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**The Impact of Gravity versus Suction-driven Therapeutic Thoracentesis on Pressure-related Complications: the GRAVITAS Multicenter Randomized Controlled Trial**

Running Head: GRAVITAS Multicenter RCT

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ABBREVIATIONS LIST

REPE: re-expansion pulmonary edema

VAS: visual analog scale

ABSTRACT

Background: Thoracentesis can be accomplished by active aspiration or drainage with gravity. We investigated whether gravity drainage could protect against negative-pressure related complications, such as chest discomfort, re-expansion pulmonary edema or pneumothorax, compared to active aspiration.

Methods: This prospective, multicenter single blinded randomized controlled trial allocated patients with large free-flowing effusions estimated ≥ 500 mL 1:1 to active aspiration or gravity drainage. Patients rated chest discomfort on 100 mm visual analog scales before, during, and after drainage. Thoracentesis was halted at complete evacuation or for persistent chest discomfort, intractable cough, or other complication. The primary outcome was overall procedural chest discomfort scored five minutes post-procedure. Secondary outcomes included measures of discomfort and breathlessness through 48 hours post-procedure.

Results: One hundred forty-two patients were randomized with 140 in the final analysis. Groups did not differ for the primary outcome (mean VAS score difference 5.3 mm, 95% CI -2.4 to 13.0, $p = 0.17$). Secondary outcomes of discomfort and dyspnea did not differ between groups. Comparable volumes were drained in both groups but procedure duration was significantly longer in the gravity arm (mean difference 7.4 minutes, 95% CI 10.2 to 4.6, $p<0.001$). There were no serious complications.

Conclusions: Thoracentesis via active aspiration and gravity drainage both appear safe and result in comparable levels of procedural comfort and dyspnea improvement. Active aspiration requires less total procedural time.

Trial Registration: Clinicaltrials.gov, number NCT03591952

## Introduction

Thoracentesis is among the most common procedures performed in clinical medicine[1–3]. Although considered a low-risk procedure, complications rates in excess of 5% have been reported, and appear more common when large pleural fluid volumes are aspirated and perhaps when vacuum suction is utilized[4,5]. Multiple complications, including pneumothorax ex-vacuo, re-expansion pulmonary edema (REPE), and chest discomfort, have been associated with increasingly negative pleural pressure developing as fluid is withdrawn if the lung is not fully re-expandable[6–11]. Pleural pressure lower than -20 cm $H_2O$ has traditionally been considered excessively negative, based primarily on data obtained from early animal models[3,8–10,12].

Despite the association between pleural pressure and complications, a recent trial of routine pleural manometry during therapeutic thoracentesis, which had been proposed as a possible safeguard against such complications, failed to result in improvement in patient comfort or reduction in serious complications[13]. Another potential method to mitigate the risk of negative pressure-related complications is drainage by gravity, which may result in significantly less negative pleural pressure than aspiration by suction or vacuum. We hypothesized that gravity drainage would result in less chest discomfort, a common negative-pressure related complication of thoracentesis, compared to suction drainage in a randomized, single-blinded fashion.

## Materials and Methods

### Study Design and Participants

We conducted a randomized, controlled, single-blind trial at 10 US academic medical centers. Patients referred to interventional pulmonology for thoracentesis were screened. Eligible patients were ≥18 years old with symptomatic pleural effusions estimated at least 500 mL in volume, defined as such if one of the following criteria were met: effusion occupying at least one third of the hemithorax on chest radiograph[14], maximum anteroposterior depth of effusion at least one third the anteroposterior dimension of the hemithorax on the axial computed tomography image immediately superior to the dome of the hemidiaphragm[15], or effusion spanning at least three interspaces on ultrasonography with depth at least 3 cm in one or more interspaces in a patient sitting upright[16]. Patients were excluded if effusions did not appear free-flowing due to septations or loculation present on pre-procedure imaging, they were unable to sit for the procedure, or unable to provide informed consent. All participants provided written informed consent. This study was approved the institutional review boards at each participating center (**Table S1**).

