Systematic review of robotic radical cystectomy functional and quality of life outcomes

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Abstract

This systematic review summarizes the urinary continence, male sexual function, and female sexual function outcomes after robotic-assisted radical cystectomy (RARC). Greater intracorporeal diversion use, longer followup, and clearly stated urinary continence definitions have revealed RARC urinary continence rates for orthotopic ileal neobladders that are similar to those after open radical cystectomy (ORC) when using the strictest continence definitions. Nerve-sparing technique appears to be well-used in most studies, with short-term and long-term RARC potency rates similar those after ORC when using the strictest potency definitions. Level 1 evidence using validated questionnaires suggests that quality of life outcomes are also similar.

Introduction

The first robotic-assisted laparoscopic radical cystectomy (RARC) with extracorporeal urinary diversion,[1] as well as RARC with intracorporeal neobladder,[2] were both described in 2003. Since then, high-quality data on the short-term and long-term oncological outcomes have been comparable between open radical cystectomy (ORC) and RARC.[3-6] Randomized controlled trials have shown similar perioperative outcomes and complication rates,[3,4] yet increased costs and prolonged operative times of RARC compared to ORC have remained a concern. However, high-volume centers have reported improved operative times, efficient robotic surgery teams, and less complications that may lower overall financial costs.[7,8] Despite the increased use of RARC, only benefits associated with minimally invasive surgery have been clearly demonstrated.[9]

With similar oncological and perioperative morbidity of RARC in comparison to ORC, we sought to review patient-reported quality of life and functional outcomes. The purpose of this systematic review was to summarize and analyze the current body of literature surrounding patient-reported urinary continence, sexual and erectile function, and health-related quality of life (HRQOL) outcomes after RARC.

Methods

A systematic literature search was performed on PubMed using the search terms "(robot) AND (cystectomy)" in April 2020 in accordance with PRISMA guidelines. Manuscripts encompassing human subjects who underwent RARC with reported outcomes on urinary continence, sexual function, erectile function, and HRQOL outcomes were included. Studies from all years, languages, study designs, and length of patient followup were included. All abstracts that resulted from this query were separately reviewed by two authors (JJ and DM) for aspects relating to urinary continence, erectile function, and HRQOL outcomes after RARC. Discrepancies were resolved by open discussion between the two authors. The abstracts of all studies cited in the reference lists of manuscripts from the PubMed query were reviewed and included within this review if relevant. Studies regarding simple cystectomy, partial cystectomy, salvage cystectomy, complications, uretero-enteric fistulas, and animal studies were excluded from this review. All manuscripts that met inclusion criteria were maintained within an electronic database.

Manuscripts that met inclusion criteria were critically reviewed for primary data concerning urinary continence, sexual function, erectile function, and HRQOL outcomes after RARC. Only the most recent study with the longest followup was included among studies with overlapping patient populations. The number of patients, proportion of nerve-sparing technique, proportion of intracorporeal urinary diversion, median followup, patient- vs. physician-reported outcome, urinary continence definition, and proportion of urinary continent patients for each definition were extracted or calculated from each manuscript. The daytime and nighttime continence rates according to each study's strictest continence definition and longest followup are displayed in this manuscript. The patient characteristics displayed in this man-

uscript reflect the actual number and proportion of patients with urinary continence data. The number of patients, proportion of nerve-sparing technique, median followup, patient- vs. physician-reported outcome, potency definition, and proportion of potent patients for each definition were extracted or calculated from each manuscript. The potency rates according to each study's strictest potency definition and longest followup are displayed in this manuscript. The patient characteristics displayed in this manuscript reflect the actual number and proportion of patients with erectile function data. HRQOL findings from randomized controlled trials are summarized. The patient characteristics displayed in this manuscript reflect the number and proportion of patients that completed the questionnaires at the latest followup period. With the variability of data, a meta-analysis would not be possible. All non-randomized control trials concerning urinary continence, sexual function, erectile function, and HRQOL outcomes after RARC with less than 50 patients were ultimately excluded.

