Received: 5 June 2024 | Accepted: 1 September 2024

DOI: 10.1002/ueg2.12675

ORIGINAL ARTICLE

ueg journal WILEY

The physiological determinants of symptom burden in cirrhosis with ascites

Nikhilesh R. Mazumder[1,2] | Filip Jezek[3] | Sardar Ansari[4] | Elliot B. Tapper[1,2] | Anna S. Lok[1]

[1]Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, Michigan, USA

[2]Gastroenterology Section, VA Ann Arbor Healthcare System, Ann Arbor, Michigan, USA

[3]Department of Molecular and Integrative Physiology, University of Michigan, Ann Arbor, Michigan, USA

[4]Department of Emergency Medicine, University of Michigan, Ann Arbor, Michigan, USA

Correspondence

Nikhilesh R. Mazumder, VA Medical Center, Room B747, 2215 Fuller Road, Ann Arbor, 48105 MI, USA.
Email: mazumde@med.umich.edu

Funding information

National Institutes of Health, Grant/Award Number: U01DK130113; American College of Gastroenterology, Grant/Award Number: Junior Faculty Development Award

Abstract

Background & Aims: Paracentesis is commonly used to manage patient discomfort due to ascites. The relationship between ascites pressure, ascites volume, and patient discomfort has not been elucidated.

Methods: We prospectively enrolled adult patients with non-malignant ascites undergoing outpatient therapeutic paracenteses from 2021 to 2024 at a tertiary care hospital. Patients completed a validated symptom questionnaire (ASI-7, maximum score 35) before, immediately after, and 1 week after paracentesis. An open-ended manometer was used to measure ascites pressure at the beginning and end of paracentesis. Mixed effect linear regression was performed to evaluate the relationships between patient characteristics, pressure, volume, and symptoms.

Results: One hundred and fifty paracentesis procedures among 48 unique patients with an average Model for End Stage Liver Disease-Sodium 3.0 of 16.7 were included. An average of 6.5 L was drained, which reduced abdominal pressure from a mean of 13.7 to 6.0 cm H_2O (10.1 to 4.4 mmHg, $p < 0.001$) and mean symptom score from 22.6 to 6.5 ($p < 0.001$). Regression models identified that symptoms and abdominal pressure linearly correlated above a pressure of 6 cm H_2O or ASI-7 score of 16 ($p < 0.01$). Taller patients required about 670 ml additional drainage per inch above the cohort mean height (5′8″) to achieve the same symptom relief.

Conclusions: Pressure measured at the bedside can be used to explore changes in abdominal pressure during paracentesis. Pressure, volume, and patient level factors such as height contribute to patient symptoms but cannot fully explain discomfort associated with ascites and relief after paracentesis.

KEYWORDS

ASI-7 score, MELD, paracentesis, patient reported outcomes, portal hypertension, pressure, volume

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2024 The Author(s). United European Gastroenterology Journal published by Wiley Periodicals LLC on behalf of United European Gastroenterology.

INTRODUCTION

Ascites is the most common complication of cirrhosis and has significant implications on patient survival and quality of life.[1–3] Request for paracentesis is largely driven by patients' symptoms. The most common symptoms associated with ascites are captured in the seven question Ascites Symptom Inventory (ASI-7) and are thought to be mediated by the pressure exerted by ascitic fluid on the digestive tract, abdominal wall and diaphragm.[4,5] Paracentesis can resolve this pressure but clinicians prefer to limit the frequency of procedures and the amount of fluid drained for fear of post-paracentesis circulatory dysfunction and renal injury.[6] Moreover, symptoms do not always correlate with fluid burden with some patients requesting paracentesis due to intolerable symptoms despite minimal ascites on imaging while others do not complain of symptoms with significant ascites present. These clinical observations suggest that symptoms related to ascites may be more complex than a simple volume-symptom relationship. Indeed, the exact relationship between ascites volume, abdominal pressure, and patient reported symptoms has not been delineated. In fact, one study found that patients with malignant ascites found no additional relief or durability of symptom improvement with paracentesis above a threshold volume.[7] In patients with cirrhosis and ascites, symptom relief may be achieved with as little as 5 L drained without changes to plasma volume, suggesting that large volume paracentesis with risk of Acute Kidney Injury (AKI) is not necessary for symptom control.[8]

A better understanding of the relationship between volume drained and pressure would aid clinicians and patients in balancing symptom improvement after paracentesis with the risk of having too much fluid removed. The objective of this study was to determine the association between pressure, volume, and symptom burden and recurrence in a prospective cohort of ambulatory patients undergoing paracentesis.

Key summary

Summarise the established knowledge on this subject

- Ascites is the most common decompensation of cirrhosis, degrades quality of life, and is often managed by paracentesis.
- The dynamics between ascites pressure, volume removed, and symptom relief during paracentesis have not been investigated.
- This is in part due to the lack of an established method to measure ascites pressure during paracentesis.