### Randomization

Patients were randomly assigned to thoracentesis with fluid drained by gravity (gravity group) or manual aspiration using a syringe (control group). The allocation sequence was generated by computer, using permuted blocks of four and six, stratified by each institution, with 1:1 allocation ratio. Allocations were assigned by opening a sealed opaque envelope prepared by a research assistant (LR) who did not participate in enrollment decisions. Envelopes were opened after placement of the thoracentesis catheter in the pleural space to prevent allocation bias on baseline measures. Patients were kept unaware of their assignment to gravity or suction as catheters were introduced into the posterior hemithorax and proceduralists remained behind the patient for the duration of the procedure.

Study Procedure

Patients were positioned in an upright seated position. Thoracic ultrasonography identified ideal catheter placement location. Overlying skin was anesthetized by local infiltration of plain 1% lidocaine before insertion of an 8F over-needle-style catheter (Safe-T-Centesis, BD, Franklin Lakes, NJ, USA or Arrow-Clarke Pleura-Seal, Teleflex, Morrisville, NC, USA) under standard sterile precautions. In the suction arm, pleural fluid was aspirated actively using a 60 mL syringe. In the gravity arm, the catheter was attached to a drainage bag placed approximately 100 cm below the catheter insertion site via straight tubing of the same length. If fluid did not spontaneously fill the tubing to start drainage into the bag, a syringe was used to prime the tubing with approximately 5 mL of pleural fluid.

Complete evacuation of the pleural space was the goal of all procedures. Drainage was stopped early for persistent chest discomfort consistent with excessively negative pleural pressure (pressure-like in the central anterior chest, neck, or jaw, worse with inspiration), intractable cough, worsening dyspnea, vagal reaction, or if other complication occurred. Reason for drainage termination, volume drained, and procedure time (catheter-in to catheter-out) were documented.

Patient-centered data were obtained using 100 mm horizontal visual analog scales (VAS), with labels “No discomfort at all” at 0 mm and “Worse possible discomfort” at 100 mm. For queries regarding breathlessness, the word “breathlessness” replaced “discomfort.” These scales are well-validated for patient-reported pain and breathlessness measurements[17–19]. Patients were asked to rate their degree of overall chest discomfort and breathlessness on the day of the procedure as well as current degree of chest discomfort prior to procedure start, after thoracentesis catheter was placed, prior to catheter removal, and immediately after catheter removal. Five minutes after catheter removal, patients indicated their overall degree of procedure-related chest discomfort from procedure start to that moment, as well as current degree of breathlessness. At 24 hours and 48 hours post-procedure, patients

were contacted to rate their degree of chest discomfort by providing a number from 0 to 100, with 100 being the worst possible discomfort. The Modified Borg Scale for Dyspnea, well-validated for dyspnea measurements in lung disease with a minimal clinically important difference of 1 unit[20], was used to assess breathlessness pre-procedure and 5 minutes, 24 hours, and 48 hours post-procedure.

All patients underwent post-procedure thoracic ultrasound to assess for the presence of more than scant remaining pleural fluid as well as chest radiograph to determine the degree to which lung re-expansion occurred and to assess for pneumothorax and REPE.

Outcomes

The primary outcome was patient-reported overall procedural chest discomfort assessed by VAS five minutes post-procedure. This primary outcome, also used in a recent similar trial conducted by this group[13], was chosen because it is clinically relevant, patient-centered, and chest discomfort represents the most frequent complication of thoracentesis which has been attributed to excessively negative pleural pressure[6,7,21]. Secondary outcomes were discomfort by VAS prior to catheter removal, immediately after catheter removal, at 24 hours, and at 48 hours; breathlessness by VAS and Borg at 5 minutes post-procedure and by Borg at 24 hours and 48 hours post-procedure, volume drained, procedure duration, and frequency of complete lung re-expansion as assessed by post-procedure thoracic ultrasound and chest radiograph. Post-procedure radiographs were also inspected for pneumothorax or REPE.

Statistical analysis

Baseline VAS chest discomfort scores reported in the TIME2 trial[22] and previously reported VAS pain score minimum clinically important difference[17] were used to inform the power calculation. Using a two-sample t-test, a sample size of 128 patients (64 in each group) was determined to have 80% power

to detect a 15 mm decrease in VAS chest discomfort score (SD 30 mm) with gravity drainage with probability of a type I error set at $\alpha=0{\cdot}05$.

