



Does office-based flexible cystoscopy provide better pain perception than rigid cystoscopy: a systematic review and meta-analysis

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Background: The aim of our study is to determine whether flexible cystoscopy (FC) leads to less pain perception than rigid cystoscopy (RC).

Methods: Eligible studies were identified through three common databases, including PubMed, the Cochrane Library and Embase. We systematically reviewed studies comparing FC to RC, and extracted data from randomized trials from December 1, 1984 to January 12, 2021, with no language restrictions. Methodological rigor, and risk of bias were evaluated by two independent reviewers using Cochrane Collaboration's tools. The analysis was completed via STATA version 14.2.

Results: We initially identified 463 studies, and four articles met the criteria for inclusion. Overall, we did not observe a significant difference between FC and RC regarding pain perception [standard mean difference (SMD): -1.19; 95% CI: -2.69 to 0.32], and there was significant heterogeneity among studies ($I^2=97.6%$, $P<0.001$). This was consistent with the results stratified by gender (male patients, SMD: -0.96, 95% CI: -2.50 to 0.59; female patients, SMD: -1.42; 95% CI: -4.49 to 1.64).

Conclusions: Our study revealed that RC is a tolerable procedure, and FC may not be more comfortable than RC. However, further larger well-designed trials are warranted to demonstrate our findings, and explore whether FC is more beneficial to patient sexual function, anxiety, quality of life, and lower urinary tract symptoms than RC.

Keywords: Flexible cystoscopy (FC); rigid cystoscopy (RC); pain perception

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Introduction

It is universally acknowledged that cystoscopy is the one of the most common outpatient procedures in urology clinical

practice. Patients are usually recommended to undergo cystoscopy when they have hematuria, regular surveillance or under suspicion of bladder cancer after transurethral

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resection of non-muscle-invasive bladder tumor, recurrent lower urinary tract symptoms, and intractable urinary tract infections (1,2). However, many patients are afraid of this clinical examination due to pain perception (2). Currently, researchers have conducted many trials to seek potentially adjuvant therapy to alleviate patient pain during cystoscopy, especially for male patients. The proposed nonpharmacological methods included increasing irrigation pressure (3-5), delaying the instillation time of topical anesthetics in the urethra (6-8), allowing patients to watch the procedure process (9-11), listening to music (12,13), hand-holding (14), urinating during FC (15), and virtual reality distraction (16). All these interventions are practical, inexpensive, and harmless.

In many countries flexible cystoscopy (FC) is the preferred out-patient method, however, rigid cystoscopy (RC) is indispensable ascribed to its better visual performance, lower costs and easier operation compared to FC. Whether FC provides better pain perception is still a controversial issue, and thereby we conduct this meta-analysis to explore the effect of different cystoscopy on pain perception in patients undergoing cystoscopy in the outpatient clinic. We present the following article in accordance with the PRISMA reporting checklist (available at <http://dx.doi.org/10.21037/apm-21-316>).

Methods

Search strategy

A systematic review and literature search were conducted according to the PRISMA guidelines (17). Eligible studies were identified through three common databases including PubMed, the Cochrane Library and Embase from December 1, 1984 to January 12, 2021 regardless of language, and the related reference lists were also retrieved manually. The used keywords or mesh terms in this study were “flexible”, “rigid”, and “cystoscopy”. Details of search strategy on PubMed were as follows: ((flexible [Title/Abstract]) AND (((((((((((Cystoscopy [Title/Abstract]) OR (Cystoscopies [Title/Abstract])) OR (Cystoscopic Surgical Procedures [Title/Abstract])) OR (Cystoscopic Surgical Procedure [Title/Abstract])) OR (Procedure, Cystoscopic Surgical [Title/Abstract])) OR (Procedures, Cystoscopic Surgical [Title/Abstract])) OR (Surgical Procedure, Cystoscopic [Title/Abstract])) OR (Surgery, Cystoscopic [Title/Abstract])) OR (Surgical Procedures, Cystoscopic [Title/Abstract])) OR (Cystoscopic Surgery [Title/

Abstract])) OR (Cystoscopic Surgeries [Title/Abstract])) OR (Surgeries, Cystoscopic [Title/Abstract])) AND (rigid [Title/Abstract]).