What are the significant and/or new findings of this study?

- We describe a novel technique to measure ascites pressure at the bedside and compare its changes with patient reported symptoms before and after paracentesis.
- We find that taller patients require more fluid removal to achieve the same relief.
- We find that patient relief is not fully explained by the pressure-volume dynamics of paracentesis.
- The results of this paper support that paracentesis is not 'one size fits all' and requires a personalized approach.

METHODS

Patient population

We included patients over 18 years old with non-malignant, portal hypertensive ascites undergoing therapeutic paracentesis in our dedicated hepatology outpatient paracentesis unit between November 2021 and February 2024. Portal hypertensive ascites was defined as ascites with a Serum Albumin Ascites Gradient >1.1.[9,10] Therapeutic paracentesis was defined as any paracentesis with intended drainage of >3 L. Decision to refer for paracentesis, quantity of ascites to be removed, and other clinical management (e.g., diuretic dosing) were determined solely by the clinical team and patient, according to standard of care.

Patients were excluded if they had a history of liver transplantation or transjugular intrahepatic portosystemic shunt placement or if they were unable or unwilling to provide consent. Given that the results from this study might inform a future model to balance symptomatic benefit against possible post paracentesis kidney injury, we also excluded patients with stage 4 or worse chronic kidney disease. We excluded patients with advanced kidney disease because of the looser correlation between creatinine change and Glomerular Filtration Rate at higher serum creatinine. Additionally, patients on dialysis do not need judicious paracentesis on the basis of renal concerns. Institutional review board approval was obtained for the study and all patients provided written informed consent for the study. Creatinine results within 14 days prior to the paracentesis date were used to calculate renal function. Laboratory results in 30 days of the paracentesis date were used to calculate Model for End Stage Liver Disease-Sodium (MELD) score.[11]

Ascites pressure measurements

Patients underwent site selection, preparation, and paracentesis per standard of care while supine at an approximately 30-degree angle. After ascites flow was established, Opening pressure (OP) was obtained under zero flow conditions with an open-ended manometer (Rocket medical) inline with the tubing used to drain the ascites to measure pressure in centimeters of water (cm H_2O) in relation to the right atrium (Figure S1). The location of the right atrium was the standard anatomic location at the midaxillary line at the level of the nipple line. Drainage was restarted after each pressure measurement

by turning a 3-way stopcock, and pressure measurements were repeated in the same manner each time the suction canister was changed, approximately every 1.5 L. All pressure measurements were performed at end expiration with suction disconnected, under local atmospheric pressure conditions. Pressure measurement was halted if the patient was repositioned or if abdominal pressure was applied to the patient's abdomen to enhance flow.

Patient reported outcomes

The ASI-7 tool was used to assess ascites related symptoms. This tool has been previously validated in determining the symptom burden in patients with ascites.[4,5] It is comprised of seven questions (See Table S1): stomach heaviness, discomfort from bloating, difficulty moving from bloating, stomach heaviness while supine, difficulty breathing while walking, difficulty eating due to bloating, and difficulty in taking a deep breath. Each question is rated on a scale of 0–5 with a score of 5 representing the most bothersome symptoms. The maximum score was 35 and minimum was zero. ASI-7 was assessed pre- and immediately post-paracentesis, and on day seven after paracentesis.

In a sensitivity analysis, consented patients who presented for abdominal symptoms and underwent ASI-7 scoring but were found to have insufficient ascites for paracentesis were compared to symptoms for patients who did undergo drainage.

Statistical analysis

Descriptive statistics with mean (standard deviation) or median (interquartile ranges [IQRs]) and count (percentage) were calculated. Ascites pressure at the start, end, and during the procedure was correlated to changes in total ASI-7 score as well as the scores of each individual component. Chi-squared and paired *t*-tests were used for comparisons of categorical and continuous variables as appropriate.

To investigate the determinants of ASI-7 scores, linear regression was performed. First, pressures were compared to their corresponding ASI-7 scores at the start and end of the procedure. ASI score was first treated as a continuous variable, and then to determine if there was a non-linear effect, it was treated as a categorical variable.

Next, changes in ASI-7 score after paracentesis (i.e., patient perceived relief) were modeled with covariates such as pressure, volume removed, and height (centered at the cohort mean, to standardize for patient size) using a random-effects model to account for patients who contributed data from more than one paracentesis. This approach would also help account for patient level effects such as baseline pain levels, pain tolerance, and unmeasured covariates that contribute to abdominal pain and relief. Linear models of pressure-volume relationship were used to evaluate the stiffness (compliance) in each patient. Lastly, time to the next procedure in days was modeled. Initially this was to be modeled with Poisson regression but due to overdispersion of the data, negative binomial regression was performed instead.

