TITLE: Outcomes of early endoscopic realignment versus suprapubic cystostomy and delayed urethroplasty for pelvic fracture related posterior urethral injuries: a systematic review.

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ABSTRACT:

Context: The evidence base for optimal acute management of pelvic fracture related posterior urethral injuries needs reviewed because of evolving endoscopic techniques. Current standard of care is suprapubic cystostomy followed by delayed urethroplasty (DU).

Objective: To systematically review the evidence base comparing early endoscopic realignment (EER) with cystostomy and DU regarding stricture rate, need for subsequent procedures and functional outcomes.

Evidence acquisition: systematic search in Medline, Embase, Cochrane central register of controlled trials, Cochrane database of systematic review, and clinicaltrials.gov without time- or language-limitations. Both medical subject heading (MeSH) and free text terms as well as variations of root word were searched. Randomised controlled trials (RCTs), non-randomised comparative studies (NRCS) and single arm case series were included, so long as ≥10 patients were enrolled. Data were narratively synthesised in light of methodological and clinical heterogeneity. The risk of bias of each included study was assessed.

Evidence synthesis:
No RCTs were found. Six non-randomised comparative studies (NRCS) and met inclusion criteria and were selected for data extraction. Non-comparative studies (NCS) with more than 10 participants were included resulting in seven eligible studies.

From the comparative papers the results of 219 patients were reported, 142 in the realignment group and 77 in the group undergoing cystostomy with delayed repair. The non-comparative studies reported on a further 150 cases. An overall stricture rate of 49% was evident in the endoscopic realignment group. Of these patients, 50% (28.1% overall) could be managed by endoscopic procedures and 40.3% (18.5% of intervention group) required anastomotic repair.

Conclusion:
No RCTs were found and the included non-randomised studies have heterogeneous populations and a high degree of bias. About half of the patients were free of stricture and thus did not undergo delayed urethroplasty in case EER had been performed.

INTRODUCTION:

Blunt trauma to the male pelvis with pelvic ring disruption, will result in posterior urethral injuries (PUI) in up to 10% of patients (1). Certain pelvic fracture subtypes have a higher association with urethral disruption. Fractures not involving ischiopubic rami have almost no elevated risk. Koraitim found the subtypes at higher risk are straddle injuries, in which all four pubic rami are fractured, or Malgaigne fractures, involving disruption through ischiopubic rami anteriorly as well as through the sacrum or sacroiliac joint posteriorly (2). Long-term morbidity of PUIs is substantial, including urethral stricture, erectile dysfunction and urinary incontinence.

The early management of PUI aims to reduce this long-term morbidity but remains controversial to date. This controversy is based on different treatment options that have been proposed in the early management.

These options include: immediate (<48h after trauma) or primary delayed urethroplasty (2-14d after trauma), immediate or primary delayed urethral realignment or suprapubic cystostomy with delayed (>3 months after trauma) urethroplasty.
Suprapubic cystostomy with delayed urethroplasty can always be considered in the early phase, but a long period of disability and discomfort due to the suprapubic catheter are clear disadvantages to this treatment strategy. Therefore, this strategy has been challenged by immediate or primary delayed realignment (if possible endoscopic) whenever the clinical condition of the patient allows it.
The aim of realignment is to correct severe distraction injuries rather than to prevent a stricture. Some authors report a lower stricture rate than with suprapubic catheter placement alone (3-5). If scarring and subsequent stricture formation occurs, the restoration of urethral continuity is easier. For short, non-obliterative strictures, internal urethrotomy can be attempted (3-5). For longer strictures, or in the case of failure of an internal urethrotomy, urethroplasty is required (3).

The debate against early realignment includes the view that complete urethral disruptions will not result in healing following primary realignment. The reported success rates could be explained by a number of partial urethral injuries which are likely to heal with a suprapubic catheter alone.
Primary realignment in the acute phase is also technically and logistically difficult. In case of failure, it may make subsequent urethroplasty more difficult (6, 7).
The EAU trauma guideline panel conducted a systematic review on this subject to verify the outcomes of early endoscopic realignment compared to cystostomy with delayed urethroplasty.

2. Evidence acquisition

2.1 Search strategy and selection criteria

The review was performed according to preferred reporting items for systematic reviews and meta-analysis (PRISMA) (fig. 3). The search strategy is described in detail in Supplementary File 1. In short, Medline (from 1946), Embase (from 1974), Cochrane Central Register of Controlled Trials , Cochrane Database of Systematic Reviews (from 2005) and clinicaltrial.gov without time, publication format and language limitations were searched for all relevant publications. Both medical subject heading (MeSH) and free text terms as well as variations of root word were searched. Key terms related to traumatic urethral strictures were combined using the set operator AND with key terms related to endoscopy realignment or cystostomy or urethral /suprapubic catheterisation. Animal studies, studies in children, case reports and letters were excluded. We also searched for any systematic reviews or RCTs related to urethra injury and pelvic fracture even no treatment interventions were mentioned. As there were only a few comparative non-randomised studies (NRCS), non-comparative studies (for example, single arm case series) (NCS) were included. A systematic literature search was initially performed in April 2015. An update on the search was done in April 2016.

2.2 PICO (Patients, intervention, comparator, outcomes):

Included patients were men with traumatic urethral posterior distraction injuries

An intervention group was formed of patients undergoing early (< 14 days) endoscopic realignment (EER). The comparator group was a patient cohort with cystostomy and delayed (> 3 months) urethral repair (SPS + DU).

Primary outcomes were stricture rates and need for auxiliary procedures. Secondary outcomes were posttraumatic urinary incontinence and impotence.

