catheter for the management of benign pleural effusion. Chest 2006;130(Suppl):271.

DISCUSSION

DR BETTY C. TONG (Durham, NC): Thank you for the opportunity to discuss this paper. Dr Freeman, congratulations on an interesting and thought-provoking study, and thank you for providing me with a copy of the manuscript in advance.

Your study demonstrated that both talc pleurodesis and tunneled pleural catheter are highly effective in treating benign pleural effusion. There were no differences between the groups in terms of reintervention and heart failure score, which could be viewed as a surrogate for symptom palliation. With two seemingly equivocal methods of treatment, patient preferences, then, should move to the forefront in terms of surgical decision making. You reported in the manuscript that patients were counseled preoperatively regarding pros and cons of both methods and that the procedure selected was based on these stated preferences. So in addition to symptom palliation, how did the groups compare in follow-up with regard to pain, quality of life, and ultimately patient satisfaction with their choice of treatment?

And secondly, perhaps the most obvious question in our current culture of "Obamacare" and cost containment pertains to both short- and long-term cost differences between the two groups and how this should be factored into the decision-making process moving forward. If there were a cost differential, how would you reconcile a lower cost choice with one that may be more expensive over the long term but perhaps less morbid and preferable to the patient? Thank you again. I look forward to hearing your comments.

DR FREEMAN: Thank you very much. I appreciate you reviewing the manuscript and I think your questions are very appropriate. Patient counseling is always difficult, and I as a surgeon have a mantra that outcomes for patients that are subjective really depend on what they go into the surgery thinking. And so if they come in my office and they have already been talked to and they want a tunneled pleural catheter and you don't give them that, you are going to have a hard time having them have subjective good outcomes, whereas if they get what they think they need and it is medically indicated, they are going to have, in their mind, a better outcome. In our practice, we do individualize the treatment to the patient, we take into consideration their wishes, and in that respect I think, at least from what I see, our satisfaction is about equal.

Your second question is a more difficult question and a very appropriate question. If we look at the Washington University study where they did a cost analysis of tunneled pleural catheter versus pleurodesis, the tipping point was a survival of about 90 days where the costs flipped from tunneled pleural catheter to pleurodesis. And so you do have to reconcile that in benign disease such as heart failure. At least in the preliminary work that we have done, the decrease in morbidity and decrease of length of stay I think extends that. Our next project is to look at that in a more formal way.

DR JOSHUA ROBERT SONETT (New York, NY): Rich, a great study as always, excellent and interesting topic. My question is, if I took it right, 65% of the patients at 6 months still had their catheter in place, is that correct?

DR FREEMAN: That is correct, yes.

DR SONETT: So is this going to be a lifetime of a tunneled pleural catheter? Don't they increase their chance of infection rate over time and what is going to happen? I just saw somebody with a horrible chest that has had one in for 2 years. At some time there is liable to be an end with these and they are going to eventually get infected, that has been our experience, and I don't even think they are really FDA approved for life.

DR ROBERT J. CERFOLIO (Birmingham, AL): They are not. Three months, the company says 3 months, but we all cheat in malignant disease.

DR SONETT: Of course. So what is the plan long term and did you ever think maybe at a certain time, like 3 months, doxycyline or bleomycin through that catheter after having good lung apposition for 2 or 3 months to try to ultimately get them free of the catheter. Thanks. Excellent study. Appreciate it.

DR FREEMAN: The infection rate that we have seen is low. We have great support staff who talk to these patients almost every week, and if there is a sign of infection, we see them early and we often remove the catheter.

What to do with the patients long term is a very good and difficult question. As you saw, the national statistics are that about half of these people will die over a 5-year period. That is not 90 days like we see in malignancy. The majority of patients do resolve their benign effusion. Sometimes it does take 10 to 12 months, but they do resolve, at least in my experience. They are FDA approved for benign disease.

DR DANIEL L. MILLER (Atlanta, GA): I have one question. We still use a traditional Denver shunt at times. When a patient is not going to be a transplant candidate in the future and a patient does not want to have a catheter hanging out of their side, we actually still use a true Denver shunt even though they have got to push it multiple times and they get a little sore at the beginning, but that is what we have used for chronic heart failure. So in your patients, do you offer them a Denver shunt at all, because I think that is something that we have gotten away from when the tunneled pleural catheter came out. Do you offer that at all or do have any experience with the Denver shunt?

DR FREEMAN: It is a great question, Dan, and I am influenced by my early experiences with those particular catheters where we were lucky to get the patient out of the postanesthesia care unit sometimes with them functioning. I personally have not used them in many years.