Statistical analysis was conducted in R version 3.3.1 according to pre-specified statistical analysis plan. Analysis was modified intention to treat, such that all patients with any procedure or outcome data were analyzed. Descriptive statistics included means, standard deviations, and ranges for continuous parameters, and percentages and frequencies for categorical parameters. Investigations for outliers and assumptions for statistical analysis, e.g., normality and homoscedasticity, were made. Comparisons between gravity and suction groups were made using the t-test for continuous variables and Chi-square test for categorical variables. There were no pre-specified sub-analyses. Two post-hoc analyses were performed. Multivariable linear regression was used to assess the association between the primary outcome and drainage method with the adjustment of nonlinear effect of current chest discomfort pre-procedure using a restricted cubic spline with three knots. Additionally, a per-protocol analysis of the primary outcome was conducted excluding suction procedures performed by any mechanism other than protocol-directed manual aspiration. A data monitoring committee was not established to oversee this trial as both methods of pleural fluid drainage studied are considered standard of care. The trial was registered at clinicaltrials.gov under identifier NCT03591952.

**Results**

Between October 11, 2018 and April 5, 2019, 201 patients were screened and 142 randomized to thoracentesis with gravity or suction drainage (**Figure 1**). Two subjects in the gravity group were withdrawn by investigators before pleural fluid was removed or outcome data obtained, one for discovery of a non-free-flowing effusion requiring alternative procedure and the other because equipment to perform the study procedure was unavailable. The final analysis included 62 patients who underwent gravity drainage and 78 who underwent aspiration via suction. This imbalance resulted from ten sites enrolling simultaneously from distinct permuted block randomization schedules. Once the recruitment target was met, all sites immediately stopped enrolling; this imbalance represents a swing of 8 allocations across all sites.

Patients assigned to each group were well-matched on baseline characteristics (**Table 1**). Average chest discomfort on the day of procedure did not differ between groups (mean difference in VAS scores 3.9 mm, 95% CI -5.6 to 13.5). Current chest discomfort immediately before procedure start did differ between groups (suction VAS score 22.9 ± 25.0 mm vs. gravity 12.3 ± 18.1).

The primary outcome of overall procedural chest discomfort measured by VAS five minutes post-procedure did not differ between suction and gravity groups (mean difference in VAS scores 5.3 mm, 95% CI -2.4 to 13.0, p = 0.17; **Table 2** and **Figure 2**). Likewise, there was no difference between suction and gravity groups for any patient-reported secondary outcome, including intraprocedure or post-procedure VAS discomfort scores (**Table 2** and **Figure 3**), post-procedure VAS and Borg dyspnea scores (**Table 3** and **Figure 4**), or pre-to-post procedure differences in VAS discomfort and dyspnea scores (**Tables 2 and 3**). Post-hoc analyses of the primary outcome, one adjusting for current chest discomfort pre-procedure and the other a per-protocol analysis excluding 11 suction procedures performed with continuous wall suction instead of protocol-dictated manual syringe aspiration, also

found no difference between suction and gravity groups (**Table S2-3 and Figures S1-3**). Primary and secondary outcomes were similar when the Wilcoxon rank sum test was used (**Table S4**). More than 1500 mL was drained in 31 procedures (17 gravity, 14 suction) with no difference between groups on any outcome measures within this subset and no complications occurred in these patients.

The volume of fluid drained in each group was equivalent (mean 1264 ± 724 mL in suction vs. 1165 ± 543 mL gravity, mean difference 99 mL, 95% CI -113 to 310, p=0.89). Procedure duration was significantly shorter in the suction group (mean duration 10.5 ± 6.1 minutes vs. 17.8 ± 9.7, mean difference 7.4 minutes, 95% CI 4.6 to 10.2, p<0.001). See **Table 4** and **Figure 5**.

Reasons for thoracentesis cessation and final diagnoses of all effusions are detailed in **Tables 4** and **5**. In both groups, drainage stopped spontaneously in approximately half of procedures and the other half were stopped early for chest discomfort, with a small minority stopped for other reasons. Post-procedure ultrasound revealed more than scant residual pleural fluid in approximately half of patients in each arm, with similar reasons for drainage discontinuation between groups (**Table S5**).

No significant adverse events were observed. One pneumothorax was documented on post-procedure chest radiograph in the suction group, with approximately 2 millimeters of apical pleural separation. During this procedure, a small amount of air was noted to be entrained via the thoracentesis catheter while attaching the drainage apparatus and the pneumothorax had resolved several hours later. There were no instances of pneumothorax ex-vacuo, expanding pneumothorax, re-expansion pulmonary edema, or bleeding complication.