2.2 Data collection and data extraction

Following de-duplication, two review authors (PJ.E., E.V.) independently screened all abstracts and full-text articles for relevance to the defined inclusion and exclusion criteria. Any disagreements were resolved by discussion or by consulting a third review author (N.L.). The references cited in all full-text articles were also assessed for additional relevant articles. There were no limitations on study design or language and also conference abstracts were included. Studies with less than 10 patients per arm were excluded. No time-restriction was used. A standardised data extraction form was used. Surgical data, stricture incidence, functional outcomes (urinary continence, sexual outcomes) and re-treatment information were extracted.

2.3 Risk of bias in individual studies

Two reviewers (PJ.E and E.V) assessed the 'risk of bias' (RoB) of each included study independently. A modified version of the RoB assessment tool was used in assessing NRCSs (8). A list of the five most important potential confounders for harm and benefit outcomes was developed a priori with clinical content experts (EAU Trauma guideline panel). The potential confounding factors were: age, preoperative continence rate, associated injuries, type of intervention and body mass index (BMI). The included studies were assessed on whether the outcomes could have been influenced by baseline imbalance or lack of adjustment in analysis for the pre-specified confounders. RoB in single arm case series, focus was redirected to addressing external validity (applicability of results to different people, places

or time) by assessing whether study participants were selected consecutively or representative of a wider patient population. Attrition bias, selective outcome reporting and whether an a priori protocol was available (indicating prospective study design), was also assessed. This is a pragmatic approach informed by the methodological literature (9, 10). The systematic review was entered into the register of PROSPERO. (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015027974)

2.4 Statistical analysis

Methodological and clinical heterogeneity of the included studies meant that meta-analysis was inappropriate. Instead, a narrative synthesis was performed due to the methodological and clinical heterogeneity of the included studies (https://www.york.ac.uk/crd/guidance/). Possible reasons for heterogeneity were explored using the available information such as differences in the population studied, the treatment given, or the way in which the outcomes were assessed. Intended formal subgroup analysis was not possible due to the inclusion of NRCS. Therefore, any subgroup differences were discussed narratively to explore potential effect size differences based on the subgroups mentioned above. A planned sensitivity analysis to assess the robustness of our review results, by repeating the analysis only including studies with an overall medium to low risk of bias, was not possible.

3. Evidence synthesis

3.1 . Quality of the studies

Two reviewers independently screened 570 abstracts, of which 84 papers were selected for full-text screening: 29 were comparative studies (mainly retrospective and non-randomised) and 55 were single arm case series (fig3). There was significant heterogeneity in the assessment and treatment evaluation in these studies. Ultimately, six NRCS and seven NCS reporting on ≥10 patients met inclusion criteria. After the update search (04/2016) one

more NRCS was added of 62 studies identified. Risk of bias is summarised in Figure 1 (NRCS) and 2 (NCS).

3.2. Study details

One NRCS out of five and one NCS out of seven are conference abstracts (11, 12). Recruitment periods ranged from 1987 to 2013, publication dates from 2001 to 2015 (table1).

3.2.1.Patients

From the *comparative* papers (NRCS) the results of 219 patients were retrieved: 142 in the realignment group and 77 in the group with cystostomy with delayed repair. Heterogeneous populations were evident in the included studies. Only one conference abstract excluded partial injuries (11). Three studies excluded bladder neck involvement (11, 13, 14).

Allocation to different treatment groups was not randomised in any study. In three papers patients were allocated to the cystostomy group if they were haemodynamically unstable (15), significant associated lesions or if endoscopic realignment was not successful (14-16).

In the *non- comparative* papers (NCS) data of 150 patients could be extracted. Only two of the papers have strict exclusion criteria. Patients with severe associated injuries who needed laparotomy were excluded by Abdelsalam (17), partial injuries were excluded by Kim et al. (18). Four non-comparative papers initially placed suprapubic catheter in all patients (4, 17, 19, 20).

One paper did not exclude all cases with open realignment (12).

Details on partial ruptures or rupture classification (Colapinto) were available in three of the NRCS. There were no significant differences between the two groups (14, 15).

Details of diagnostic assessment were not given by all papers (4, 12, 13, 14). Radiographic studies (retrograde and/or antegrade urethrography) were performed in the majority of NRCS (11,15,16,21) and NCS (17-20, 22).

Two of the NRCS papers used only retrograde cystoscopy (flexible and radiographic control) (14, 15). Four other papers used a combination of retrograde and antegrade cystoscopy (through the cystostomy) (11, 13, 16, 21). All the NCS papers combined retrograde and antegrade realignment.

3.3. Outcomes

3.3.1 Post-traumatic stricture rate (table2)

All included studies evaluated stricture incidence with uroflowmetry. In almost all reports, a maximum urinary flow rate (Qmax) of < 15ml/s or subsequent urethral intervention was considered as treatment failure or indication of subsequent urethral manipulation. One paper defined stricture as moderate or severe according to the frequency of urethrotomies (15). In the abstract from Abdalla (11) two asymptomatic patients with a Qmax of < 15ml/s were not treated.

Stricture rates range from 10 to 40% in the delayed treatment group. Two papers report a stricture rate of 100% in the cystostomy group but this evaluation was done before the delayed urethroplasty (13, 14).

For endoscopic realignment in NRCS the selected papers report stricture rates ranging from 14.3 (14) – 100% (11). In NCS papers strictures were observed in 25 (19) – 73.7% (22) of patients.