Study selection

We used the PICOS method to identify eligible patients. Patients (P): patients who could communicate with operators normally; intervention (I): patients in experimental group underwent FC; comparison (C): comparing FC to RC; outcomes (O): pain perception was measured by visual analogue pain scale (VAS); study design (S): randomized controlled trials; exclusion criteria included the following items: (I) no systemic sedation or analgesia before cystoscopy; (II) current urinary infection; (III) presence of current pain in the pelvic region (e.g., bladder pain syndrome or interstitial cystitis); (IV) pregnancy; (V) prior urethral surgery; (VI) cystoscopy with other interventions; (VII) data not available; (VIII) meeting abstracts. *Figure 1* showed the flowchart of study selection process in this study.

Data extraction and quality assessment

We firstly imported the retrieved publications into the Endnote. Two independent authors screened the search results based on the title, abstract, and final full text. Discrepancies are settled through discussion. Two independent reviewers used the preformulated tables to extract data. The following data were extracted: the first author's name, year of publication, country, period, age, sample size, local anesthesia, selection criteria, pain perception, and cystoscopy type.

Two independent authors evaluated the methodological quality of the studies according to the Cochrane Collaboration's Risk of Bias (RoB) tool in Review Manager software. This tool primarily evaluates 7 domains: random sequence generation (selection bias); allocation concealment (selection bias); blinding of participants and personnel (performance bias); blinding of outcome assessment (detection bias); incomplete outcome data (attrition bias); selective reporting (reporting bias); other bias (such as funding sources). Moreover, two reviewers independently rated the level of evidence of the included articles through the Oxford Centre for Evidence-Based Medicine criteria (18); This scale graded studies from strongest (level 1) to weakest (level 5) strength of evidence according to study design and data quality.

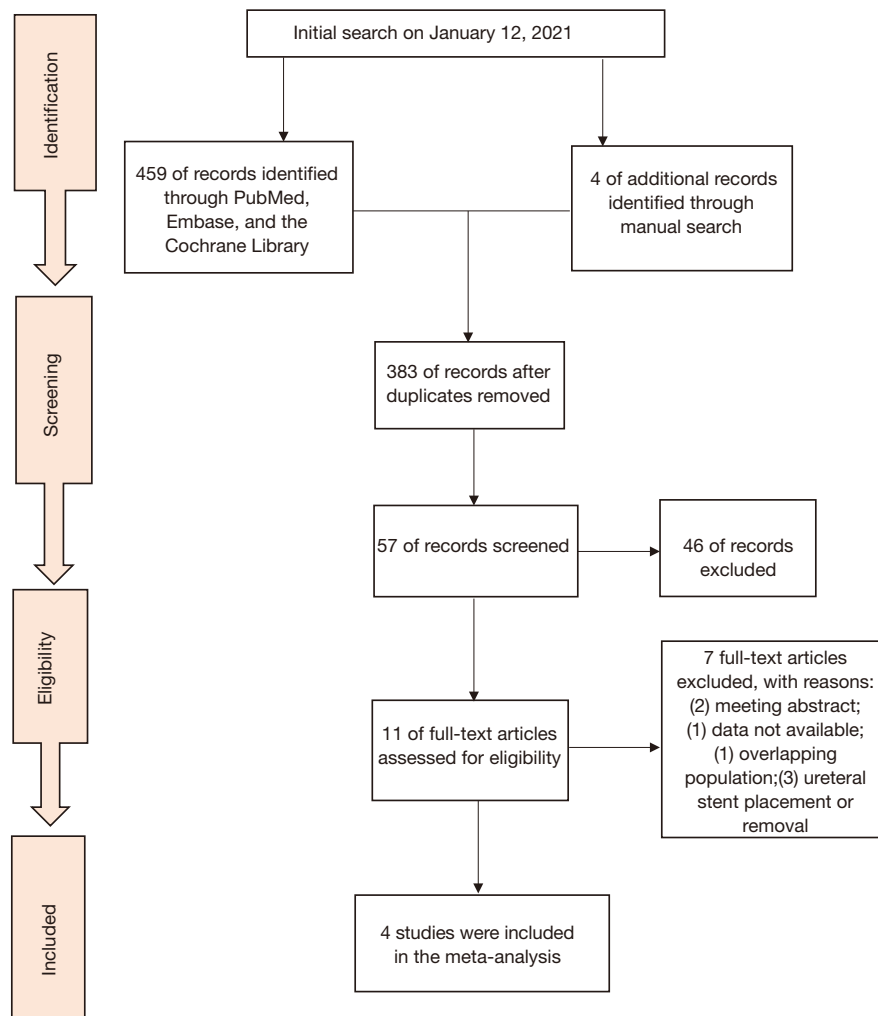


Figure 1 The flowchart of study selection in this study.

