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Pressure bag irrigation vs manual pressure and gravity drainage for reducing patient discomfort during flexible cystoscopy, A Study protocol for a randomised double blinded controlled trial

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Abstract

Background Flexible cystoscopy is widely used for the diagnosis and surveillance of various urological conditions and is commonly performed in an outpatient setting under local anaesthesia. Various adjuncts have been proposed to reduce patient discomfort, with the most notable being the manual bag squeeze method. This approach elevates irrigation fluid pressure, induces hydrodistension, and has received a strong recommendation from the European Association of Urology (EAU). However, the manual bag squeeze method is limited by inconsistencies in the pressure applied by individuals and the need for additional staff members to perform the procedure. This trial aims to assess the efficacy of standardised pressure bags in elevating irrigation fluid pressure during flexible cystoscopy and its impact on reducing mean pain scores, compared to conventional gravity drainage and the manual bag squeeze manoeuvre.

Methods A randomised, controlled, double blinded, single-centre, parallel-group trial will be conducted. Participants scheduled to undergo flexible cystoscopy will be recruited, screened for eligibility and randomised to one of three study groups: (1) Intervention 1 – Pressure bag Group, (2) Intervention 2 – Manual bag squeeze group, and (3) Control – Gravity drainage group with a simulated bag squeeze. Randomisation will be stratified based on participants' history of prior flexible cystoscopy. The primary outcome is the mean pains score reported by participants immediately after the procedure, assessed using a Numerical Rating Scale (NRS). Secondary outcomes include Patient Reported Outcome Measures (PROMIS) surveys at day 7 post flexible cystoscopy to evaluate for pain intensity (1a), Pain inference (short form 6a) and emotional distress-anxiety (Short form 4a), as well as the incidence of complications reported at day 30 post-procedure.

Discussion This trial will evaluate the role of pressure bags to elevated fluid irrigation pressure and its effect on reducing patient discomfort during flexible cystoscopy using a rigorous methodology. If proven to be effective, pressure bag fluid irrigation has the potential to be implemented as one of the standards of practice for flexible cystoscopies.

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Keywords Flexible Cystoscopy, Pain Management, Pressure Bag, Numerical Rating Scale (NRS), Randomised controlled trial, Irrigation fluid pressure

Introduction

Background and rationale

Flexible cystoscopy is a commonly used in the diagnosis and surveillance of various urological conditions. Cystoscopy involves the insertion of a fibre-optic camera into the bladder through the urethral meatus, enabling direct visualisation of the lower urinary tract. The use of sterile irrigation fluid during the procedure enhances visual clarity. Similarly, flexible cystoscopy employs a flexible camera and is typically performed under local anaesthesia in an outpatient clinical setting. In contrast, rigid cystoscopy is typically performed under a general anaesthetic, and is generally reserved for cases where additional interventions, such as biopsies or the removal of tumours or bladder stones, are anticipated. The avoidance of general anaesthesia and its associated complications are advantageous to the routine use of flexible cystoscopy for diagnostic purposes and the healthcare economic burden associated with its use is significantly cheaper compared to rigid cystoscopy [1, 2]. Furthermore, it optimises the allocation of operating theatre resources, allowing healthcare facilities to reserve operating theatre time for confirm cases of urological pathologies rather than diagnostic investigations.

The use of flexible cystoscopy in male patients is associated with greater comfort and tolerability compared to rigid cystoscopy when performed under local anaesthesia, as highlighted in the European Association of Urology (EAU) Guidelines [3, 4]. The distinct anatomical differences between male and female patients can influence the location and degree of pain caused by cystoscopy [5]. Males experience greater resistance and pain as the cystoscope passes through the urethral membrane compared to females and as such, prior studies have focused on minimising pain during flexible cystoscopies primarily on male patients.

Despite the administration of local anaesthesia, flexible cystoscopy in males still causes varying degrees of discomfort, often influenced by patient-specific and disease-related factors [6, 7]. Prior studies have demonstrated varying time-points of procedural discomfort during flexible cystoscopy, suggesting that the most significant pain occurring during passage of the external urethral sphincter [8]. Amongst the studied interventions evaluated to mitigate discomfort, the manual 'bag-squeeze' manoeuvre has been identified as the most clinically practical [9]. Other proposed adjuncts included the use of nitrous oxide gas, midazolam, intraurethral lidocaine gel with varying intraurethral dwelling times and volumes, plain lubricant gel, music, stress balls, DVD videos, live cystoscopy viewing for patients, virtual reality-based distraction, and transcutaneous electrical nerve stimulation (TENS) [10–18]. While these methods have shown varying degrees of effectiveness, their practical application in clinical settings is often constrained by inherent limitations.