3.3.2. Urinary incontinence (table3)

Urinary incontinence was not assessed in a standardised fashion. Three studies (7,17,19) reported the number of pads used/day. The other studies made a decision based on patients reporting only. Incontinence was considered to be present for a case if it met the criteria of the reporting article. Across the included studies, incontinence rates were around 10% without remarkable difference between treatment groups.

3.3.3. Erectile dysfunction (table3)

Erectile dysfunction was not assessed by standardised questionnaires but was mainly self-reported, or not reported at all (14). In NRCS and NCS, ED ranged from 5-45% of included patients.

3.3.4. Subsequent procedures (SP) (table 4)

Strictures treated after suprapubic cystostomy and delayed urethroplasty could be treated endoscopically in up to 40% of patients. The necessity to perform urethroplasty in 100% of cases in the Hadjizacharia paper reflects the stricture rate as discussed above. The paper does not provide stricture rates or need for subsequent procedures after urethroplasty (14). Similarly, in Johnsen et al, 78.6% of patients underwent urethroplasty, with 3/13 (21,4%) patients with suprapubic cystostomy refusing further intervention (13).
In failed EER cases with stricture formation, 14.3% (14) - 50% (11) could be managed endoscopically, as compared to 0% (14, 19) - 57.9% (22) requiring urethroplasty.

4. Discussion

Acute management of PUIs is challenging and complex. They are usually associated with more serious and even life-threatening injuries. This is one of the reasons why it is not essential to have bladder drainage (either suprapubic or transurethral) the first hours after trauma. However, it is preferable to have it as quick as possible in order to monitor urinary output, treat retention and minimise extravasation. A gentle attempt of urethral catheterisation is unlikely to do any additional damage. If urethral catheterisation is not successful, suprapubic catheter should be placed (23). Diagnosis of PUI relies on retrograde urethrography which is able to differentiate between a complete or partial injury. This injury to the urethral mucosa will lead to fibrosis and scarring with risk of stricture formation. A partial injury might heal without consequences, with a non-obliterative stricture or with an obliterative stenosis. A complete injury is a distraction defect between the mucosal edges. The gap between them is filled with scar tissue, which will lead to an obliterative stenosis.

Early realignment is an option in the acute management of partial and complete injuries. In a partial injury, realignment and transurethral catheterisation avoids extravasation of urine in the surrounding tissues reducing the inflammatory response. In a complete injury, it aims to correct severe distraction rather than to prevent a stricture. It is wrong to assume that urethral healing is attributable to a urethral catheter, because healing will occur regardless of it.

In this review, about half of the patients treated with EER were free of recurrence. These good results can be explained in part by inclusion of partial injuries. The fact that partial injuries might heal without consequences is supported by a hallmark animal study (24), which demonstrated that if 1/3 of the urethral circumference is preserved, a full spontaneous restoration of the urethral patency is possible with urethral catheterisation only. One paper explicitly excluded partial injuries and they describe a stricture ratio of only 53% cases (18). This is in contrast of the above-mentioned animal study, where all animals with a complete urethral distraction developed a stricture. However, in the animal study, the distraction defect was 5cm. After realignment, the urethral mucosal edges can be approximated in close contact to each other, promoting the urethral regeneration. Furthermore, it is sometimes difficult to discriminate between partial and complete injuries. So it is possible that some complete injuries might be misdiagnosed partial injuries. Nevertheless the potential benefit of avoiding a subsequent stricture in some of the patients after EER remains very interesting. It supports the practice of organizing an attempt of realignment when the patient is stabilised and other major injuries have been treated. Until this time bladder drainage can be secured by cystostomy. With the cystostomy in place, realignment can be performed in an antegrade and/or retrograde fashion. When patients with PUI are taken to operating theatre for any kind of intervention, they could be considered for any kind of realignment. Barrett et al. conducted a systematic review (25) about acute management of urethral injuries. They discuss 2 reports of endoscopic realignment (14, 15) but mainly other methods of realignment as an open procedure (Davis interlocking sounds, railroading, etc.). Their meta-analysis of stricture ratio favours primary realignment.

Two papers concluded that urethroplasty with anastomotic repair has worse outcomes after previous manipulation (26, 27). Singh et al. concluded that previous manipulation negatively influences subsequent anastomotic repair (26). Their intervention group consisted of 7 endoscopic realignment cases and 8 urehtroplasties. Culty et al. retrospectively analysed a urethroplasty database and concluded that patients with failed realignment or urethrotomies had more restenosis and worse satisfactory rates after urethroplasty (27). One could also state that failed realignment cases probably were those cases with more severe trauma and tissue damage. This demonstrates how difficult it is to compare different trauma patients. Furthermore, it is difficult to retrieve the definition of failed realignment. It can be that realignment was not possible and aborted. In this case, we hypothesize that it will not negatively influence further outcomes. However it is possible that a failed realignment was a wrong realignment, where the urethral catheter was not inserted in the bladder but in the pelvic hematoma. This mistake might be recognised in a delayed fashion if the suprapubic catheter was also maintained. We hypothesize that this wrong realignment can have a negative further impact. However, with endoscopic realignmet, direct visual control should minimize the risk of 'wrong' realignment.

There is too much publication bias to conclude which patients will have the most benefit from EER. Only one abstract (11) and one NCS paper excluded partial injuries (18) and they report respectively a 100% and a 53.3% failure rate. Kim et al. published 7/15 patients requiring no further treatment after EER. These results are especially remarkable because most patients had concomitant bladder or other organ injuries indicating severe trauma. The other papers have included partial injuries and so their results could be accounted on this. It seems common sense that those partial injuries (in stable patients) would be the ideal candidates for EER but subgroup analysis couldn't be performed to prove this statement.