**Discussion**

In this multicenter, randomized, controlled, single-blind trial we assessed two standard-of-care methods for draining pleural fluid during therapeutic thoracentesis with regards to clinically-relevant patient-centered primary and secondary outcomes. We did not find any difference between active pleural fluid aspiration and gravity drainage related to patient comfort, including chest discomfort measured by VAS or breathlessness measured by VAS and Modified Borg. In both groups, chest discomfort increased during the procedure before returning to pre-procedure baseline approximately 24 hours later (**Figure 3**) and breathlessness continued to improve through 48 hours post-procedure (**Figure 4**). The only significant difference between groups was the time required to drain equivalent volumes of fluid, with gravity requiring a mean additional 7.4 minutes. There were no significant complications in either group. Both methods of pleural fluid drainage appear safe and result in comparable levels of procedural comfort and improvement in dyspnea, with active aspiration requiring less overall time.

Major complications of therapeutic thoracentesis, including chest discomfort, pneumothorax ex-vacuo, and re-expansion pulmonary edema, have been associated with increasingly negative pleural pressures, occurring when fluid is excessively aspirated in the setting of non-expandable lung[3,6–10]. The presence of non-expandable lung, with a prevalence of 40% in a recent similar trial[13], is difficult to predict before therapeutic thoracentesis. Recent work has focused on whether direct monitoring of pleural pressures via manometry might prevent pressure-related complications. A recent randomized trial found that routine use of a digital pleural manometer during therapeutic thoracentesis conferred no benefit[13]. The current study sought to evaluate whether changing the degree of negative pressure applied to the pleural space during therapeutic thoracentesis would improve patient comfort.

Despite the frequency with which thoracentesis is performed and association between pleural pressure and complications, optimal drainage methods have not been extensively studied. As a result,

significant variation exists in drainage techniques, with intermittent suction via manual syringe aspiration, continuous suction via vacuum bottle or wall-based suction, and drainage to gravity all considered standard of care. These methods all apply negative pressure to the pleural space but to different and often variable magnitudes. Kelil and colleagues measured ex-vivo pressures generated by evacuated bottle, 60 mL Luer-lock syringe, and wall suction with regulator turned to maximal continuous suction. Maximum negative pressures measured were -963 cm $H_2O$, -802 cm $H_2O$, and -706 cm $H_2O$, respectively[23]. Alraiyes and colleagues, measuring negative pressures during therapeutic thoracentesis using digital manometers positioned in-line between thoracentesis catheter and drainage line, noted maximal negative pressures of approximately -250 cm $H_2O$ aspirating with a 60 mL syringe and -115 cm $H_2O$ with evacuated bottle[24]. The gravity drainage method utilized in this study generated constant negative pressure of approximately -17 cm $H_2O$, significantly lower than all active-suction pleural fluid aspiration methods (**Figures S4-5**).

No prior studies have compared pleural fluid drainage by gravity to active aspiration. Senitko and colleagues randomized 100 patients to drainage by manual syringe aspiration or evacuated bottle and found more complications in the latter group, though some questioned whether this study was adequately powered[4,25]. Sagar and colleagues, in a brief letter, report a complication rate of 0.012% using maximal wall suction to aspirate pleural fluid[25]. Kim and colleagues reported no increase in complication rate after switching from evacuated container to wall suction in a prospective observational series involving 421 thoracenteses[26], though objective chest discomfort measurements were not reported.

We hypothesized that gravity drainage would result in less chest discomfort. One criticism of intermittent pleural manometry-guided thoracentesis is the significant “blind time” between pleural pressure measurements, when highly negative pressures might be generated by active aspiration methods if the lung reaches its limit of normal expandability between measurements[13,27]. Excessively

negative intrapleural pressures might be avoided by an aspiration mechanism which does not utilize a degree of suction in the excessively negative range. However, our findings suggest that this strategy does not protect against chest discomfort. There are several potential explanations for this finding. While gravity drainage involves a significantly lower degree of suction, it does still apply negative pressure to the pleural space, and despite the studied gravity apparatus exerting negative pressure ex-vivo below the threshold of "excessively negative," excessively negative pleural pressure could still develop in the breathing patient with nonexpandable lung due to swings in pleural pressure with respiration. Additionally, the relationship between intrapleural pressure and chest discomfort is inconsistent. In a large prospective series, Feller-Kopman and colleagues noted only 22% of patients who developed chest discomfort had excessively negative pleural pressure and 9% of patients with excessively negative intrapleural pressure had no symptoms[7]. Others have noted the development of pneumothorax ex-vacuo despite use of pleural manometry with avoidance of excessively negative pleural pressure[21,28]. Heidecker and colleagues have suggested local non-uniform stresses exerted on the visceral pleura, rather than global pressure within the pleural space, might explain these findings[21].