Sedatives and anxiolytics, such as Nitrous Oxide gas and Midazolam, have been shown to effectively alleviate procedural pain. However, their use is associated with significant adverse effects, including respiratory depression, nausea and vomiting [18–20]. Consequently, these agents often necessitate cardiorespiratory monitoring and the involvement of trained anaesthetic staff, which restricts their feasibility in outpatient settings—a key advantage of flexible cystoscopy [21]. A recent systematic review by Raskolnikov et al. [12] assessed the efficacy of lidocaine impregnated lubricant gel during flexible cystoscopy, reporting a statistically significant reduction in pain. However, this effect was time-dependent, with greater efficacy observed with longer dwell times. Despite this, the clinical significance of the observed reduction – measured as a 0.2 decrease on the VAS – remains unclear [12]. Additionally, interventions such as music, stress balls, live cystoscopy viewing for patients, virtual reality-based distraction, plain lubricant gel and transcutaneous electrical nerve stimulation did not result in any significant pain reduction [14–18].

A recent randomised controlled trial by Berjoui et al. (2020) examined the efficacy of the 'bag squeeze' manoeuvre for generating pressure irrigation during flexible cystoscopy [10]. This involves a staff member manually compressing the irrigation fluid bag to increase pressure, as opposed to the conventional method of fluid drainage via gravity. The increased pressure induces hydrodistension, easing the passage of the flexible cystoscope across the membranous urethra. This study demonstrated that the 'bag-squeeze' manoeuvre significantly reduced mean pain scores, as measured with a VAS, from 3.39 (95% CI 2.99–3.78) in the control group to 1.91 (95% CI 1.60–2.22) in the intervention group. This technique has since been strongly recommended by the European Urology Guidelines for usage as a proposed standard of

care [4]. However, this study highlighted several limitations, limiting its reproducibility. The human difference in the manual pressure applied during the 'bag-squeeze' manoeuvre introduces inconsistency, while the need for an additional staff member to perform the technique increases staffing requirements and associated costs.

In this study, we aim to perform a prospective randomised, blinded trial to investigate improvements in procedural pain from flexible cystoscopies with a pressure-irrigation fluid. This will be achieved through use of fluid-pressure bags which can be set to standardised level to avoid the variability in a 'bag-squeeze' technique and decreases the number of staff required during the procedure. Manual bag squeeze can result in fluid flow rate of 6 - 10 mls/second on Uroflow through flexible cystoscope. Pressure bag setting of 350 mmHg was found to be required to create flow rate of 10 mls/second on Uroflow through flexible cystoscope. This intervention could represent a simple, cost-effective solution that is widely available and easily applied. If proven to be an effective means of reducing pain during flexible cystoscopies, pressure bag fluid irrigation has the potential to be implemented as one of the standards of practice for flexible cystoscopies.

Objectives

Aim 1: To Investigate whether different types of fluid irrigation pressures during flexible cystoscopy results in decreased pain

Using standardised pressure bags found in more healthcare institutions, we hope to see a reduction in mean pain scores using validated questionnaires self-reported by patients. If proven to be effective, this will represent an easily accessible, easily reproducible and cost-effective simple intervention with potential to be implemented as standard practice. We hypothesise that pressure bag fluid irrigation, at a set standardised pressure will significantly reduce patients' pain during flexible cystoscopy when compared to gravity drainage and comparable to the 'bag-squeeze' technique.

Aim 2: To investigate pain interference in usual daily activities following cystoscopy with different types of fluid irrigation pressures and assess for any complications at day 30 with either methods

All participants in our study will undergo two follow up evaluations post cystoscopy, at day 7 and another at 30 days. Although the majority of post-cystoscopy complications – particularly urinary tract infections (UTIs) – are expected to manifest within 7–14 days, the 30 day timepoint is retained as a precautionary measure to capture any delayed or atypical presentations. A UTI is defined as (1) a symptomatic presentation that results in an antibiotic prescription documented in the medical records, or (2) a positive urine culture in a symptomatic patient.

Trial design

This study is designed as a parallel group, randomised, double-blinded controlled trial. Patients will be randomly allocated into three groups to evaluate whether pressure bag irrigation (Intervention 1) reduces pain scores compared to conventional fluid irrigation drainage against gravity (control) and manual bag-squeeze (Intervention 2) as supported by the EAU guidelines. This study protocol follows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines. This study was approved by Institutional review boards at the Western Sydney Local Health District (WSLHD) Human Research Ethics Committee (HREC) with ethics approval obtained (2023/PID00688) and was registered in ANZCTR (ACTRN12623000799651). Written Informed consent will be obtained from all participants.