RESULTS

Procedural and patient characteristics

A total of 150 therapeutic paracenteses performed on 48 unique patients were included, with a median of 2 (IQR 1–3) procedures per patient. Patient and procedural characteristics are displayed in Table 1. Thirty-three (68%) patients were male, and their average age was 62.2 years at enrollment. The most common cause of liver disease was metabolic-dysfunction associated steatosis (n = 21, 44%), followed by alcohol (n = 17, 35%). At the time of paracentesis, patients had mean serum sodium of 135 mmol/L, total bilirubin 3.4 mg/

TABLE 1 Characteristics of patients and procedures.

Patient characteristics[a]	
n	48
Male sex, *n* (%)	33 (68)
Mean age, years (SD)	62.2 (12.6)
Etiology of liver disease, *n* (%)	
Metabolic associated steatohepatitis	21 (44)
Alcohol	17 (35)
Hepatitis C	4 (8)
Other	6 (13)
Sodium, mmol/L	135 (5)
Total bilirubin, mg/dl	3.4 (4.0)
Creatinine, mg/dl	1.2 (0.4)
Albumin, g/dl	3.3 (0.5)
MELD 3.0	16.7 (6.5)
Platelets, K/μl	118 (56)
Ascites characteristics	
Total Number of paracenteses	150
Median number of procedures per patient (IQR)	2 (IQR 1–3)
Opening pressure (OP), cm H_2O	13.7 (5.4)
Closing pressure, cm H_2O	6.0 (5)
Volume drained, L	6.5 (2.1)
Elastance (E), cm H_2O/L	1.51 (0.44)
Median days to next paracentesis (IQR)	9 (7–14)
Days to next paracentesis, *n* (%)	
<10 days	74 (49.3)
11–20 days	44 (29.3)
21+ days	16 (10.7)
Missing/no follow up	16 (10.7)

Abbreviations: BUN, Blood urea nitrogen; INR, International normalized ratio; MELD 3.0, Model for End-Stage Liver Disease 3.0.

[a]Values presented as mean (SD) unless otherwise noted. Labs presented as per procedure.

dl, international normalized ratio 1.3, and serum creatinine 1.2 mg/dl, with a corresponding mean MELD 3.0 score of 16.7. Mean serum albumin was 3.3 mg/dl and platelets 118 K/μl.

During therapeutic paracentesis, an average of 6.5 L was drained, which decreased the OP from a mean of 13.7 to 6.0 cm H_2O (10.1 to 4.4 mmHg, $p < 0.001$). Only 43 procedures of 150 (28.6%) reached a final pressure of 0 cm H_2O.

Drivers of patient symptoms

Abdominal pressure at the beginning and end of the procedure was significantly associated with patient reported symptoms ($n = 145$, 1.75 cm H_2O increase per 5 ASI-7 points, $p < 0.001$). When pressure-symptom relationship pre- and post-paracentesis was separately analyzed, OP and pre-paracentesis ASI-7 score had a stronger relationship (2.0 cm H_2O per 5 ASI-7 points, $p < 0.001$) (Figure 1a) compared to last pressure and post paracentesis ASI-7 score (0.8 cm H_2O per 5 ASI-7 points, $p = 0.06$) (Figure 1b), supporting prior observations that symptoms can be improved with small decreases in pressure. This pressure-symptom relationship was approximately linear (blue line Figure 1c). Above an ASI score of 16, higher pressure corresponded to statistically significantly ($p < 0.006$) increase in abdominal pressure above baseline pressure of 6.0 cm H_2O (Figure 1c, 95% CI above dotted line).

Patients with insufficient fluid for paracentesis

Sixteen patients presented to the paracentesis unit because of abdominal symptoms, consented and completed ASI-7 questionnaire but did not have sufficient ascites to drain. Compared to patients who underwent paracentesis, this group of patients had a lower mean total ASI-7 score (17.5 vs. 22.6, $p = 0.04$) and had less difficulty