Results

A total of 614 manuscripts were generated from the PubMed search query, with only 51 manuscripts meeting inclusion criteria after abstract review. An additional six manuscripts that met inclusion criteria were identified from the reference lists. This data is summarized in Supplementary Fig. 1.

A total of 23 studies reporting primary data on urinary continence after RARC were identified. Four studies were excluded because they encompassed a patient population updated in more recent studies, while another study was excluded due to only graphical representation of data. The remaining 14 studies were excluded for having less than 50 patients. Four studies containing more than 50 patients, published from 2013–2019, ultimately captured 341 patients with urinary continence data (Table 1). Marked heterogeneity in nerve-sparing reporting/use, followup period, and continence definitions were noted. No clear urinary continence patterns were identified in relation to publication year, nerve-sparing technique, intracorporeal urinary diversion or followup period.

A total of 15 studies reporting primary data on potency after RARC were identified. Five studies were excluded because they encompassed a patient population updated in more recent studies, while eight were excluded for having less than 50 patients. Two studies containing more than 50 patients, published from 2013–2015, ultimately captured 163 patients with potency data (Table 2). Of note, these studies also met the urinary continence inclusion criteria and are included in Table 1. Marked heterogeneity in nerve-sparing reporting/use, followup period, and potency definitions were noted. While no clear potency patterns were identified in relation to publication year or followup period, nerve-sparing technique appeared to improve potency.

A total of four randomized controlled trials reporting primary data on HRQOL using validated questionnaires met inclusion criteria (Table 3). These four randomized studies, published from 2014–2020, included a total of 301 patients that completed the questionnaires at the latest followup period. Although only two studies used the same questionnaire, no study identified a significant difference between ORC and RARC at any time point.

Discussion

Despite the increased uptake of RARC and focus on oncological, perioperative, and cost outcomes, relatively few studies have compared functional and quality of life outcomes after RARC. Although other reviews have been published on this topic, ours is the first systematic review since 2015.[10] We focused on randomized trial outcomes and patient-reported outcomes at the highest level of evidence. Since this time, multiple large series with long-term followup have been published. Our review of the current body of literature suggests

Table 1. Comparison of studies evaluating urinary continence after RARC

Author	Year	Patients	Nerve-sparing (%)	Intracorporeal diversion (%)	Followup (mo)	Patient vs. physician reported outcome	Daytime definition	Daytime rate (%)	Nighttime definition	Nighttime rate (%)
Prospective studies										
Tyritzis[13]	2013	70	58 bilateral; 4 unilateral	100	12	Patient	0–1 pads	69	0–1 pads	57
Brassetti[23]	2019	137	N/A	N/A	12	Patient	Complete absence of leak	79	N/A	N/A
Retrospective studies										
Sim[24]	2015	73	70 bilateral	100	32	Patient	<1 pad	89	<1 pad	68
Gok[25]	2019	61	89 bilateral; 5 unilateral	100	27	Patient	0–1 security pads	61	Dry with no protection	41

The strictest urinary continence definition with the longest followup was used. RARC: robotic-assisted radical cystectomy.

Table 2. Comparison of studies evaluating erectile function after RARC

Author	Year	Patients	Nerve-sparing (%)	Followup (mo)	Patient vs. physician reported outcome	Potency definition	Potency rate (%)
Prospective studies							
Tyritzis[13]	2013	62	58 bilateral; 4 unilateral	12	Physician	IIEF >25 w/ or w/o PDE5I	47
Retrospective studies							
Sim[24]	2015	101	70 bilateral	32	N/A	N/A	37

IIEF: International Index of Erectile Function; PDE5I: phosphodiesterase type 5 inhibitor; RARC: robotic-assisted radical cystectomy.

that the urinary continence, erectile function, and HRQOL outcomes after RARC are similar to those after ORC.