This review revealed that 1 out of 2 recurrences after EER can be treated with endoscopic incision. These findings are in line with those of Moudouni et al (16). We cannot confirm whether the subsequent urethroplasty in the other recurrences was more difficult or less successful. Tausch concluded that endoscopic realignment cases had more re-interventions and that time to

definitive resolution was longer than in patients with cystostomy and delayed urethroplasty (6). They analysed only patients that were referred for urethroplasty. We regarded this a major confounder because previous treatment probably failed. But we realise that repeated urethrotomies and other manipulations could result in a longer time until definitive resolution. For some patients this could be bothersome and a disadvantage of endoscopic treatment. In which way this could influence patient satisfaction, is an interesting question that needs to be investigated.

No major differences between groups were observed in terms of erectile dysfunction and incontinence. Therefore, it can be assumed that these complications are merely related to the severity of the injury itself rather than the method of initial management (15). Erectile dysfunction is observed in 34% of patients with pelvic fracture related urethral injury in the systematic review from Blashko et al (28). They also concluded that lower dysfunction rates in the endoscopic realignment group were probably due to less severe injury or differences in reporting erectile dysfunction.

A systematic review of literature was carried out but no randomised clinical trials were found. This is not unsurprising as it is difficult to conduct multicentre RCTs in the setting of trauma. Trauma is by definition an unexpected event. This results in patients transferred as an urgency to the nearest hospital instead of the most competent. Transfer to the appropriate department and planning of the EER can be hindered by logistic limitations. To date no well-designed comparative trials have been conducted. Some papers claim to be comparative but a rigorous evaluation of the methods revealed that control groups consisted of failed endoscopic realignment. Others had a serious selection bias: cases with associated injuries or a severe distraction defect were included in the control group (i.e. suprapubic cystostomy and delayed urethroplasty). Therefore it is very likely that the urethral trauma has been more extensive then in patients with successful endoscopic realignment. Again comparing results of these groups can be misleading. This was also one of the reasons why a meta-analysis and further statistical analysis was not performed. In general NCS were more rigorous concerning inclusion and exclusion criteria. The highest level of evidence of included series was level 3 (29). This is the major limitation of this review.

From this review of the existing literature it is clear that a considerable number of urethral ruptures by pelvic fracture can be healed by EER, but others may be harmed by the procedure or it may be less cost effective. Based on the basic principles of wound healing and a few animal experiments one can expect that EER is most successful when the distance between both disrupted ends is short. This is the majority of cases. An attempt to EER can be advocated in the first 2 weeks after trauma in these patients if their condition allows.
To develop a better view on the right indications of EER we should develop multicentre observational studies, in which all attempts, failures and successes of EER are registered.

Conclusion:

This systematic review revealed there are no well conducted comparative studies of EER versus cystostomy and delayed urethroplasty. The mainstay of reports are case series with a high degree of bias and heterogeneity. EER might resolve the urethral injury in about half of PUIs and this supports an attempt of EER when the patient is stabilised in the first 2 weeks after trauma. Because of the many possible publication bias we could not identify those patients, which will benefit of the procedure or will be possibly harmed.

Author contributions:

Elshout PJ: Protocol development, Data collection or management, Data analysis, Manuscript writing/editing
Erik Veskimae: Data collection or management, Data analysis, Manuscript writing/editing
Nicolaas Lumen: Protocol development, Data analysis, Manuscript writing/editing
Steven MacLennan: Data analysis, Manuscript writing/editing
Cathy Yuan: Data collection or management
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Franklin Kuehhas: Protocol development
N.D. Kitrey: Protocol development
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D.J. Summerton: Protocol development

Conflict of Interest: This systematic review is conducted on behalf of the EAU trauma guideline panel.

Ethical Standards: This systematic review is written and submitted according to the Guidelines of the Committee on Publication Ethics (COPE).