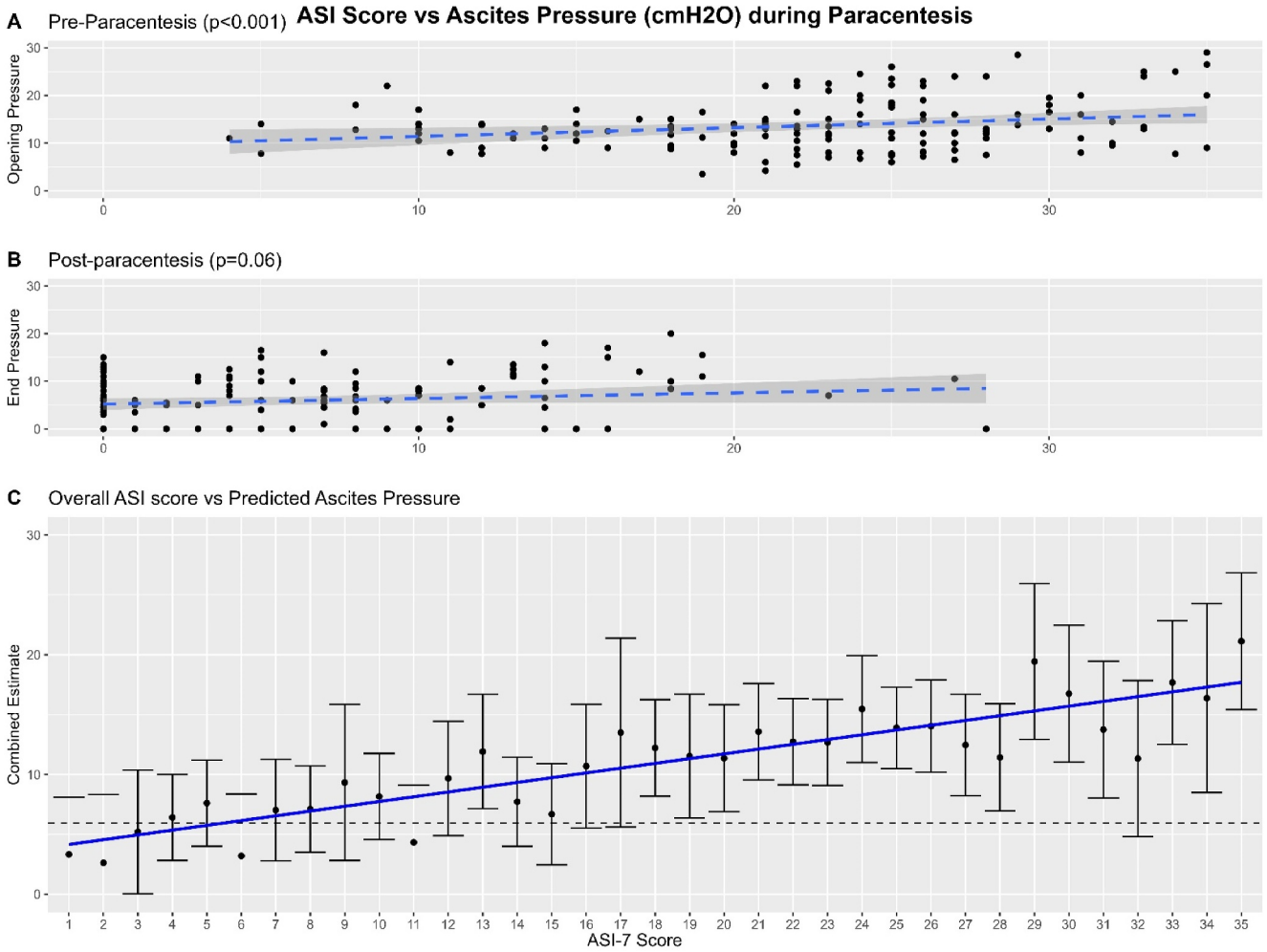


FIGURE 1 Correlation of abdominal pressure and ASI-7 score. (a) ASI-7 Score prior to procedure start is significantly correlated with higher Ascites Pressure ($p < 0.001$). (b) ASI-7 Score and pressure suffer from a floor effect at 0, no significant correlation was found ($p = 0.06$). (c) When combined, increasing ASI-7 score and abdominal pressure are noted especially at higher scores and pressures, for instance ASI-7 > 16 ($p < 0.01$). Further increases in symptomatology correspond to measurable increases in abdominal pressure above baseline (dotted line) with an approximately linear relationship (blue line). ASI, Ascites Symptom Inventory.

with breathing while walking (2.38 vs. 3.6, $p = 0.02$) and difficulty eating (1.94 vs. 2.9, $p = 0.05$). However, the patients who presented with insufficient ascites to drain had a higher total ASI-7 score compared to post-paracentesis ASI-7 score of those who did have paracentesis (17.5 vs. 6.5, $p < 0.001$), with higher scores in all domains except for 'difficulty breathing while walking' and 'difficulty with deep breaths'.

Predictors of symptom relief

Dynamics of symptom relief and return as reflected by ASI-7 are displayed in Figure 2 (Top Panel). Immediately after paracentesis, patients experienced marked symptom relief reflected in a drop in total ASI-7 from 22.6 to 6.5 ($p < 0.001$). All ASI-7 components were statistically significantly improved immediately after paracentesis; however, patients reported the least absolute improvement in 'difficulty breathing while walking' (3.6 to 2.0, $p < 0.001$). Prior to paracentesis, 4/149 ASI-7 scores were at the ceiling level of 35 (2.7%). Immediately after paracentesis, 38/146 ASI scores were reported as 0 for a floor effect of 26%. Mean total ASI-7 decrease from pre- to post- paracentesis was not statistically different between those procedures where the final pressure reached to 0 cm H_2O versus not (drop in ASI score 16.34 vs. 15.26 $p = 0.48$) despite a larger pressure drop (−9.6 cm H_2O vs. −6.9 cm H_2O, $p < 0.001$) and a larger volume removed during the procedure (7.3 vs. 6.1 L, $p < 0.001$) in patients whose last pressure was zero.