Urinary continence

Incontinent urinary diversion, continent cutaneous diversion, and orthotopic neobladder have been described in the ORC and RARC literature. In addition to the various diversions, continence rates in RARC are influenced by age, mental status, intact and innervated urethral sphincter, urethral length, low-pressure and large capacity reservoir, absence of bacteriuria, and complete voiding.[11] Orthotopic neobladders were first created in an extracorporeal manner, but studies have progressively moved towards intracorporeal. Many intracorporeal neobladders have been described, but some of the most commonly used ones include the pyramid pouch, u-shaped neobladder, USC-modified Studer neobladder, and Karolinska-modified Studer neobladder.[12] The wide variety of urinary diversions and large number of variables that influence urinary continence have made the comparison of continence outcomes after RARC difficult.

In a systematic review by the Pasadena consensus panel in 2015, the authors noted that there were widespread differences in patient selection, data collection, followup period, nerve-sparing use, and outcome definition that limited their ability to draw any conclusions on urinary continence outcomes after RARC.[10] Similar to the findings of the Pasadena consensus panel, there still remains marked heterogeneity in outcome definitions between series that make objective comparisons difficult. However, there appears to be a trend towards greater intracorporeal diversion use, longer followup, and clearly stated urinary continence definitions in more recent series. The movement towards more uniform techniques and definitions will allow for objective analyses and meta-analyses in the future.

Male sexual function (potency)

Potency is another highly investigated functional outcome after radical cystectomy. In the systematic review by the Pasadena consensus panel in 2015, the authors noted the presence of small sample sizes, use of non-validated definitions/evaluations, absence of long-term followup, and wide variety in use of nerve-sparing technique that limited their ability to draw any conclusions on erectile function after RARC.[10] Similar to the their findings, there still remains marked heterogeneity in outcome definitions between series that make objective comparisons difficult. In contrast to the urinary continence data, there does not appear to be a trend towards the use of objective and uniform measurements of potency. Nerve-sparing technique appears to be well-used in most studies, with a combination of short-term and long-term outcomes reported.

An understanding of the long-term potency rates from more typical RARC populations may be more useful for physicians and patients. In one prospective study, 47% of patients who underwent bilateral nerve-sparing had an International Index of Erectile Function (IIEF) >25 with or

Table 3. Health-related quality of life outcomes after RARC from prospective randomized clinical trial

Author	Year	Surgical approaches	Patients	Questionnaire	Domains	Summary of findings
Messer[21]	2014	ORC vs. RARC	25	FACT-VCI	Physical, social/family, emotional, functional with single items that pertain to cystectomy	No significant differences at 3, 6, 9, and 12 months
Bochner[3]	2015	ORC vs. RARC	52	EORTC QLQ-C30	Global health, cognitive, emotional, physical, role, social, financial, and symptoms	No significant differences at 3 and 6 months
Khan[4]	2016	ORC vs. LRC vs. RARC	46	FACT-BL, FACT-G	Physical, social/family, emotional, functional with single items that pertain to bladder cancer	No significant differences at 8 months
Becerra[22]	2020	ORC vs. RARC	178	FACT-VCI, SF-8	Physical, social/family, emotional, functional with single items that pertain to cystectomy; physical and mental health	No significant differences at 6 months

EORTC QLQ-C30: European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire; FACT-BL: Functional Assessment of Cancer Therapy-Bladder Cancer; FACT-G: FACT-General; FACT-VCI: FACT-Vanderbilt Cystectomy Index; ORC: open radical cystectomy; LRC: laparoscopic radical cystectomy; RARC: robotic-assisted radical cystectomy; SF-8: Short-Form 8 Health Survey.

without phosphodiesterase type 5 inhibitor (PDE5I) at 12 months postoperatively.[13] More specifically, 31% and 50% of nerve-spared men were potent without medication and with PDE5I, respectively. In contrast, only 10% and 5% of non-nerve spared men were potent without medication and with PDE5I, respectively. No statistical analysis was performed to compare these differences, but potency appears to be substantially improved with nerve-sparing. These potency rates are similar to the rates in contemporary ORC series, which range from 29–79%.[14-17] Similar to the interpretation of the urinary continence data, a closer analysis of the ORC data shows that potency rates after RARC are similar to those after ORC when using the strictest potency definitions.