Methods

Study setting

This study will be performed in the Endoscopy Unit of the outpatient department at Westmead Hospital, Sydney Australia. Westmead Hospital is a major public healthcare facility and tertiary referral centre located in Western Sydney. Participants scheduled to undergo flexible cystoscopy at this single-centre public hospital will be recruited for the trial following the provision of written informed consent. After enrolment and randomisation, participants will undergo flexible cystoscopy, during which immediate post-procedural pain scores will be recorded. Additionally, follow up data will be collected at 7 days and 30 days post procedure to assess for any complications requiring a medical review.

Eligibility criteria

Eligible participants who meet the inclusion and exclusion criteria, (Table 1) will undergo a screening process conducted by one of two methods: (1) One of two urology registrars from the investigative team will review patients with upcoming flexible cystoscopy appointments via the electronic medical record (eMR) and contact eligible patients to describe the study and obtain informed consent remotely, which will be documented using the Research Electronic Data Capture System (REDCap). Otherwise, (2) Clinicians working in the outpatient clinics who book patients for flexible cystoscopy can contact one of the two urology registrars who will then screen the patient for eligibility, contact eligible patients, obtain informed consent and document in REDCap, as appropriate. A modified institutional Patient Informed

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Male	Chronic pelvic pain
Older than 18 years of age	Bladder Pain Syndrome or Interstitial Cystitis
No previous complications during flexible cystoscopy	Chronic pain syndrome
No anticipated additional procedure is to be required during cystoscopy (such as, urethral dilatation, removal of ureteric stent)	History of meatal stenosis, urethral stricture or bladder neck contracture
	Use of analgesia within 24 h of cystoscopy
	Presence of Indwelling urethral catheter within 24 h of cystoscopy

Consent Form (PICF – Appendix A) will be used in which the investigative team will outline to each eligible patient, emphasising the purpose of the study, randomisation, duration, patient's rights and responsibilities, along with potential risks and benefits. Each participant will be provided with ample opportunity to ask questions and review the provided information in their own time prior to providing consent to participate.

Participants who are found to initially meet the inclusion criteria and are randomised but required an unanticipated additional procedure during flexible cystoscopy (such as, urethral dilatation) will be excluded from the analysis.

Interventions

Routine Flexible cystoscopies will be performed at Westmead Public Hospital's Endoscopy Unit. All participants will be in the supine position and receive 10 ml of instillagel (Lidocaine 2% gel) immediately prior to their flexible cystoscopy insertion. Intraurethral lidocaine gel will remain within all participants urethra for 1 min, prior to insertion of the cystoscope in accordance with recommended scope of current clinical guidelines and common practice. To ensure allocation concealment, a physical barrier will be placed in front of the fluid irrigation bag setups (Fig. 1). The second assistant, responsible for retrieving the opaque envelopes containing the allocation details for each patient, will review the allocation and ensure the correct intervention or control is applied. The second assistant will then pass the giving set line, attached to the corresponding bag (pressure bag, bag-squeeze manoeuvre, or gravity drainage with simulated bag-squeeze), around the physical barrier to the first assistant. The first assistant will subsequently hand it over to the proceduralist at the appropriate stage of the procedure. The height of all irrigation bags is standardised at 60 cm above the participants bladder and all patients undertook flexible cystoscopy using a 16 Fr Olympus cystoscope. All irrigation fluids will utilise 1 L bags of sterile water for irrigation.

Intervention 1: pressure bag irrigation

We employ the 'INFU-SURG' 1000 ml Pressure infuser for the pressure bag intervention study arm. This is a registered class 1 medical device within the Australian Register of Therapeutic Goods (ARTG). 'INFU-SURG' holds the CE Mark (CE 2797/BSI Group) relevant to the European economic area attesting to its conformity with relevant EU health, safety, and environmental protection standards. In addition to this, 'INFU-SURG' is used internationally; by using this pressure infuser, we ensure adherence to standard-of-care usage for elevating irrigation fluid pressure during flexible cystoscopy. Appendix C contains the full Clinical Investigation Plan (CIP) related to our use of IFU-SURG pressure bags.1 Litre of sterile water for irrigation is placed inside the pressure bag and set at 350 mmHg of pressure attached to an MD Devices giving set. Prior UroFLow study has demonstrated that at this setting, a flow rate of 10 ml/s passing through the cystoscope was achieved.

Intervention 2: manual bag-squeeze

A designated staff member, referred to as the 'second assistant' will be responsible for performing the manual bag-squeeze manoeuvre for all patients assigned to this intervention arm. This approach aims to minimize variability in the manoeuvre by preventing differences in manual input from multiple staff members. This designated individual will endeavour to maintain consistent pressure throughout the duration of the flexible cystoscopy, from its entry into the urethra to its passage into the bladder. At predetermined intervals throughout the study, approximate pressure levels achieved during the bag-squeeze manoeuvre will be intermittently assessed using a UroFlow machine. While not a primary endpoint, these measurements will serve as ancillary data, providing insight into the consistency of pressure application.