Of paramount importance in considering a randomized trial in which no difference was found between groups is whether a type II error has occurred. This trial was appropriately powered using superiority design to detect a clinically meaningful difference in VAS discomfort score, with planned enrollment of at least 64 patients in each arm. Variability of the primary outcome did not exceed variability assumed for the power calculation (actual overall SD 22.9 versus assumed SD of 30). We did see an imbalance in allocation away from the planned 1:1 ratio due to ten sites enrolling simultaneously from distinct permuted block randomization schedules. Repeat power calculation using the final allocation numbers confirms this trial remains appropriately powered (power of 83%). There were very few post-randomization exclusions. There was complete outcome data on all patients. Among 201 screened patients, only 47 (23%) were excluded before randomization, the majority of which (37 of 47)

for effusions which were too small by objective radiographic criteria, supporting the external validity of our findings.

Baseline characteristics were similar between groups, except for lower immediate pre-procedure chest discomfort in the gravity group. If gravity drainage was more comfortable within the predefined time points, as hypothesized, we should certainly have seen lower chest discomfort scores on the primary outcome after starting at a lower baseline level of discomfort, and post-hoc analysis adjusting for immediate pre-procedure chest discomfort concurred with the primary analysis. Furthermore, all secondary outcomes related to discomfort, including pre-to-post change in discomfort, failed to identify a difference between groups. Eleven thoracenteses allocated to suction were accomplished with continuous wall suction rather than protocol-directed manual syringe aspiration. Both methods have been shown to produce comparable levels of negative pressure as reviewed above, with one study associating continuous suction with more discomfort and higher incidence of other complications[4]. If true, this should also have biased toward finding a difference between these groups, which we did not, and post-hoc per-protocol analysis excluding wall suction cases concurred with the primary analysis. Thus, we are confident on the basis of the data integrity that this study represents a true negative for the primary outcome analysis.

This study has several limitations. It was not powered to detect differences in re-expansion pulmonary edema or pneumothorax ex-vacuo, which would require prohibitively large sample sizes. Manometry was not utilized during thoracenteses in this trial so the precise negative pressures being applied in vivo by the two studied methods is not known however based on prior data this has not been shown to impact symptomatic outcomes and thus was deemed to be an unnecessary measurement. The most pertinent intra-procedure pressure measurement would be the pressure within the pleural space measured via independent catheter or channel from the drainage catheter, which was not practically feasible. It is possible that the post-procedure timepoints selected for discomfort measurements did not

fully capture the degree of procedural discomfort experienced, although our data with highest discomfort just prior to catheter removal with downward trend in discomfort scores thereafter suggests we are not missing a later peak in discomfort.

**Conclusions**

We conclude that pleural fluid drainage via suction and gravity drainage are equivalent in terms of patient comfort, with both increasing discomfort and relieving dyspnea by comparable magnitudes. Both also appear safe, with no significant complications occurring in this trial. Gravity drainage did require additional time to accomplish drainage, though proponents of gravity drainage note that this is "hands-off" time which some find more convenient. These two aspiration methods, one faster but "hands-on" and the other slower but more "hands-off," can be used interchangeably by individual providers according to their personal preferences and the clinical setting.

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Study concept and design: RJL, FM, NMR, LY, OBR

Acquisition of data: RJL, SS, HBG, OBR, LR, JKP, ZSD, LGD, JCC, JA, CW, TMS, KRD, NJ, SA, LY, FM, DFK, HL

Analysis and interpretation of data: RJL, FM, NMR, HC, RWL, CG, JTH, SS, HGB, JKP, JCC, LY, DFK, HL

Drafting of the manuscript: RJL, FM, NMR, LY

All authors participated in critical revision of the manuscript for important intellectual content and provided final approval to submit this version of the manuscript and have agreed to be accountable for all aspects of the work.