The concepts that nerve-sparing technique and preoperative erectile function may affect potency after radical cystectomy have been described in the ORC literature.[18] One study compared patient demographics and preoperative characteristics between patients who did and did not maintain potency after RARC, defining potency as "erection sufficient for penetration."[19] The study did not include nerve-sparing technique or preoperative erectile function into the analysis, but found that urinary diversion type, operative time, blood loss, transfusion rates, hospital length of stay, number of lymph nodes sampled, pathological stage, surgical margin status, patient followup, and recurrence were not statistically different between those who were and were not potent. Despite attempts by these authors to identify factors affecting potency, more data using validated questionnaires and objective measurements are needed to draw appropriate conclusions.

Female sexual function

While most literature has focused on male sexual function after RARC, there has been some research on female sexual function by preserving the inferior hypogastric plexus in sex-sparing RARC. The greatest experience on this topic is from a series of 11 female patients with ≤cT2 disease and an absence of bladder neck, trigone, or urethral tumor at time of transurethral resection.[20] Sexual function was measured using the Female Sexual Function Index questionnaire, which includes six sexual domains.[20] Arousal and orgasm domains were not significantly different from their baseline at 12 months postoperatively, but were significantly lower at three months postoperatively.[20] Lubrication, satisfaction, pain, and global score were significantly lower compared to baseline at 12 months postoperatively, but improved from the three-month postoperative visit.[20] Most patients (73%) were sexually active at 12 months postoperatively.[20] The baseline characteristics, perioperative complications, and long-term complications were not significantly different between these 11 sex-spared RARC patients and 36 standard RARC patients; however, daytime continence was significantly improved in the sex-spared cohort.[20] This very early and limited data suggests that acceptable sexual function can be achieved in females after RARC.

Health-related quality of life

Radical cystectomy remains one of the most morbid operations in urology, with many studies investigating the impact on quality of life. As emphasis on HRQOL increases, validated questionnaires were created to capture the challenges that were specific to oncology, and more specifically bladder cancer. Four prospective, randomized clinical trials were performed that compared HRQOL between ORC and RARC. The first study used the Functional Assessment of Cancer Therapy-Vanderbilt Cystectomy Index (FACT-VCI) to compare patients.[21] The authors found no significant difference from baseline total scores and individual domains at three, six, nine, and 12 months postoperatively in the ORC or RARC cohorts. There were also no significant differences in HRQOL between ORC and RARC on multivariate analysis, except an isolated lower physical well-being score at six months in the ORC group. The second prospective, randomized clinical trial analyzed HRQOL between ORC and RARC by comparing the European Organization for the Research and Treatment of Cancer Quality of Life 30-item core questionnaire (EORTC QLQ-C30) at three and six months postoperatively.[3] No statistical differences in quality of life change from baseline at three or six months postoperatively were identified in any domain. The third prospective, randomized controlled study compared ORC, laparoscopic radical cystectomy (LRC), and RARC, with quality of life assessed with FACT-Bladder Cancer (FACT-BL) and FACT-General (FACT-G).[4] Similar to the prior studies, this study did not find any significant difference between the three approaches.

The RAZOR trial captured the largest number of patients and recently published their HRQOL results — which used the FACT-VCI and Short-Form 8 Health Survey (SF-8) — comparing ORC and RARC cohorts at three and six months postoperatively.[22] There were no significant differences between the cohorts at any time point for any of the FACT-VCI outcomes or SF-8 composite scores. Upon subset analyses by urinary diversion, there were no significant differences at any time point, except for a lower FACT-BL-Cys in continent urinary diversion patients at three months. Physical composite scores were significantly more positive in the continent urinary diversion patients at six months, while mental composite scores were not significantly different between the two diversions at any time point. Although the urinary continence and potency data after RARC is heterogeneous and largely retrospective, there is high-quality evidence to suggest that the HRQOL outcomes after ORC and RARC are similar.