Control: gravity drainage with simulated bag-squeeze

Similarly, the 'second assistant' will be responsible for simulating a bag-squeeze for all patients allocated to the control group which employs conventional fluid

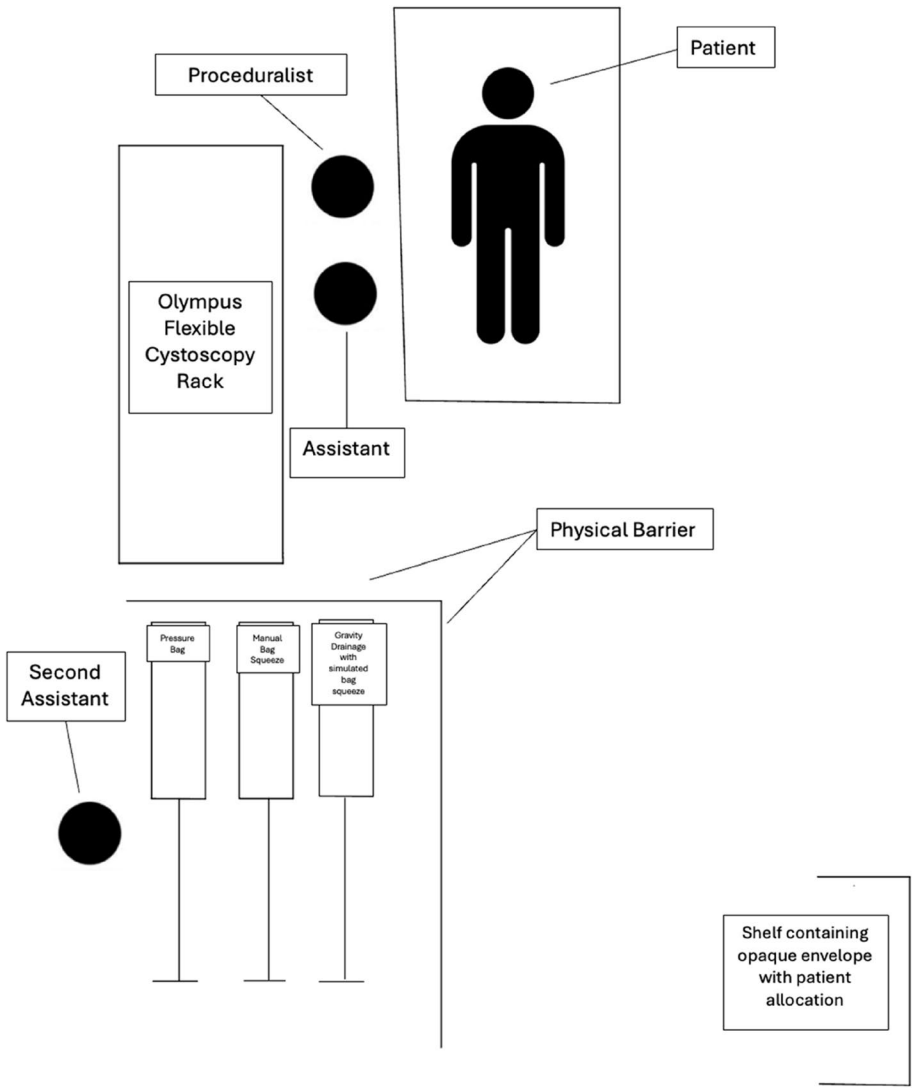

Fig. 1 Endoscopy room trial layout

irrigation pressures due to gravity drainage. The role of the simulated bag-squeeze is to ensure allocation concealment from the proceduralist and first assistant during the procedure.

Outcomes

Primary outcome measure

The mean pain score as reported by participants immediately following flexible cystoscopy, as assessed using a Numerical Rating Scale-NRS (Fig. 2). Each participant will be asked to score their peak pain levels experienced during flexible cystoscopy prior to leaving the procedure room, ensuring appropriate standardisation of timing of pain assessment of participants across the three study arms.