To explore the height-based effect (height was used as an indicator of patient and abdominal cavity size), we calculated a patient level slope of the pressure-volume curve that is an estimated decrease in pressure following a 1 L volume drainage for each patient, also known as the elastance. Patient height was negatively associated with elastance (Figure 3. Elastance 1.49 at 68 inches with decrease in 0.05 per inch above this height, $p < 0.001$). In other words, these symptom-independent results demonstrate that taller patients experienced less pressure reduction with the same volume removed during paracentesis.

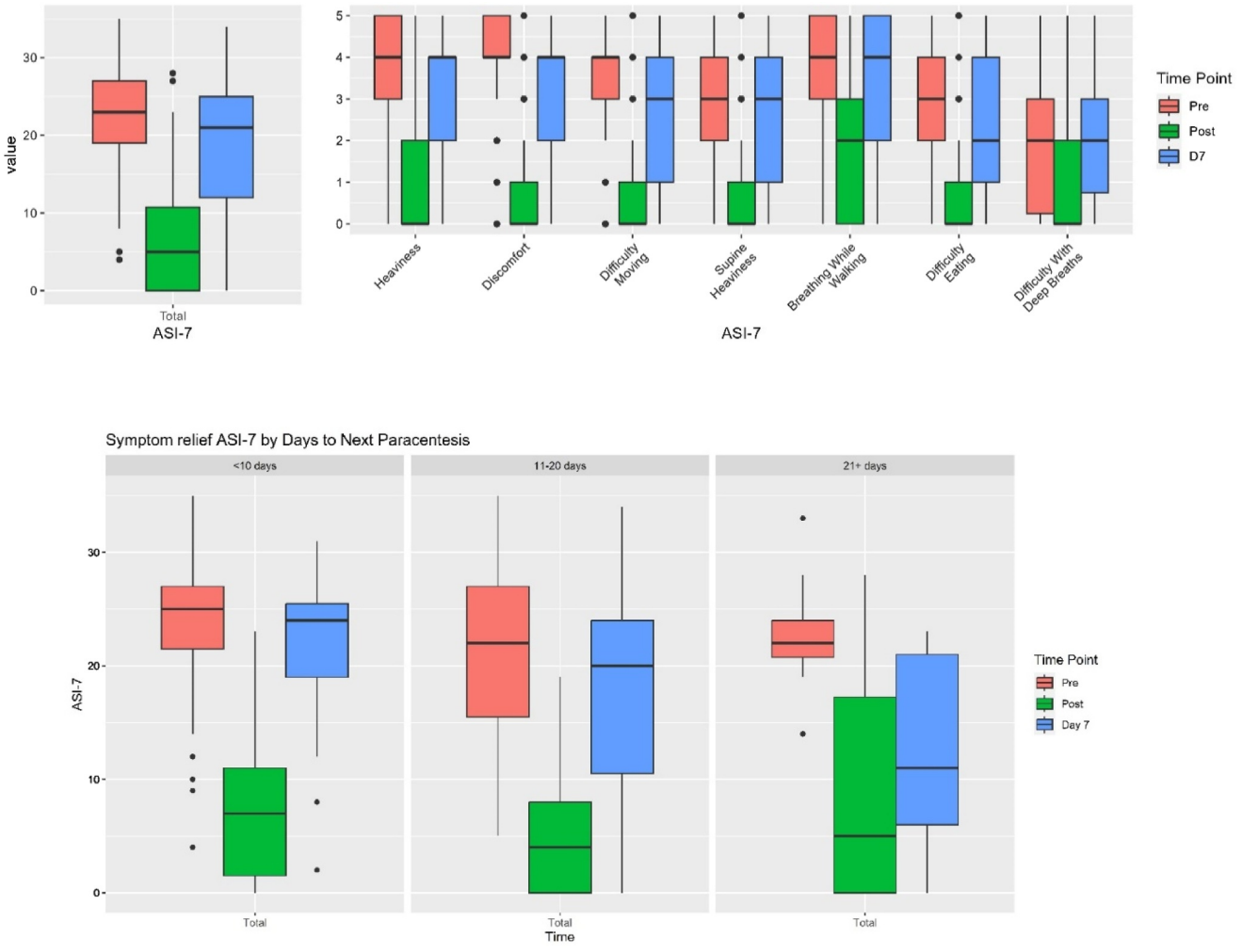


FIGURE 2 Symptom response to paracentesis. (Top) ASI scores, before ($n = 145$), at the end ($n = 142$) and 7 days after ($n = 83$) therapeutic paracentesis. Significant drops in patient symptoms occurred in all components of ASI-7 immediately after paracentesis ($p < 0.001$ for all). (Bottom) After 7 days, patients who went on to undergo paracentesis in <10 days ($n = 71$, mean 8 days) had the same symptoms as those who went on to wait 11–20 days ($n = 42$, mean 12.6 days; Total ASI-7 22.5 vs. 19.6, p = NS). ASI, Ascites Symptom Inventory.