This manuscript is the first systematic review since 2015 to analyze the functional and quality of life outcomes after

RARC. Our search methodology was systematic and thorough to fully capture the relevant literature. In contrast to previous systematic reviews, our manuscript only reports the data of patients with urinary continence, potency, and HRQOL outcomes. Prior systematic reviews report patient numbers, nerve-sparing proportion, intracorporeal diversion, and followup values of entire patient cohorts, which chiefly encompass patients with the oncological outcomes and primary endpoints. The majority of the functional and HRQOL data are secondary endpoints of larger studies that have primary oncological endpoints. As a result, the subset of patients with reported functional and HRQOL data have different characteristics compared to the larger study cohorts. Given the heterogeneity of the functional and HRQOL assessments between studies, a high-quality meta-analysis could not be performed.

Conclusions

Few studies have analyzed the functional and quality of life outcomes after RARC. There remains marked heterogeneity in urinary continence and potency outcome definitions between historical series that make objective comparisons difficult. Trends toward greater intracorporeal diversion use, longer followup, and clearly stated urinary continence definitions have revealed RARC urinary continence rates for orthotopic ileal neobladders are similar to those after ORC when using the strictest urinary continence definitions. Similarly, nerve-sparing technique appears to be well-used in most studies, with short-term and long-term RARC potency rates similar those after ORC when using PDE5I under the strictest potency definitions. Lastly, level 1 evidence using validated questionnaires suggests that the HRQOL outcomes after ORC and RARC are similar.