Secondary outcome measures

The secondary outcome measures include:

1. Patient reported outcome measures (PROMIS) surveys at 7 days post-cystoscopy (Appendix B). These surveys will be provided to patients electronically on their nominated email address and will assess for Pain intensity (1a), Pain inference with activities of daily living (Short Form 6a), and Emotional Distress-Anxiety (Short Form 4a).
2. Complications of urinary tract infection, haematuria or urinary retention within 30 days after flexible cystoscopy. This analysis will be performed by one of two urology registrars in the investigative team who will review the electronical medical records (eMR)

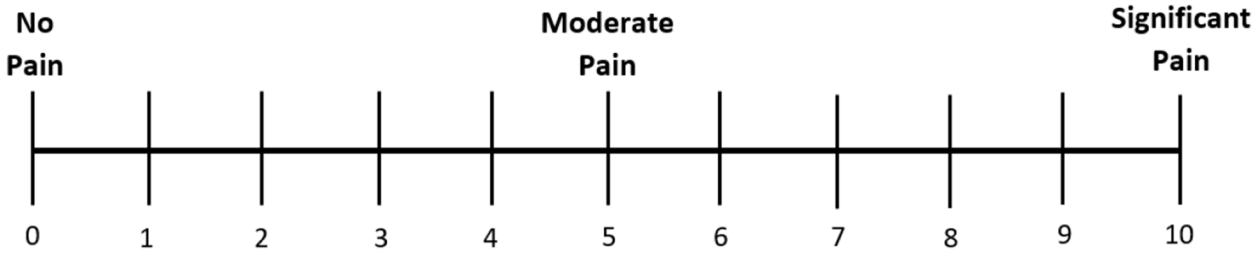

Fig. 2 NRS pain distress rating for participant's flexible cystoscopy experience

along with contacting the patients for a short interview.

Participant timeline

Eligible participants for the study will be identified through a review of the electronic medical records (eMR) or flexible cystoscopies scheduled via outpatient clinics. Screening for eligibility will be performed by one of two urology registrars from the investigative team. Patients deemed eligible will be contacted prior to the procedure and provided with the Patient Information and Consent Form (PICF), allowing them 3 days to review the materials and consider their participation. Emphasis will be placed on ensuring that individuals understand they should not provide consent if they feel uncomfortable. Subsequently, participants will be contacted no later than one day prior to their procedure to obtain informed consent remotely. During this interaction, the voluntary nature of participation will be reiterated.

Sample size

Sample size calculation was performed using nQuery advisor to compare immediate post-procedural pain scores amongst the three groups – control (gravity drainage), manual bag-squeeze, and pressure bag irrigation – using two-sided superiority tests. Drawing on prior research (e.g., Berjoui et al. 2020), we assumed a mean pain score of approximately 3.4 in the control arm, a clinically relevant mean difference of 1.5–2.0 points on a 10-point NRS, and a standard deviation of about 2. For a two-sample comparison (intervention vs control), with a two-sided alpha of 0.05 and a target power of at least 80%, we estimated that 26 control participants would be sufficient to detect this difference against one intervention arm. However, because the trial includes two intervention arms and we also aim to sufficiently power secondary comparisons (e.g., intervention 1 vs intervention 2), we expanded the total sample size.

With an overall alpha of 0.05, a total of 190 participants (30 in the control group and 80 in each intervention group), was determined to provide adequate power (80–90%) to detect a clinically meaningful effect. This allocation ratio enables comparisons of each intervention versus the control arm and preserves sufficient sample size for a secondary comparison between the two interventions.

Specifically, we plan to recruit 80 participants in each intervention arm (pressure bag irrigation and manual bag-squeeze) and 30 participants in the control arm, yielding a total sample size of 190. This allocation was further guided by calculations indicating that 75 participants per arm would be required to achieve at least 90% statistical power, using a two-sided t-test with a significance level of 0.04, an equivalence margin of 1, and an expected difference of 0.

The overall significance level for the study is set at 0.05, and we will apply appropriate adjustments for multiple comparisons in the final analysis.

Recruitment

At Westmead Hospital, approximately 30 flexible cystoscopies are performed each week, 70% of which are male. The recruitment of 190 participants (30 control, 80 per intervention arm) is expected to take 100 weeks given the current process of recruitment and the anticipation of intermittent delays secondary to clinic rescheduling and staff availability. Regular review of clinic schedules and the electronic medical records (eMR) will be performed by two urology registrars to identify eligible patients, along with early engagement of eligible participants. Recruitment will be finalised no later than the day before the procedure, integrated into the routine pre-procedural screening conducted for these flexible cystoscopy lists. Flexible cystoscopies are performed in the outpatient

Endoscopy Unit at Westmead Hospital by the Urology senior resident medical officer who will be blinded and not involved in the study further. Recruitment for this study commenced in February 2024, and as of the time of this study protocol submission, 68 participants have been enrolled.

Allocation & blinding

Sequence generation

Once a participant is deemed eligible and provides consent and is thereby enrolled, we will employ a stratified, blocked randomisation approach generated by a web-based platform (www.randomizer.org). Participants will be stratified according to prior flexible cystoscopy experience, as this variable may influence procedural tolerance drawing on previous negative experiences, thereby possibly resulting in biased self-reported pain scores [22]. Within each stratum, the allocation sequence is created using permuted blocks of variable sizes to ensure balanced group assignment while reducing predictability. This randomisation software operates without replacement, maintaining a strictly non-repetitive assignment of participants to one of the three study arms (gravity drainage control, manual bag-squeeze, and pressure bag).