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References

1. Bjurlin MA, Fantus RJ, Mellett MM, Goble SM. Genitourinary injuries in pelvic fracture morbidity and mortality using the National Trauma Data Bank. J Trauma. 2009;67(5):1033-9.
2. Koraitim MM. Predictors of erectile dysfunction post pelvic fracture urethral injuries: a multivariate analysis. Urology. 2013;81(5):1081-5.
3. Leddy LS, Vanni AJ, Wessells H, Voelzke BB. Outcomes of endoscopic realignment of pelvic fracture associated urethral injuries at a level 1 trauma center. Journal of Urology. 2012;188(1):174-8.
4. Moudouni SM, Patard JJ, Manunta A, Guiraud P, Lobel B, Guille F. Early endoscopic realignment of post-traumatic posterior urethral disruption. Urology. 2001;57(4):628-32.
5. Mouraviev VB, Coburn M, Santucci RA. The treatment of posterior urethral disruption associated with pelvic fractures: Comparative experience of early realignment versus delayed urethroplasty. Journal of Urology. 2005;173(3):873-6.
6. Tausch TJ, Morey AF. The case against primary endoscopic realignment of pelvic fracture urethral injuries. Arab Journal of Urology. 2015;13(1):13-6.
7. Lumen N, Hoebeke P, De Troyer B, Ysebaert B, Oosterlinck W. Perineal Anastomotic Urethroplasty for Posttraumatic Urethral Stricture With or Without Previous Urethral Manipulations: A Review of 61 Cases With Long-Term Followup. Journal of Urology. 2009;181(3):1196-200.
8. Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, et al. Evaluating non-randomised intervention studies. Health Technol Assess. 2003;7(27):iii-x, 1-173.
9. Viswanathan M, Nerz P, Dalberth B, Voisin C, Lohr KN, Tant E, et al. Assessing the impact of systematic reviews on future research: two case studies. J Comp Eff Res. 2012;1(4):329-46.
10. Dalziel K, Round A, Stein K, Garside R, Castelnuovo E, Payne L. Do the findings of case series studies vary significantly according to methodological characteristics? Health Technol Assess. 2005;9(2):iii-iv, 1-146.
11. Abdalla MA, Ibrahim TM, Abdel Latif AM. Initial management of pelvic fracture urethral distraction injury: Urethral realignment versus suprapubic tube. European Urology, Supplements. 2015;Conference:30th Annual Congress of the European Association of Urology, EAU15 Madrid Spain. Conference Start: 20150320 Conference End: 4. Conference Publication: (var.pagings). 14 (2) (pp e340).
12. El Kady A, El Ghoneimy M, Rasool MA, Hamid MA, Badawy H. Outcome of primary urethral realignment in the management of posterior urethral disruption. Journal of Urology. 2014;Conference:2014 Annual Meeting of the American Urological Association, AUA Orlando, FL United States. Conference Start: 20140516 Conference End: 21. Conference Publication: (var.pagings). 191 (4 SUPPL. 1) (pp e35).
13. Johnsen NV, Dmochowski RR, Mock S, Reynolds WS, Milam DF, Kaufman MR. Primary Endoscopic Realignment of Urethral Disruption Injuries--A Double-Edged Sword? J Urol. 2015;194(4):1022-6.
14. Hadjizacharia P, Inaba K, Teixeira PGR, Kokorowski P, Demetriades D, Best C. Evaluation of immediate endoscopic realignment as a treatment modality

for traumatic urethral injuries. Journal of Trauma Injury, Infection and Critical Care. 2008;64(6):1443-9.
15. Ku JH, Jeon YS, Kim ME, Lee NK, Park YH. Comparison of long-term results according to the primary mode of management and type of injury for posterior urethral injuries. Urologia Internationalis. 2002;69(3):227-32.
16. Moudouni S, Tazi K, Koutani A, ibn Attya A, Hachimi M, Lakrissa A. Comparative results of the treatment of post-traumatic ruptures of the membranous urethra with endoscopic realignment and surgery. Progres en urologie : journal de l'Association francaise d'urologie et de la Societe francaise d'urologie. 2001;11(1):56-61.
17. Abdelsalam YM, Abdalla MA, Safwat AS, Elganainy EO. Evaluation of early endoscopic realignment of post-traumatic complete posterior urethral rupture. Indian Journal of Urology. 2013;29(3):188-92.
18. Kim FJ, Pompeo A, Sehrt D, Molina WR, Mariano Da Costa RM, Juliano C, et al. Early effectiveness of endoscopic posterior urethra primary alignment. Journal of Trauma and Acute Care Surgery. 2013;75(2):189-94.
19. Shrestha B, Baidya JL. Early endoscopic realignment in posterior urethral injuries. Journal of Nepal Health Research Council. 2013;11(23):62-5.
20. Sofer M, Mabjeesh NJ, Ben-Chaim J, Aviram G, Bar-Yosef Y, Matzkin H, et al. Long-term results of early endoscopic realignment of complete posterior urethral disruption. J Endourol. 2010;24(7):1117-21.
21. Boulma R, Kallel Y, Sellami A, Gargouri MM, Rhouma SB, Chlif M, et al. Endoscopic realignment versus delayed urethroplasty in the management of post traumatic urethral disruption: Report of 30 cases. Tunisie Medicale. 2013;91(5):332-6.
22. Leddy L, Wessells H, Voelzke B. Outcomes of endoscopic realignment of posterior urethral injuries at a Level 1 trauma center. Journal of Urology. 2011;Conference:2011 Annual Meeting of the American Urological Association, AUA Washington, DC United States. Conference Start: 20110514 Conference End: 9. Conference Publication: (var.pagings). 185 (4 SUPPL. 1) (pp e4).
23. Lumen N, Kuehhas FE, Djakovic N, Kitrey ND, Serafetinidis E, Sharma DM, et al. Review of the current management of lower urinary tract injuries by the EAU trauma guidelines panel. European Urology. 2015;67(5):925-9.
24. Weaver RG, Schulte JW. Experimental and clinical studies of urethral regeneration. Surg Gynecol Obstet. 1962;115:729-36.
25. Barrett K, Braga LH, Farrokhyar F, Davies TO. Primary realignment vs suprapubic cystostomy for the management of pelvic fracture-associated urethral injuries: A systematic review and meta-analysis. Urology. 2014;83(4):924-9.
26. Singh BP, Andankar MG, Swain SK, Das K, Dassi V, Kaswan HK, et al. Impact of Prior Urethral Manipulation on Outcome of Anastomotic Urethroplasty for Post-traumatic Urethral Stricture. Urology. 2010;75(1):179-82.
27. Culty T, Boccon-Gibod L. Anastomotic urethroplasty for posttraumatic urethral stricture: previous urethral manipulation has a negative impact on the final outcome. Journal of Urology. 1374;177(4):1374-7.
28. Blaschko SD, Sanford MT, Schlomer BJ, Alwaal A, Yang G, Villalta JD, et al. The incidence of erectile dysfunction after pelvic fracture urethral injury: A systematic review and meta-analysis. Arab Journal of Urology. 2015;13(1):68-74.