Competing interests: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

References

1. Menon M, Hemal AK, Tewari A, et al. Nerve-sparing robot-assisted radical cystoprostatectomy and urinary diversion. *BJU Int* 2003;92:232-6. https://doi.org/10.1046/j.1464-410X.2003.04329.x
2. Beecken WD, Wolfram M, Engl T, et al. Robotic-assisted laparoscopic radical cystectomy and intra-abdominal formation of an orthotopic ileal neobladder. *Eur Urol* 2003;44:337-9. https://doi.org/10.1016/S0302-2838(03)00301-4
3. Bochner BH, Dalbagni G, Sjoberg DD, et al. Comparing open radical cystectomy and robot-assisted laparoscopic radical cystectomy: A randomized clinical trial. *Eur Urol* 2015;67:1042-50. https://doi.org/10.1016/j.eururo.2014.11.043
4. Khan MS, Gan C, Ahmed K, et al. A Single-center, early-phase, randomized, controlled, three-arm trial of open, robotic, and laparoscopic radical cystectomy (CORAL). *Eur Urol* 2016;69:613-21. https://doi.org/10.1016/j.eururo.2015.07.038
5. Parekh DJ, Reis IM, Castle EP, et al. Robot-assisted radical cystectomy vs. open radical cystectomy in patients with bladder cancer (RAZOR): An open-label, randomized, phase 3, non-inferiority trial. *Lancet* 2018;391:2525-36. https://doi.org/10.1016/S0140-6736(18)30996-6
6. Hussein AA, Elsayed AS, Aldhaam NA, et al. Ten-year oncological outcomes following robot-assisted radical cystectomy: Results from the international robotic cystectomy consortium. *J Urol* 2019;202:927-35. https://doi.org/10.1097/JU.0000000000000386
7. Leow JJ, Reese SW, Jiang W, et al. Propensity-matched comparison of morbidity and costs of open and robot-assisted radical cystectomies: A contemporary population-based analysis in the United States. *Eur Urol* 2014;66:569-76. https://doi.org/10.1016/j.eururo.2014.01.029
8. Morii Y, Osawa T, Suzuki T, et al. Cost comparison between open radical cystectomy, laparoscopic radical cystectomy, and robot-assisted radical cystectomy for patients with bladder cancer: A systematic review of segmental costs. *BMC Urol* 2019;19:110. https://doi.org/10.1186/s12894-019-0533-x
9. Rai BP, Bondad J, Vasdev N, et al. Robotic versus open radical cystectomy for bladder cancer in adults. *Cochrane Database Syst Rev* 2019;4:CD011903. https://doi.org/10.1002/14651858.CD011903.pub2
10. Yuh B, Wilson T, Bochner B, et al. Systematic review and cumulative analysis of oncologic and functional outcomes after robot-assisted radical cystectomy. *Eur Urol* 2015;67:402-22. https://doi.org/10.1016/j.eururo.2014.12.008
11. Collins JW, Wiklund NP. Totally intracorporeal robot-assisted radical cystectomy: Optimizing total outcomes. *BJU Int* 2014;114:326-33. https://doi.org/10.1111/bju.12558
12. Tan WS, Lamb BW, Kelly JD. Evolution of the neobladder: A critical review of open and intracorporeal neobladder reconstruction techniques. *Scand J Urol* 2016;50:95-103. https://doi.org/10.3109/21681805.2016.1141318
13. Tyritzis SI, Hosseini A, Collins J, et al. Oncological, functional, and complications outcomes of robot-assisted radical cystectomy with totally intracorporeal neobladder diversion. *Eur Urol* 2013;64:734-41. https://doi.org/10.1016/j.eururo.2013.05.050
14. Hekal IA, El-Bahnasawy MS, Mosbah A, et al. Recoverability of erectile function in post-radical cystectomy patients: Subjective and objective evaluations. *Eur Urol* 2009;55:275-83. https://doi.org/10.1016/j.eururo.2008.06.072
15. Vilaseca A, García-Cruz E, Ribal MJ, et al. Erectile function after cystectomy with neurovascular preservation. *Actas Urol Esp* 2013;37:554-9. https://doi.org/10.1016/j.acuro.2013.02.012
16. Jacobs BL, Daignault S, Lee CT, et al. Prostate capsule sparing vs. nerve-sparing radical cystectomy for bladder cancer: Results of a randomized, controlled trial. *J Urol* 2015;193:64-70. https://doi.org/10.1016/j.juro.2014.07.090
17. Colombo R, Pellucchi F, Moschini M, et al. Fifteen-year single-center experience with three different surgical procedures of nerve-sparing cystectomy in selected organ-confined bladder cancer patients. *World J Urol* 2015;33:1389-95. https://doi.org/10.1007/s00345-015-1482-y
18. Hernández V, Espinos EL, Dunn J, et al. Oncological and functional outcomes of sexual function-preserving cystectomy compared with standard radical cystectomy in men: A systematic review. *Urol Oncol* 2017;35:539.e17-29. https://doi.org/10.1016/j.urolonc.2017.04.013
19. Haberman K, Wittig K, Yuh B, et al. The effect of nerve-sparing robot-assisted radical cystoprostatectomy on erectile function in a preoperatively potent population. *J Endourol* 2014;28:1352-6. https://doi.org/10.1089/end.2014.0315
20. Tuderti G, Mastroianni R, Flammia S, et al. Sex-sparing robot-assisted radical cystectomy with intracorporeal padua ileal neobladder in female: Surgical technique, perioperative, oncological and functional outcomes. *J Clin Med* 2020;9:577. https://doi.org/10.3390/jcm9020577
21. Messer JC, Punnen S, Fitzgerald J, et al. Health-related quality of life from a prospective, randomized clinical trial of robot-assisted laparoscopic vs. open radical cystectomy. *BJU Int* 2014;114:896-902. https://doi.org/10.1111/bju.12818
22. Becerra MF, Venkatramani V, Reis IM, et al. Health-related quality of life of patients with bladder cancer in the RAZOR trial — a multi-institutional, randomized trial comparing robot vs. open radical cystectomy. *J Urol* 2020;204:450-9. https://doi.org/10.1097/JU.0000000000001029
23. Brassetti A, Tuderti G, Anceschi U, et al. Combined reporting of surgical quality, cancer control, and functional outcomes of robot-assisted radical cystectomy with intracorporeal orthotopic neobladder into a novel trifecta. *Minerva Urol Nefrol* 2019;71:590-6. https://doi.org/10.23736/S0393-2249.19.03566-5
24. Sim A, Balbay MD, Todenhöfer T, et al. Robot-assisted radical cystectomy and intracorporeal urinary diversion — safe and reproducible? *Cent Eur J Urol* 2015;68:18-23. https://doi.org/10.5173/ceju.2014.466
25. Gok B, Atmaca AF, Canda AE, et al. Robotic radical cystectomy with intracorporeal Studer pouch formation for bladder cancer: experience in 98 cases. *J Endourol* 2019;33:375-82. https://doi.org/10.1089/end.2019.0036