Allocation concealment and implementation

Allocation concealment will be maintained throughout the duration of the study using opaque, sealed envelopes. Each envelope will contain the group allocation for the individual patient, as determined by the random sequence generated by the computer-based randomiser tool. The envelopes, sequentially numbered, will be prepared prior to the procedural list by a member of the investigative team not involved in data collection or analysis. During the trial, a second assistant, independent of the proceduralist and first assistant, will retrieve and open the appropriate envelope for each patient immediately prior to the commencement of the procedure (Fig. 1). The second assistant will open the envelope behind the secure barrier to ensure that allocation remains concealed from both the proceduralist, first assistant and the participant. Subsequently, the second assistant will prepare the corresponding intervention or control, assigned to that patient. For the pressure bag group, a giving set attached to a pressure bag set at 350 mmHg will be provided to the first assistant. For the manual bag-squeeze group, an identical giving set will be applied by the second assistant behind the physical barrier. For the control group, an identical giving set to the other two study arms will be provided, accompanied by a simulated bag squeeze to ensure blinding.

Blinding

This study is double blinded in design, ensuring that both the participants and proceduralist remain unaware of the group allocation. The urology registrar responsible for participant screening, recruitment and randomisation is not involved in any subsequent stages of the study, including data collection, or analysis. Blinding is extended to other key investigators in this trial. Data collectors, data analysts and outcome adjudicators are all blinded to group assignments. Once Data collection has concluded, the proceduralist will complete a 'blinding assessment questionnaire', in which they will be asked to infer the study arm to which each patient was assigned. This procedure will allow for evaluation of the effectiveness of the blinding process.

Data collection methods

Participant baseline demographics (age, Date of Birth [DOB], medical record number, co-morbidities, medications, prior flexible cystoscopy) are collected on confirmation of enrolment and provision of informed consent. Proceduralist experience (< 3 months, 3–12 months, or > 12 months) will also be recorded. Outcome data will be collected at (1) baseline (mean pain score), immediately after either Intervention 1 or 2, or control group, (2) PROMIS surveys will be reviewed at day 7 and responses recorded and (3) Patient telephone interview at day 30 to assess for any medical complications following flexible cystoscopy. 1–3 remainder prompts will be provided to each patient yet to complete their day 7 surveys and multiple (1–3) attempts will be made at contacting patients at day 30, along with eMR review regarding any recent emergency department presentations. Missing outcome data will reported.

Data management

Outcome data will be transcribed into the Research Electronic Data Capture (REDCap) system (www.project-redcap.org/). This data includes demographic and procedural data from the electronic medical records (eMR), along with outcome information (post procedure pain score, PROMIS survey scores). This data is entered into REDCap by one member of the investigative team who is blinded to allocation. For quality assurance, double-check protocols for data entry, including spot audits and automated validation rules in REDCap are employed. Automatic audit trails capture every data entry and modification that is inputted into the database. Initially, data will be re-identifiable, however once participants dataset has been completed or the study is completed, then the participants DOB and medical record number will be redacted to ensure the final data is deidentified. Final

participant data is stored for a minimum of seven years from the date of the last entry as per New South Wales's laws regarding storage of patient records. The maximum retention period for the deidentified data will be ten years before it is permanently destroyed. The principal investigator is the data custodian for the database. Please refer to Appendix D for the full Data Management Plan (DMP).

Statistical methods

Descriptive statistics will be used to summarise participant characteristics across the three study groups. Appendix E contains the full Statistical Analysis Plan (SAP). Categorical variables will be compared using Fisher's exact, while continuous variables will be analysed using independent two sample t-tests. Prior to conducting between-group comparisons, we will use the Shapiro–Wilk test to determine whether the pain and PROMIS data are normally distributed. If the distribution is approximately normal, independent two sample t-tests will be used to compare each intervention to the control arm. Given the unequal group sizes, we will check for homogeneity of variances (e.g., using Levene's test). If there is evidence of unequal variances, we will employ the Welch's t-test which does not assume equal variances and handles unbalanced sample sizes more robustly. Should any of the continuous variables violate normality assumptions as assessed by the Shapiro–Wilk test, we will use the Mann–Whitney U test instead which can handle unbalanced groups without bias given ties are accounted for automatically in the rank calculations.