Figure 2 showed the RoB summary of the four studies (5-8). Overall, included studies had a low risk of selection bias, attrition bias and reporting bias. However, the risk of performance bias was high. The risk of detection bias was unclear due to absence of related description.

Statistical analysis

Continuous variables presented as means and corresponding standard deviations (SD) were pooled for mean difference (MD) or standard MD (SMD). The fixed effects model was used unless there exists heterogeneity ($P < 0.1$), and significance was set at $P < 0.05$. Additionally, we performed a subgroup analysis based on gender. This meta-analysis was completed by STATA version 14.2.

Results

Search results

We initially identified 463 studies, and four articles (19-22) met the criteria for inclusion. Two studies (19,20) compared FC to RC in 141 male patients, and the other two studies (21,22) investigated the two cystoscopy methods in 274 female patients. The participants came from the Netherlands, USA, Poland, and Turkey. Table 1 presented the main characteristics of included studies in this meta-analysis.

Meta-analysis results

Overall, we did not observe a significant difference between

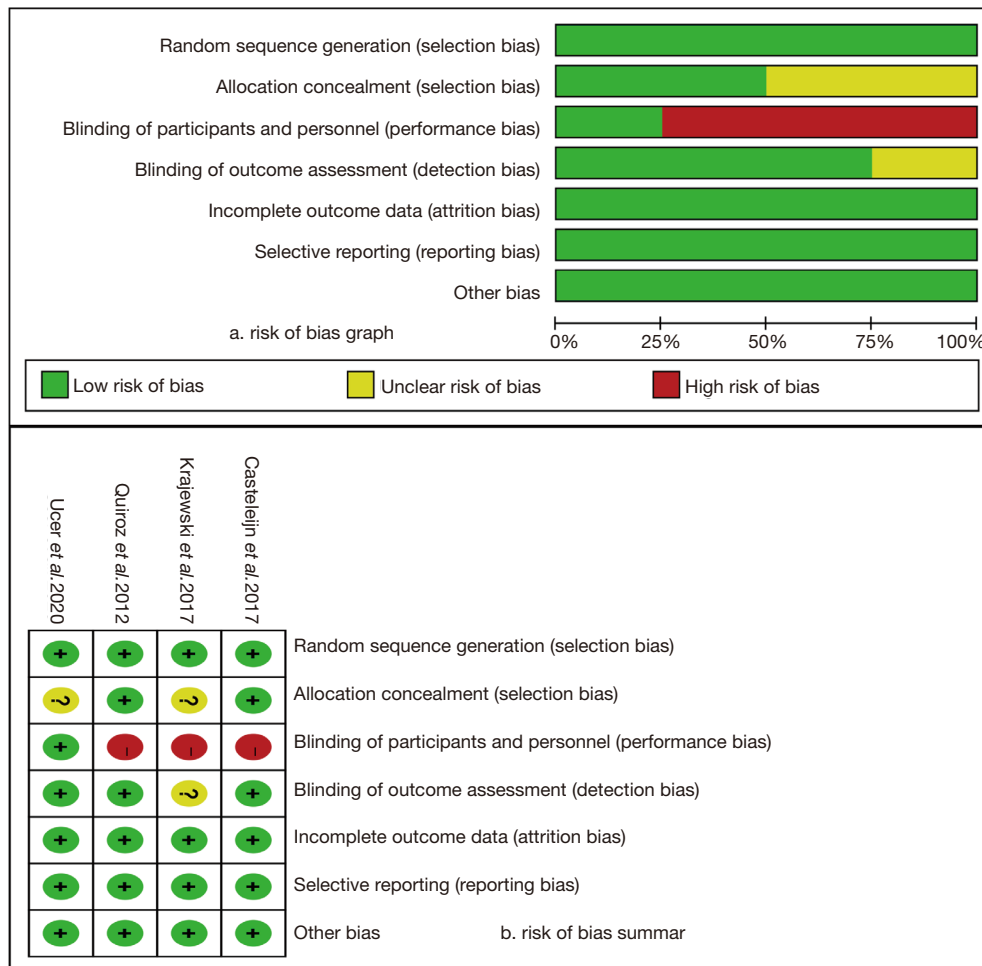


Figure 2 The methodological quality of studies included in this study.