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TABLES

Table 1. Baseline Subject Characteristics

| | **Suction (n=62)** | **Gravity (n=78)** |
|---|---|---|
| Age (years) | 62.5 (14.0) | 65.1 (13.2) |
| Male gender | 28 (45%) | 37 (47%) |
| Procedure setting | | |
| Outpatient | 33 (53%) | 43 (55%) |
| Emergency Department | 2 (3%) | 1 (1%) |
| Inpatient, regular ward | 27 (44%) | 33 (42%) |
| Inpatient, intensive care unit [a] | 0 | 1 (1%) |
| Smoking status | | |
| Current | 5 (8%) | 9 (11.5%) |
| Former | 33 (53%) | 42 (54%) |
| Never | 24 (39%) | 27 (35%) |
| Prior thoracentesis | 27 (44%) | 44 (56%) |
| With significant chest discomfort | 8 (13%) | 15 (19%) |
| Known effusion etiology | 19 (31%) | 17 (22%) |
| Malignant | 15 (24%) | 11 (14%) |
| Heart failure | 2 (3%) | 1 (1%) |
| Hepatic hydrothorax | 2 (3%) | 1 (1%) |
| Other [b] | 0 | 4 (5%) |
| Comorbidities | | |
| Malignancy | 48 (77%) | 51 (65%) |
| Heart failure | 5 (8%) | 10 (13%) |
| Chronic kidney disease | 4 (6.5%) | 11 (14%) |
| Cirrhosis | 4 (6.5%) | 6 (8%) |

Data are n (%) or mean (SD).

[a] This patient was not mechanically ventilated.

[b] Other known effusion etiologies pre-procedure: nonspecific pleuritis by prior pleural biopsy (2), post-cardiac surgery (1), drug-induced (1).

Table 2. Pre-, intra-, and post-procedure chest discomfort scores.

| | Suction (n=62) | Gravity (n=78) | Mean Difference[a] | 95% CI | P value |
|---|---|---|---|---|---|
| **Pre-procedure** | | | | | |
| Average chest discomfort [b] | 25.3 (27.0) | 21.4 (29.4) | 3.9 | -5.6 to 13.5 | 0.42 |
| Current chest discomfort, pre | 22.9 (25.0) | 12.3 (18.1) | 10.5 | 3.2 to 17.9 | 0.005 |
| **During Procedure** | | | | | |
| Current chest discomfort, open | 23.0 (24.1) | 15.1 (21.0) | 7.8 | 0.3 to 15.4 | 0.04 |
| Current chest discomfort, close | 36.0 (28.8) | 32.8 (30.0) | 3.3 | -6.7 to 13.2 | 0.52 |
| Current chest discomfort, post | 33.3 (27.1) | 30.0 (27.7) | 3.3 | -5.9 to 12.6 | 0.48 |
| **After procedure** | | | | | |
| Overall chest discomfort through 5m post [c] | 25.5 (25.0) | 20.2 (21.0) | 5.3 | -2.4 to 13.0 | 0.17 |
| Chest discomfort through 24 hours post | 19.6 (28.8) | 18.7 (25.0) | 0.9 | -8.4 to 10.3 | 0.85 |
| Chest discomfort through 48 hours post | 18.6 (25.5) | 17.2 (26.0) | 1.4 | -7.8 to 10.6 | 0.77 |
| Pre-to-post change in VAS discomfort | 11.0 (30.0) | 17.8 (31.3) | -6.8 | -17.4 to 3.8 | 0.35 |
| Pre-to-5m-post change in VAS discomfort | 3.5 (28.9) | 8.0 (24.3) | -4.5 | -13.6 to 4.6 | 0.31 |

Data are mean VAS scores (SD). VAS = visual analog scale (0-100 mm).

[a] Suction minus gravity.

[b] On the day of the procedure.

[c] Primary outcome measure.