Each intervention arm will be compared to the control arm with a two-sided alpha of 0.05, applying a multiple comparisons adjustment (e.g., Bonferroni or a hierarchical testing strategy) to maintain the family-wise error rate. If we consider a one-sided approach for certain comparisons if they arise, an alpha set at 0.025 will be used. If there are notable baseline imbalances in covariates, we will consider a propensity score weighting approach for sensitivity analyses rather than discarding observations via matching. Missing outcome data will be handled using multiple imputation methods, specifically using multivariate normal imputation (MVN), ensuring that participants who have incomplete data remain in the final analyses. The same approach will be used for analysing the NRS for pain and the patient-reported outcome measurement information system (PROMIS) scores.

Data monitoring

Data monitoring committees (DMC) are not required for the purposes of this study, given only one variable is changing in an otherwise well-established practice. This study does not plan for a formal interim analysis, given the sample size and design are powered to address the primary outcome within the predefined trial duration (Table 2). Despite this, the investigative team will conduct ongoing safety monitoring to identify any unexpected adverse effects or procedural complications. If any safety concerns arise, the primary investigator, together with the coordinating principal investigator will review the data and consider early termination of the study.

Harms mitigation

Adverse events or unexpected injuries will be systematically recorded and during outcome assessment at day 7 and day 30 post procedure, along with spontaneous participant reports throughout the trial. Each adverse event will be reviewed for severity and clinical significance. All serious adverse events will be reported to the WSLHD HREC within 72 h and documented in the trial database. A summary of any adverse events will be included in the final report write-up to ensure transparency.

Auditing

All audit activities for this trial will be conducted in accordance with the standards outlined by the Western Sydney Local Health District (WSLHD) Human Research Ethics Committee (HREC). The HREC or a delegated monitoring body is responsible for reviewing the trial's progress and may schedule an audit at least once annually or whenever deemed necessary based on a risk assessment. These audits verify compliance with applicable local regulations, Good Clinical Practice (GCP) guidelines, and standards consistent with ISO 14155. These audits are performed independently of the investigative team, thereby maintaining impartial oversight. During an audit, investigators will provide open access to all trial documentation, participant records, and database logs. Any findings or recommendations will be documented and communicated promptly to both the study team and the HREC. In cases where changes to the protocol or procedures are warranted, these will be submitted for ethical review and approval prior to implementation. This framework ensures the data integrity, participant safety, and regulatory compliance are upheld throughout the duration of the study.

Ethics & dissemination

Research ethics approval

This study protocol was approved by the Western Sydney Local Health District (WSLHD) Human Research Ethics Committee (HREC) on 11/07/2023 (2023/PID00688). Local site ethics approval was also obtained (2023/STE02392). This study is registered in the ANZCTR registry (ACTRN12623000799651).

Table 2 Intended study schedule

	Study period					
	Enrolment	**Allocation**		**Post-allocation**		**Close-out**
	Pre-randomisation	**Before flexible cystoscopy**	**Day of flexible cystoscopy**	**After flexible cystoscopy**		**Post data collection**
Timepoint (Days):	***− 3***	**− 1**	**0**	***+7***	***+30***	***(+)30—60***
Enrolment:						
Eligibility screen	X					
Informed consent		X				
Randomisation to Intervention groups or control		X				
Interventions:						
Pressure bag intervention 1			X			
Manual bag squeeze intervention 2			X			
Gravity drainage control group			X			
Assessments:						
Patient baseline characteristics	X					
Mean pain score assessment			X			
PROMIS Survey – survey monkey link sent to participants email				X		
Patient interview to assess for medical complications					X	
Data monitoring						
Demographic data input	X					
Allocation & enrolment		X				
Outcome data input			X	X	X	
Data assessment & report write-up						X

Protocol amendments

Revisions to the study protocol will be reviewed and improved by all members of the investigative team. Any amendments will be resubmitted to the ethics review board for ethics re-approval and all enrolled participants will be informed.

Consent or assent

Informed consent will be obtained by one of two urology registrars on the investigative team prior to patient randomisation and the collection of any preliminary demographic data. Following eligibility screening, potential participants will be contacted before the procedure to discuss the study in detail. If they express interest in participating, patients will recieve Patient Information and Consent Form (PICF; Appendix A) via email and may sign the consent either electronically through the secure REDCap e-consent platform, by returning a signed PDF via email, or by providing a hard copy on the day of cystoscopy. Participants will be afforded 72 h to review the PICF and consider their participation. This approach minimises the need for multiple in-person visits solely for consent process, thereby reducing participant burden and expediting recruitment.

Confidentiality

Patients will be denoted with a study identification number on enrolment. This number will be used for data registration and will initially be re-identifiable for study members until the participants dataset is completed. Following this, identifiable characteristics (such as, date of breath, medical record number) will be removed. Stored data will be password encrypted in a REDCap database, only accessible by members of the investigative team for a minimum of 7 years.