29. Phillips B. GRADE: levels of evidence and grades of recommendation. Arch Dis Child. 2004;89(5):489.

Appendix 1: Search strategy

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <March 2016>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to April 27, 2016>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>, Embase <1974 to 2016 April 28>

Search Strategy:

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1 exp urethra injury/

2 ((urethra* or lower urinary tract or LUT) adj5 (trauma or traumas or traumatic or injury or injuries or lesion* or rupture or laceration* or avulsion* or contusion* or damage*)).tw.

3 exp urethra stricture/ or (Urethral adj3 (stricture* or stenosis or stenosis or narrow* or disruption*)).tw.

4 or/1-3

5 exp pelvis fracture/

6 ((pelvic or pelvis) and (fracture or fractures)).tw,kw.

7 posterior.tw,kw.

8 or/5-7

9 4 and 8

10 exp endoscopic surgery/

11 (endoscop* or video assisted).tw,kw.

12 realignment.tw.

13 exp urethral catheter/

14 (((urethral or transurethral) and (catheter or catheters or catheterisation or catheterization)) or Felxima or VaPro).tw.

15 exp urinary diversion/

16 ((suprapubic or urinary) adj5 (diversion* or catheterisation or catheterization)).tw.

17 exp cystostomy/ or cystostom*.tw.

18 or/10-17

19 9 and 18

20 (Systematic review or meta-analysis).tw,kw. or Meta analysis/ or "systematic review"/

21 (Medline or Embase or Cochrane or Pubmed or placebo*).ab.

22 random*.mp.

23 (randomized controlled trial or controlled clinical trial).pt.

24 or/20-23

25 9 and 24

26 19 or 25

27 women/ not (men/ or (men or male).tw,kw.)

28 26 not 27

29 children/ not adult/

30 28 not 29

31 case report/ or case reports/ or case report.ti.

32 30 not 31

33 remove duplicates from 32

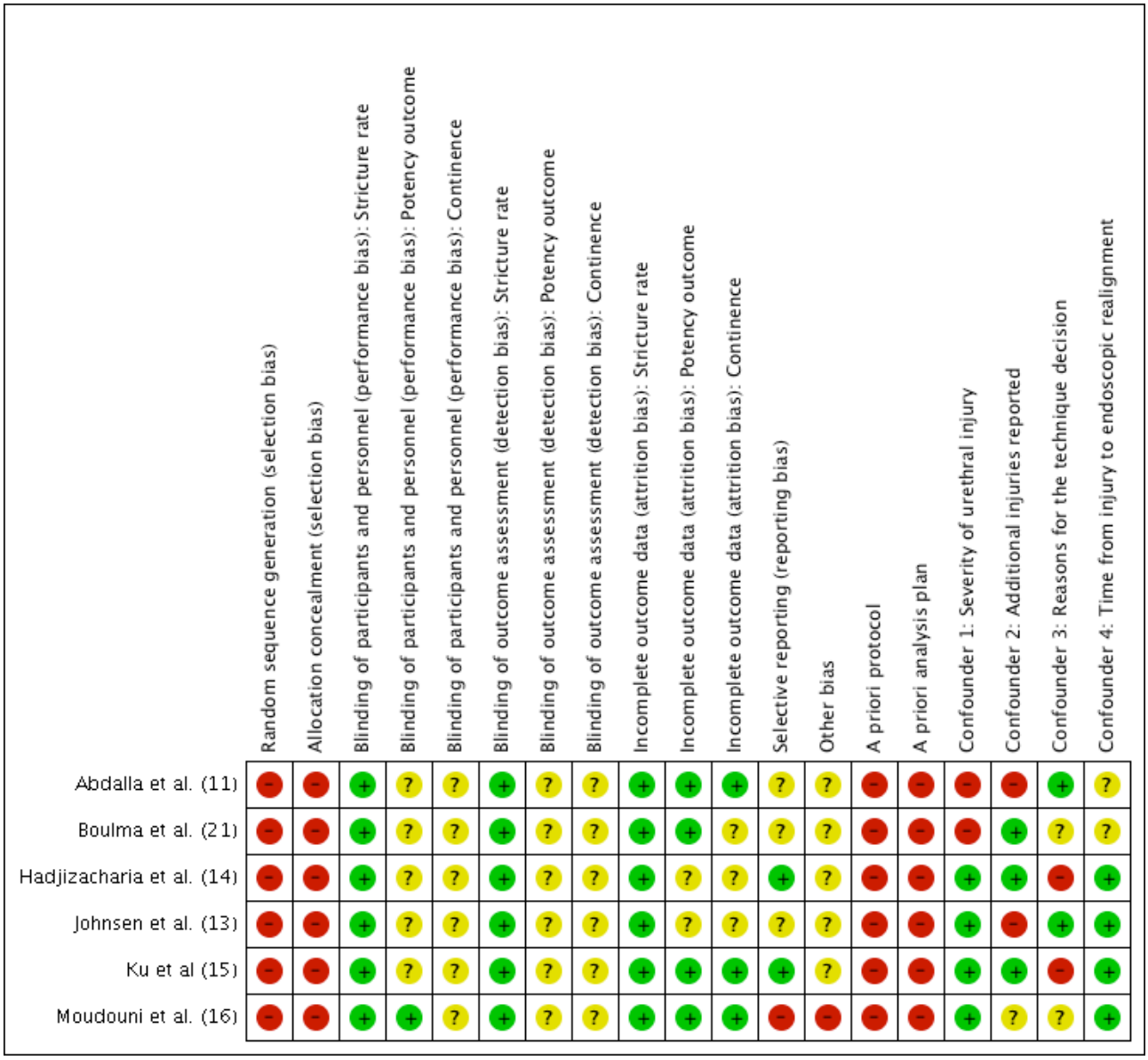

Figure 1. Risk of bias summary of non-randomised comparative studies (NRCS).