FC and RC regarding pain perception (SMD: -1.19; 95% CI: -2.69 to 0.32; *Figure 3*) with great between-study heterogeneity ($I^2=97.6\%$, $P<0.001$). This was in keeping with the results stratified by gender (male patients: SMD: -0.96, 95% CI: -2.50 to 0.59; female patients: SMD: -1.42; 95% CI: -4.49 to 1.64; *Figure 3*).

Discussion

Cystoscopy is commonly conducted with 2% lidocaine gel administering intraurethrally for several minutes to reduce pain before procedure in many urologic institutes (23,24). Nonetheless, it is difficult to achieve optimal analgesic effect due to procedural invasiveness. In 1973, Tsuchida Seigi and Sugawara Hiroatsu firstly introduced FC, which

was potentially less painful than RC (25). Subsequently, many institutions routinely performed FC in their urology outpatient, and some studies believed that FC was more comfortable than RC (20,26). The EAU guidelines reported that FC led to better compliance than RC under topical anesthetics instillation in the urethra, especially in male patients due to prostate, tight sphincter, and longer urethra (27). In the present study, no significant pain relief was identified in patients undergoing FC when compared to RC.

The friction between cystoscope and urethral mucosa leads to bleeding and pain perception. Several studies believed that the location of most painful part in FC was the membranous urethra of external sphincter (12,28). For the past decades, many investigators have proposed several

Table 1 The main characteristics of included studies in this meta-analysis

| Study | Country | Period | Patient | Age (years), mean (SD) | Local anesthesia | Cystoscopy | Inclusion criteria | Exclusion criteria | Outcomes | LoE |
|-------------------------------|-----------------|---------------|------------------------------|------------------------------------|--|--|--|--|--|-----|
| Casteleijn <i>et al.</i> 2017 | The Netherlands | 12 months | Female FC: 97 RC: 92 | FC: 58 [18] RC: 58 [17] | No | FC: 16.2 Fr (Olympus, CYF-5, Tokyo, Japan); RC: Frigid Storz cystoscope with 30-degree lens | Fist time cystoscopy, hematuria, urinary incontinence, LUTS, recurrent urinary tract infections | A history of previous cystoscopy procedures, cystoscopy with other procedures, current urinary tract infection, anatomic urethral abnormalities, presence of current pain in the pelvic region (e.g., bladder pain syndrome or interstitial cystitis), known with pain syndromes, for example vaginismus or fibromyalgia, and any analgesic use during the 24 hours before procedure | 100 mm-VAS | 2b |
| Ucer <i>et al.</i> 2021 | Turkey | Not reported | Male, FC: 20; RC: 21 | FC: 63.40 (7.08); RC: 64.23 (7.87) | 10 mL 2% lidocaine instilled into the urethra for 10 minutes | FC: 15.5 Fr (Karl Storz, Tuttingen, Germany); RC: 15.5 Fr (Olympus Europe Holding GmbH, Hamburg, Germany) | Pathologically low risk NMIBC (Ta, G1/low grade, <3 cm, primary) after first TURB | T1, G2,3/high grade, carcinoma <i>in situ</i> , recurrence tumor, >3 cm and patients who underwent re-TURB and/or intravesical treatment | 10 cm-VAS | 2b |
| Quiroz <i>et al.</i> 2012 | USA | 2009.5–2010.8 | Female, FC: 50; RC: 50 | FC: 57.6 (13.9); RC: 61.9 (14.8) | 2% Xylocaine instilled into the urethra for at least 5 minutes | FC: 16 Fr (Karl Storz 11272C); RC: 17 F, 70°-degree scope; 0° scope used for urethroscopy portion; 30°-degree scope when appropriate | Age at least 18 years, able to complete an English language written questionnaire, microscopic hematuria, >200 cc voiding dysfunction symptoms, urinary incontinence, or history of recurrent bacterial cystitis | Acute urinary infection, chronic bladder pain, pregnancy, prior urethral surgery, and urinary retention, defined as a post-void residual of greater than | 10 cm-VAS | 2b |
| Krajewski <i>et al.</i> 2017 | Poland | Not reported | Male, FC: 50; RC: 50 | FC: 69.5 (6.8); RC: 69.0 (7.3) | 2% lidocaine instilled into the urethra for at least 5 minutes | FC: 15 Fr; RC: 20 Fr | Men undergoing TURB | Age under 18 years, with indwelling catheters, with history of any but TURB surgery on genitourinary tract, CS with intervention, symptomatic urinary tract infection, and inability to cooperate with psychological evaluations. Patients taking medications affecting their mental states | Numeric rating scale: ranging from 0 (free from pain) to 10 points (unbearable pain) | 2b |

SD, standard deviation; LoE, level of evidence; RC, rigid cystoscopy; FC, flexible cystoscopy; VAS, visual analog scale; TURB, transurethral resection of non-muscle-invasive bladder tumor; NMIBC, non-muscle-invasive bladder tumor; LUTS, lower urinary tract symptoms.