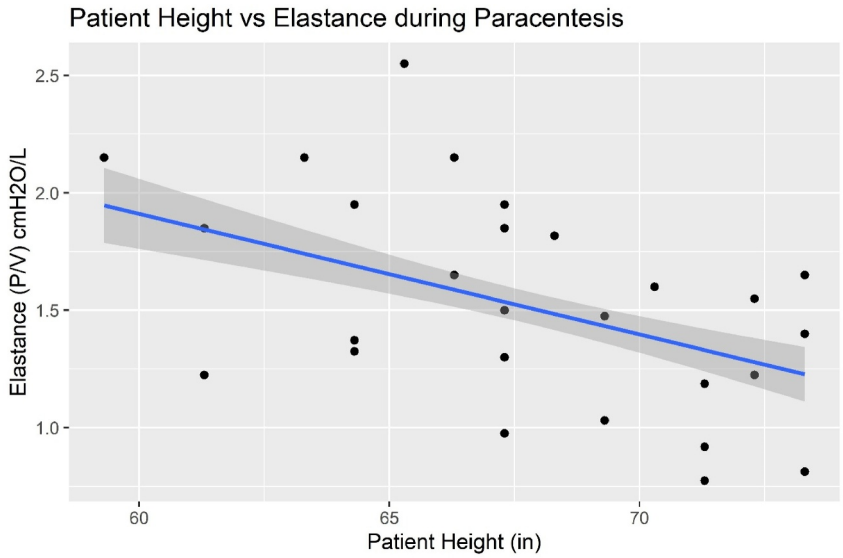


FIGURE 3 Elastance decreases with patient height. Elastance (pressure per volume) was 1.49 at the mean cohort height of 68″ with a decrease of 0.05 per inch above this height, ($p < 0.001$) explaining why taller patients experienced less pressure reduction with the same volume removed.

TABLE 2 Multilevel regression models of symptom relief after paracentesis.

	Univariate	*p*	Pressure model	*p*	Volume model	*p*
Drop in pressure (cm H_2O)	−0.37	0.001	−0.35	0.016	–	–
Volume drained (L)	−1.1	<0.001	–	–	−1.1	<0.001
Height (inches)[a]	+0.69	0.001	+0.63	0.017	+0.74	0.007
Intercept[b]	–	–	−13.9	<0.001	−9.5	<0.001
Akaike information criteria (AIC)			937.56		929.57	

Note: Models of change in ASI-7 score after paracentesis using multilevel linear regression with patient level random effects.

[a]Height in inches above cohort median of 68″.

[b]Intercept in this model is the estimated effect of a paracentesis that removed zero volume, or the portion ASI-7 score change that remains unexplained by the other variables in the model.

Results of modeling using patient level random effects are displayed in Table 2. On univariate analysis, relief from paracentesis (i.e., decrease in ASI-7 score) was associated with a drop in abdominal pressure (−0.37 ASI points per cm H_2O, $p = 0.001$) and volume drained (−1.1 ASI points per liter drained, $p < 0.001$). We investigated the effect of patient size on symptom relief after paracentesis. We found that for each inch above 68 inches (the cohort mean), patients would require an additional 1.8 cm H_2O (1.3 mmHg) drop in abdominal pressure or 670 ml of fluid drained to achieve the same decrease in ASI-7.

Predictors of need for recurrent paracentesis

Among the 150 paracentesis procedures, 134 (89%) procedures required follow - up paracentesis. Repeat paracentesis occurred after a median of 9 days (IQR 7–14).

A day 7 symptom report available after 82 (56%) procedures in 30 unique patients showed a return of symptoms but mean total ASI-7 score was still significantly improved compared to pre-paracentesis (18.3 vs. 22.6 cm H_2O, $p < 0.001$). Among patients who had follow up paracentesis (Figure 2 bottom panel), day 7 symptoms were not significantly different (22.5 vs. 19.6, p = NS) between those who had repeat paracentesis in <10 days ($n = 71$, mean 8 days) and those who had repeat paracentesis 11–20 days ($n = 42$, mean 12.6 days). Day 7 ASI-7 scores were lowest in patients who did not have repeat paracentesis or only after more than 20 days. Using negative binomial regression, the drop in ASI-7 score, drop in abdominal pressure, patient height, reaching a zero end-pressure, platelet count did not predict the number of days until the next procedure. The volume of ascites removed was only weakly related to time until next paracentesis, with a 6% lower incident rate ratio per liter ($p = 0.049$).