Table 3. Pre- and post-procedure breathlessness scores.

| | Suction (n=62) | Gravity (n=78) | Mean Difference[a] | 95% CI or $\chi^2$ | P value |
|---|---|---|---|---|---|
| **Pre-procedure** | | | | | |
| Average breathlessness, VAS [b] | 40.8 (29.4) | 37.4 (30.5) | 3.4 | -6.7 to 13.5 | 0.51 |
| Borg Dyspnea score | 3.10 (2.83) | 2.83 (2.66) | 0.26 | -0.7 to 1.2 | 0.64 |
| **After procedure** | | | | | |
| Breathlessness, VAS, at 5m post | 21.0 (22.5) | 18.2 (20.6) | 2.8 | -4.4 to 10.0 | 0.45 |
| Pre-to-post change in VAS breathlessness | -19.8 (32.8) | -19.2 (33.6) | -0.6 | -11.8 to 10.6 | 0.68 |
| Borg Dyspnea score, at 5m post | 1.90 (1.89) | 1.83 (1.73) | 0.07 | -0.5 to 0.7 | 0.90 |
| Borg Dyspnea score, at 24h post | 1.68 (1.59) | 1.67 (2.01) | 0.01 | -0.6 to 0.6 | 0.49 |
| Borg Dyspnea score, at 48h post | 1.54 (1.85) | 1.49 (2.14) | 0.05 | -0.7 to 0.8 | 0.47 |

Data are mean (SD). VAS = visual analog scale (0-100 mm).

[a] Suction minus gravity.

[b] On the day of the procedure.

Table 4. Procedure data.

| | Suction (n=62) | Gravity (n=78) | Mean Difference[a] | 95% CI or $\chi^2$ | P value |
|---|---|---|---|---|---|
| Volume drained (mL) | 1264 (724) | 1165 (543) | 99 | -113 to 310 | 0.89 |
| Thoracentesis duration (minutes) | 10.5 (6.1) | 17.8 (9.7) | -7.4 | -10.2 to -4.6 | <0.001 |
| Drainage discontinuation reason | | | | | |
| Stopped spontaneously | 28 (45%) | 34 (44%) | | | |
| Chest discomfort | 30 (48%) | 38 (49%) | | | |
| Intractable cough | 1 (2%) | 3 (4%) | | | |
| Increased dyspnea | 2 (3%) | 3 (4%) | | | |
| Vagal episode | 1 (2%) | 0 | | | |
| Complications | | | | | |
| Non-expanding Pneumothorax | 1 (2%) | 0 | | $\chi^2 = 1.27$ | 0.26 |
| Residual post-procedure effusion [b] | 32 (52%) | 41 (53%) | | $\chi^2 = 0.01$ | 0.91 |

Data are mean (SD) or n (%)

[a] Suction minus gravity.

[b] More than scant residual pleural fluid on post-procedure thoracic ultrasound

Table 5. Pleural fluid analysis and final effusion diagnoses

| | **Suction (n=62)** | **Gravity (n=78)** |
|---|---|---|
| Exudate * | 40 (64.5%) | 45 (57.7%) |
| Transudate * | 14 (23%) | 19 (24%) |
| Effusion etiology | | |
| Malignant | 27 (43.5%) | 27 (35%) |
| Heart failure | 5 (8%) | 5 (6%) |
| Chylothorax | 1 (2%) | 0 |
| Hepatic hydrothorax | 4 (6%) | 5 (6%) |
| Chronic kidney disease | 1 (2%) | 3 (4%) |
| Parapneumonic | 2 (3%) | 1 (1%) |
| Other † | 1 (%) | 4 (%) |
| Could not be determined | 21 (33%) | 33 (42%) |

Data are n (%).

* Pleural fluid analysis was not obtained in 8 control and 14 gravity effusions.

† Other etiologies included (n=1 each): trapped lung with ex-vacuo transudative effusion, multifactorial volume overload, drug-induced (dasatinib), paramalignant inflammatory.

FIGURE LEGENDS

Figure 1. Trial profile.

Figure 2. Comparison of overall procedural chest discomfort between active aspiration and gravity groups assessed by VAS five minutes after catheter removal (primary outcome). Data are medians and IQR.

Figure 3. Pre, intra, and post-procedure trend in VAS chest discomfort scores. Pre: immediately before catheter insertion. Open: immediately after catheter placement. Close: just prior to catheter removal. Post: immediately after catheter removed. 5 min post: overall procedural chest discomfort measured 5 minutes after catheter removal. Data are mean VAS scores and 95% CIs.

Figure 4. Pre- and post-procedure Modified Borg Scale for Dyspnea scores. Data are medians and IQR.

Figure 5. Comparison of volume drained and procedure duration between active aspiration and gravity groups. A) Volume drained. B) Procedure duration from catheter placement to removal. Data are means and 95% CIs.