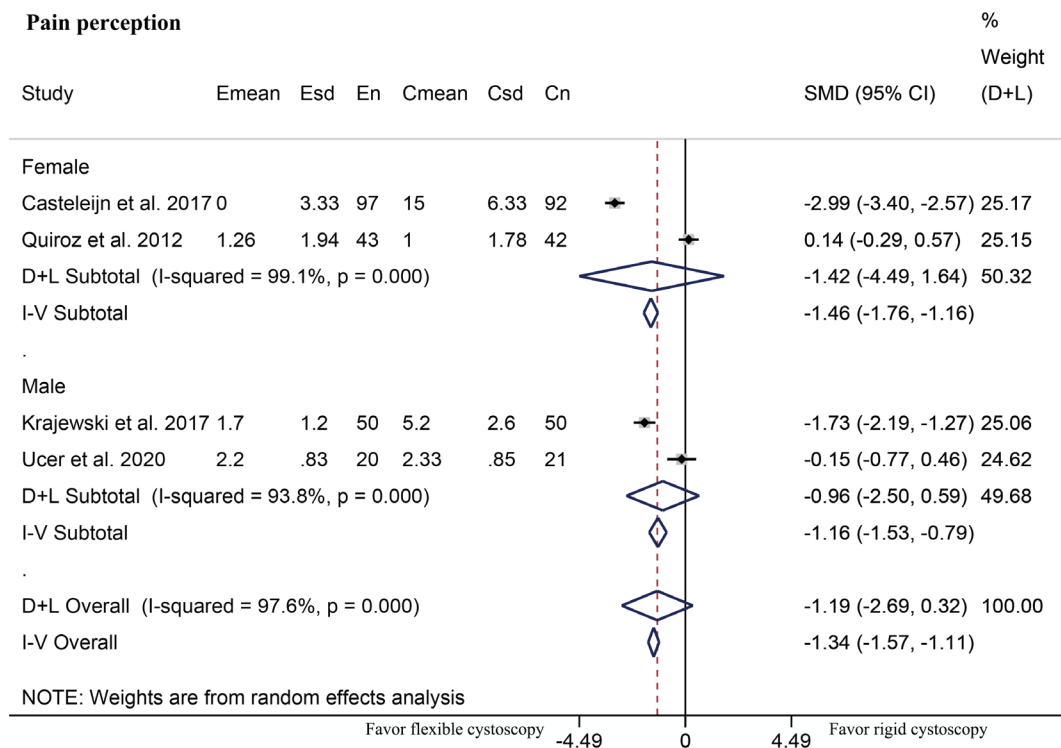


Figure 3 The pooled results of the evaluated outcomes in this study.

methods to relieve patient discomfort, such as parenteral agents (29), inhalational agents (30), watching video (9,31), Bag Squeeze (4,5), and listening to music (12,13,32-35). Besides, FC contribute to less pain than RC for patients with obvious bladder neck elevation according to our clinical experience, because RC is more likely to touch the urethral mucosa for these patients. Perhaps FC is more suitable for selective male patients, such as patients with obvious bladder neck elevation. We still need large clinical trials to confirm this finding.

It is undeniable that our study has following limitations. Firstly, the limited number of studies, sample size, different size of cystoscopy, and ethnic differences in penis prevented us from making a definite conclusion. Secondly, we were unable to evaluate the effect of FC and RC on discomfort in the Asian patients due to smaller penis size and diameter in the Asian countries than those in the western and African countries in most cases. Thirdly, we did not have the ability to further assess the influence of different cystoscopy methods on patient sexual function, anxiety, quality of life, and lower urinary tract symptoms. Furthermore, we

were also unable to assess the impact of the number of procedures on pain perception due to insufficient data.

Conclusions

Our study revealed that RC is a tolerable procedure, and FC may not be more comfortable than RC. However, further larger well-designed trials are warranted to demonstrate our findings, and explore whether FC is more beneficial to patient sexual function, anxiety, quality of life, and lower urinary tract symptoms than RC.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at <http://dx.doi.org/10.21037/apm-21-316>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/apm-21-316>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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