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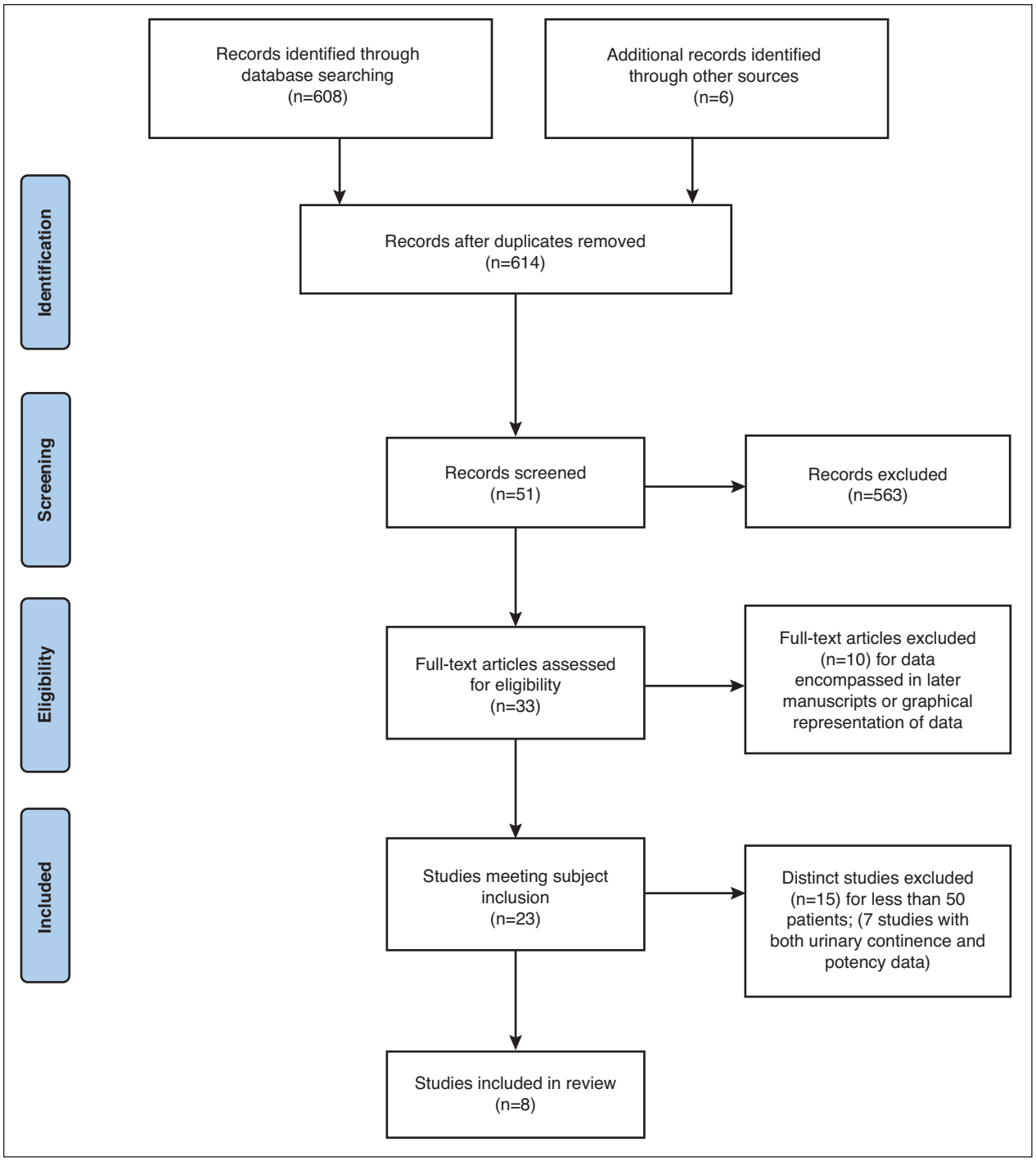

Supplementary Fig. 1. Study flow diagram.