DISCUSSION

Therapeutic paracentesis is a central part of ascites management, but data regarding the relationship between volume drained and symptom relief are limited. There is a widespread belief that greater volume removal equates to greater, longer lasting relief and that this relationship holds until all ascites is drained - so called 'total' paracentesis. This goal is often in direct contest with real concerns of care teams for post paracentesis circulatory dysfunction, electrolyte imbalance, and AKI. As a result, the paracentesis 'dose' is typically conservatively prescribed by clinicians *a priori* and adjusted via trial and error based on patient requests or complications. Thus, some patients do not attain adequate relief and others may be exposed to risk from excess drainage with diminishing returns on symptom improvement. Data clarifying the relationship between ascites volume and symptoms could improve patient satisfaction and safety while also elucidating the underlying mechanisms of ascites symptoms.

Key findings

In this study, we prospectively quantified patient symptoms and compared them directly with measured ascites pressure. We demonstrated that ascites pressure can be measured at the bedside in outpatients using a simple open-ended manometer found in lumbar puncture kits. We found that abdominal pressure is closely correlated with patient symptoms. However, we delineated three key areas of nuance. First, paracentesis planning should not be 'one-size-fits all'. We hypothesized that body size and size of the abdominal cavity may influence pressure-symptom relationship. Given that weight and abdominal circumference are affected by ascites, we used height as an indicator of abdominal cavity size. We found that taller patients achieved less symptom relief than shorter patients for the same volume of ascites drained. Our model showed that for each inch in height above the mean height in our cohort, about 670 ml of additional ascites would need to be drained to achieve the same symptom relief. Patient level modeling of elastance also demonstrated that taller patients have less pressure decrease per volume drained. Taken together, these results support the hypothesis that patient size is an important factor in the relationship between abdominal pressure and volume, and that this mediates patient relief after paracentesis.

Second, we found a linear relationship between symptoms and pressure that was statistically significant at higher pressures. Patients had a significant increase in ASI-7 score once the abdominal pressure exceeded 6.0 cm H_20, suggesting a threshold effect below which patient symptoms are not wholly attributable to abdominal pressure. This is further highlighted by the added comparison of patients who requested paracentesis for abdominal symptoms but did not have sufficient ascites to drain. These patients presented with a median symptom score of 17, similar to the level at which there was a statistical correlation between symptoms and pressure we found above. The component of the ASI-7 which was most predictive of the presence of large volume ascites was questions related to breathing and eating. ASI-7 scoring was limited by a significant floor effect after paracentesis, with 26% of patients rating their symptoms as a zero, the lowest possible score. This effect interferes with statistical inference and may contribute to the non-linearity of our findings. Future work to refine patient-reported outcomes should focus on the domains that best correlate with abdominal pressure due to ascites.

Third, the severity of symptoms reported at a given pressure varied widely between patients. This is reflected in the wide range of pressures for any given ASI-7 score (Figure 1) and quantified in our regression models with intercepts ranging from 9.5 to 13.9 points on the ASI-7 scale despite patient level random effects modeling. The finding of ASI-7 scores of $\geq$10 when pressure is extrapolated to zero suggests that a substantial proportion of the total symptom burden is not explained by abdominal pressure or volume of ascites and contribute to the better than expected improvement in post-paracentesis ASI-7 relative to the drop in pressure. Our findings highlight the difficulty in determining how much fluid to drain to provide the greatest symptom relief. The inter-patient variability is again demonstrated in day 7 symptom report, where patients ultimately undergoing paracentesis on day 8 versus 12 had similar level of symptoms. Indeed, we show that the volume removed or the degree of pressure reduction is not associated with the time to next paracentesis. This shows that many patients have differing tolerances for pain or aversion to procedures, which often influence their desire or willingness to pursue a paracentesis. Our findings indicate the need for further studies to inform the optimal paracentesis frequency and volume removal tailored to each patient and to explore complementary therapies that are capable of reducing the psychosocial impact of ascites.[12] Our findings are clinically important because they show the heterogeneity of patient response and the height dependence of patient relief after paracentesis. Given the simplicity of our bedside ascites pressure measurement, we believe this method can be applied in broad clinical settings.

Contextual factors

Our data must be interpreted in the context of the study design. First, there were no predefined criteria for the amount of fluid removed, timing of follow-up paracentesis, or dose of concomitant diuretics in this study though the dosing of intravenous albumin was standardized per our paracentesis protocol in most patients. Given that our study was exploratory, we deferred those decisions to the clinical team. Second, patients who were on recurring paracentesis schedules (e.g., weekly) may have introduced noise into our analysis of 'time to next paracentesis' as logistical considerations such as preference for day of the week and weekend closure, etc. might have dictated the timing and not symptom-driven need. Third, the open-ended manometer was placed at the level of the right atrium, which may underestimate pressure due to the gauge being higher than the paracentesis site. This would potentially bias our pressure estimates downwards and may contribute to why we did not find a strong difference between the

group who reached zero pressure compared to those who did not. We intentionally chose this location to provide a standardized hemodynamic and anatomic context for the pressure. We used height rather than Body Mass Index or body surface area as a measure of patient size in our models. While dry body weight' would have been the ideal covariate, most patients have some residual ascites or peripheral edema. More importantly, we sought to create a prediction model that could be used prior to paracentesis start for procedural planning. In the future, we hope to externally validate our models to help customize patient relief after paracentesis.