Access to data

Throughout the duration of the study, access to re-identifiable information within the database is restricted to the research team members. Enrolled participants may request access to their pertinent data before de-identification, in accordance with applicable policies. Upon the completion of the participants dataset or the conclusion of the study, the data is de-identified and retained within the final REDCap database. This non-identifiable data

can be shared with bona fide researchers upon request, in alignment with data-sharing guidelines established by the Australian Research Data Commons (ARDC).

Ancillary and post-trial care

There will be no compensation for participants as outlined in the PICF. All protocol interventions are conducted in accordance with approved regulations within New South Wales Health. Consequently, any adverse outcomes will be managed through the Medicare scheme, either via the participant's primary care provider, or through the Emergency Departments of public hospitals.

Dissemination policy

The results of this study will be disseminated to the public through scientific urology focused conferences and journals. A copy of the final report will be sent to all interested participants at the conclusion of report write-up and publication. The investigate team will determine the authorship of all planned presentation and publication works, with the order of authors reliant on the individual contribution of each author. We will not employ or use any professional writers.

Discussion

Here we describe a study protocol for a randomised, double blinded controlled trial to evaluate the role of pressure on fluid irrigation in reducing patient discomfort as opposed to conventional gravity-based drainage and manual bag-squeeze. To our knowledge, this will be the first randomised controlled trial that evaluates the use of pressure bags in elevating irrigation pressure during flexible cystoscopy to assess patient self-reported pain scores.

This study has several limitations. Firstly, this study is conducted at a single centre thus findings may have limited generalisability particularly if the study population is not representative of broader demographic or clinical groups. This concern is heightened if patient baseline characteristics reveal a homogenous racial or cultural demographic. Such homogeneity could significantly impact the subjective nature of patient self-reported mean pain scores, as ethnic and cultural differences in pain perception and may introduce variability or bias. These factors could affect the interpretation of pain scores due to differences in individual pain thresholds, cultural attitudes towards pain, or expectations [23]. Additionally, variability in operator technique and challenges in consistently maintaining target irrigation pressures, particularly during manual bag squeeze, could impact the reliability of the intervention. This limitation is mitigated by ensuring the same staff member assumes the second assistant role and whilst this aims to standardize the intervention and reduce variability, it does reduce external validity by limiting the range of operators who might perform the bag-squeeze differently in routine practice. Moreover, while blinding protocols are robust, they may be inadvertently compromised if proceduralists infer the intervention method through tactical feedback. This inherent limitation is challenging to mitigate and is a common issue in randomised trials involving clinical interventions. Finally, external factors such as room or fluid temperature, and patient positioning, may confound results. Efforts to minimise these effects include the use of standardised irrigation bag warmers, maintaining a consistent procedural room thermostat setting, and ensuring all patients are supine during flexible cystoscopy.

This study holds significant clinical implications. If elevated irrigation fluid pressure via pressure bags is demonstrated to reduce mean pain scores compared to conventional gravity-based drainage and proves to be equivalent or superior to manual bag squeeze techniques, it could provide strong evidence supporting its broader adoption in flexible cystoscopy. While this study aimed to isolate the effects of sustained manual pressure in the bag squeeze arm and continuous pressure via a pressure bag set at 350 mmHg against a strict gravity based control, we acknowledge that clinicians frequently combine these techniques in routine practice. The pressure bag approach represents a readily reproducible, wildly accessible, cost-effective and simple intervention to reduce patient discomfort. Future research, ideally multi-centre studies with a broader range of personnel would be valuable in validating and expanding upon these findings across diverse patient populations and clinical settings. Although our study offers valuable insights for local practice, further evidence from larger, more heterogenous cohorts is necessary before incorporating these findings into widespread clinical guidelines.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12894-025-01753-3.

Supplementary Material 1. Appendix A: PICF.

Supplementary Material 2. Appendix B: PROMIS Survey at Day 7.

Supplementary Material 3. Appendix C: Clinical Investigation Plan

Supplementary Material 4. Appendix D: Data Management Plan

Supplementary Material 5. Appendix E: Statistical Analysis Plan

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Not applicable.

Authors'contributions

DA is responsible for study protocol development, patient recruitment, and final report write up at the conclusion of the trial. AC is responsible for patient recruitment and study protocol development. AD is responsible for study protocol development, data input and outcome assessment. LK is responsible

for data analyses, outcome assessment and supervision. Finally, AW is the coordinating principal investigator on this study, and assumes the role of chief investigator, with responsibilities in study protocol development, patient recruitment and supervision.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study has received form ethics board approval from the Western Sydney Local Health District (WSLHD) Human Resources Ethics Committee (HREC)—2023/PID00688. Local site ethics approval was also obtained (2023/STE02392). Informed consent will be obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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