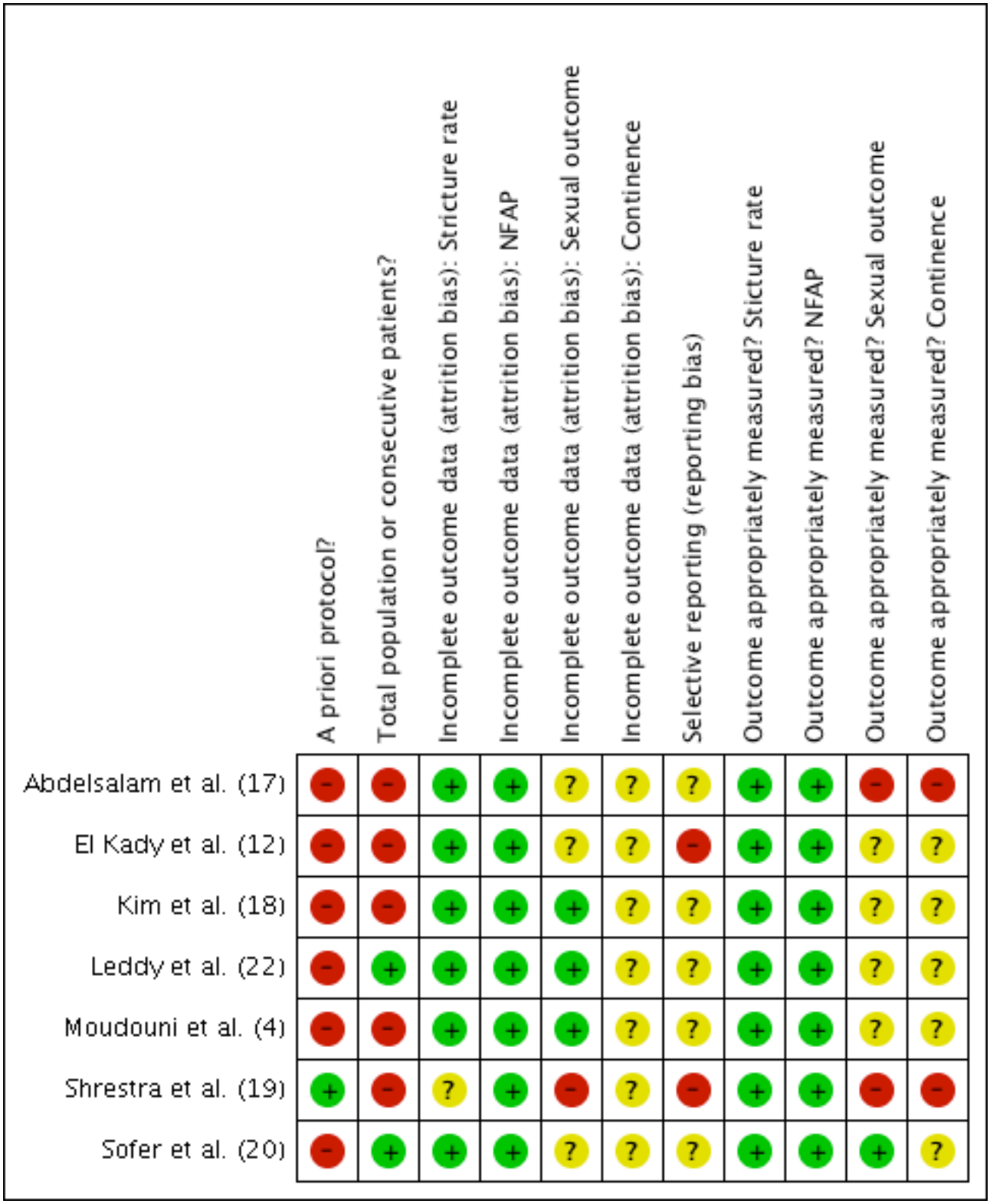

Figure 2. Risk of bias summary for non-comparative series (NCS). NFAP- need for auxillary procedure.