CONCLUSION

In summary, the physiologic underpinnings of ascites symptoms can be measured using a simple bedside technique and are related to abdominal pressure and patient height. By directly measuring abdominal pressure we found a complex relationship between volume drained and symptom relief that does not confirm that more volume removed will always lead to greater or longer lasting symptom relief. Future studies should continue to unravel the factors contributing to individual patient symptoms to help personalize paracentesis planning to achieve maximum benefit: risk ratio.

ACKNOWLEDGMENTS

NIH U01DK130113 to EBT and ACG Junior Faculty Development Award to NRM.

CONFLICT OF INTEREST STATEMENT

None of the authors have any conflicts of interest to report related to this work. Tapper has consulted for Bausch, Mallinckrodt, Axcella, Novo Nordisk, Ambys, Lipocine, Kaleido, and Takeda.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ORCID

Nikhilesh R. Mazumder https://orcid.org/0000-0001-9749-5334
Filip Jezek https://orcid.org/0000-0003-0629-7389
Elliot B. Tapper https://orcid.org/0000-0002-0839-1515
Anna S. Lok https://orcid.org/0000-0002-5811-6845

REFERENCES

1. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol. 2006;44(1):217–31. https://doi.org/10.1016/j.jhep.2005.10.013
2. Tapper EB, Zhao Z, Mazumder N, Parikh ND. Incidence of, risk factors for, and outcomes after ascites in a population-based cohort of older Americans. Dig Dis Sci. 2022;67(11):5327–35. https://doi.org/10.1007/s10620-022-07454-3
3. Tapper EB, Kanwal F, Asrani SK, Ho C, Ovchinsky N, Poterucha J, et al. Patient-reported outcomes in cirrhosis: a scoping review of the literature. Hepatology. 2018;67(6):2375–83. https://doi.org/10.1002/hep.29756
4. Onishi Y, Wakita T, Fukuhara S, Noguchi Y, Okada M, Sakaida I, et al. Development and validation of a symptom scale specific for Ascites accompanied with cirrhosis: the ASI-7. Clin Transl Gastroenterol. 2014;5(2):e48. https://doi.org/10.1038/ctg.2013.20
5. Neijenhuis M, Gevers TJG, Atwell TD, Gunneson TJ, Schimek AC, Kievit W, et al. Development and validation of a patient-reported outcome measurement for symptom assessment in cirrhotic ascites. Am J Gastroenterol. 2018;113(4):567–75. https://doi.org/10.1038/ajg.2018.18
6. Ginès P, Titó L, Arroyo V, Planas R, Panés J, Viver J, et al. Randomized comparative study of therapeutic paracentesis with and without intravenous albumin in cirrhosis. Gastroenterology. 1988;94(6):1493–502. https://doi.org/10.1016/0016-5085(88)90691-9
7. Ito T, Yokomichi N, Ishiki H, Kawaguchi T, Masuda K, Tsukuura H, et al. Optimal paracentesis volume for terminally ill cancer patients with ascites. J Pain Symptom Manage. 2021;62(5):968–77. https://doi.org/10.1016/j.jpainsymman.2021.04.010
8. Pinto PC, Amerian J, Reynolds TB. Large-volume paracentesis in nonedematous patients with tense ascites: its effect on intravascular volume. Hepatology. 1988;8(2):207–10. https://doi.org/10.1002/hep.1840080202
9. Biggins SW, Angeli P, Garcia-Tsao G, Ginès P, Ling SC, Nadim MK, et al. Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 practice guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021;74(2):1014–48. https://doi.org/10.1002/hep.31884
10. Angeli P, Bernardi M, Villanueva C, Francoz C, Mookerjee RP, Trebicka J, et al. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol. 2018;69(2):406–60. https://doi.org/10.1016/j.jhep.2018.03.024
11. Optn. Guidance to Liver Transplant Programs and the National Liver Review Board for: adult MELD exception review.
12. Holman A, Parikh N, Clauw DJ, Williams DA, Tapper EB. Contemporary management of pain in cirrhosis: toward precision therapy for pain. Hepatology. 2022;77(1), 290–304. https://doi.org/10.1002/hep.32598

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Mazumder NR, Jezek F, Ansari S, Tapper EB, Lok AS. The physiological determinants of symptom burden in cirrhosis with ascites. United European Gastroenterol J. 2024;12(9):1222–9. https://doi.org/10.1002/ueg2.12675