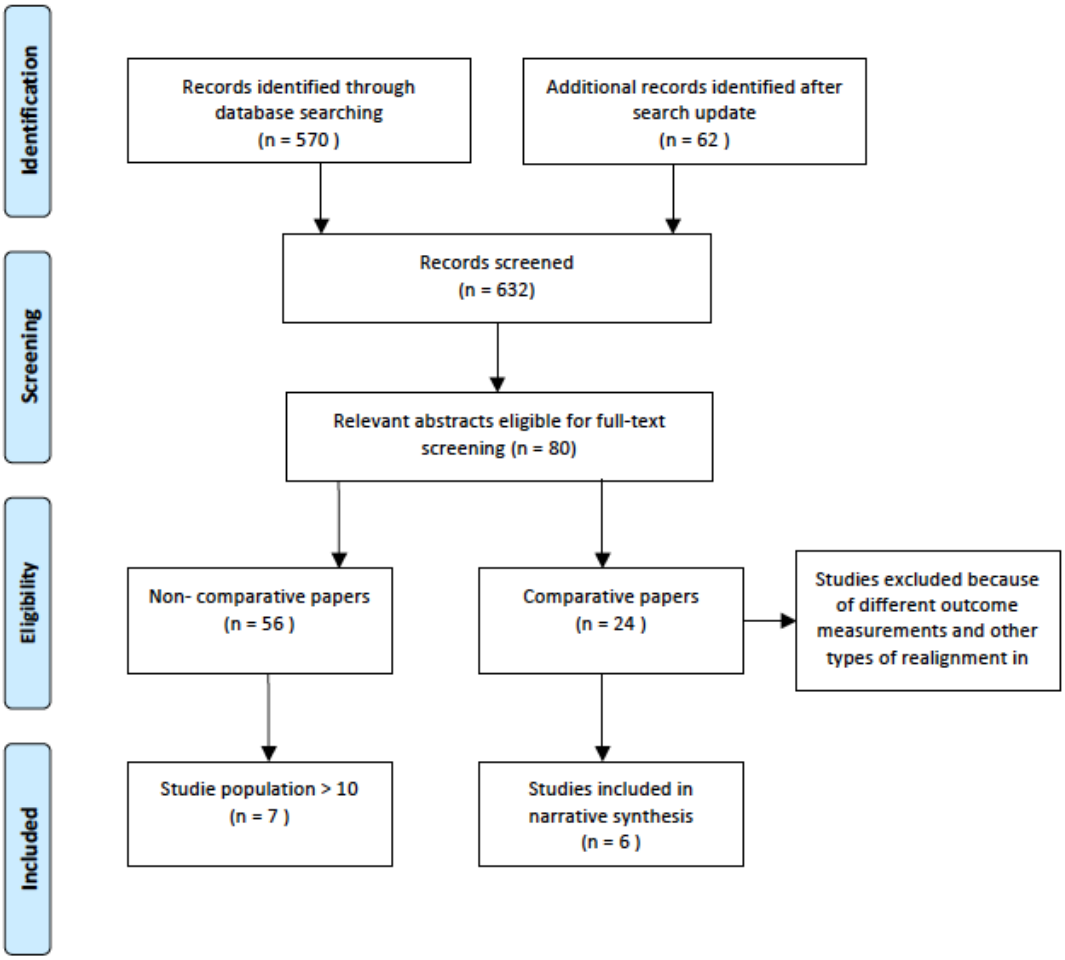

Figure 3 shows the PRISMA flow diagram of the literature search.

Tables

Table 1 Characteristics of included studies

Study ID	Year	Comparison	Study Design	Recruitment period	N patients: intervention	N patients : control	Outcomes reported	Follow up (months)
Abdalla (11)	2015	Y	Prospective NRCS	10/2009- 7/2013	16	16	SR, NFAP, UI, ED	12-30m
Boulma (21)	2013	Y	Retrospective NRCS	2/2002-3/2009	20	10	SR, NFAP, UI, ED	21
Hadjizacharia (14)	2008	Y	Proscpective NRCS	9/2000- 9/2006	14	7	SR, NFAP	7 (0-21)
Ku (15)	2002	Y	Retrospective NRCS	1990-1999	35	20	SR, NFAP, UI, ED	63.4 (19-110)
Moudouni (16)	2001	Y	Retrospective NRCS	1989- 1998	30	10	SR, NFAP, UI, ED	34 (12-72)
Johnsen (13)	2015	Y	Retrospective NRCS	1/2000-6/2014	27	14	SR, NFAP, UI, ED	40 (1-152)
Shrestha (19)	2013	N	Prospective NCS	11/2007-10/2010	20		SR, NFAP, UI, ED	6 (3-6)
Abdelsalam (17)	2013	N	Retro- and prospective NCS	5/2004-4/2009	41		SR, NFAP, UI, ED	NR
Moudouni (4)	2001	N	Retrospective NCS	4/1987-1999	29		SR, NFAP, UI, ED	83 (34-120)
El Kady (12)	2014	N	Prospective NCS	7/2011-5/2013	15		SR, NFAP, UI, ED	NR
Sofer (20)	2010	N	Retrospective NCS	NR	11		SR, NFAP, UI, ED	51 (24-84)
Leddy (22)	2012	N	Retrospective NCS	1/2004-7/2010	19		SR, NFAP, UI, ED	40 (10-80)
Kim (18)	2013	N	Retrospective NCS	1/2005-4/2012	15		SR, NFAP, UI, ED	31.8

NRCS: non randomised comparative studies

NCS: non comparative studies

NR: not reported

Table 2: Outcomes (stricture rates)

Study ID	stricture rate (n,%)	
	SPS + DU	EER
Abdalla (11)	6 (37.5%)	16 (100%)
Boulma (21)	3 (30%)	7 (35%)
Hadjizacharia (14)	7 (100%)	2 (14.3%)
Ku (15)	13 (65%)	21 (60%)
Moudouni (16)	4 (40%)	8 (26.6%)
Johnsen (13)	14 (100%)	17(63%)
Shrestha (19)		2(25 %)
Abdelsalam (17)		23(56%)
Moudouni (4)		12 (41%)
El Kady (12)		9 (60%)
Sofer (20)		5(45.5%)
Leddy (22)		14 (73.7%)
Kim (18)		8 (53%)

table 3. Functional outcomes

Study ID	incontinence outcomes (n,%)		impaired potency (n,%)	
	SPS + DU	ER	SPS + DU	ER
Abdalla (11)	2(12.5%)	0	4(25%)	2(12.5%)
Boulma (21)	0	0	2 (20%)	1 (5%)
Hadjizacharia (14)	NR	NR	NR	NR
Ku (15)	2 (10%)	3 (8.6%)	5 (25%)	10 (28.6%)
Moudouni (16)	1 (10%)	0	4 (40%)	6 (20%)
Johnsen (13)	1 (9.1%)	2 (8.7%)	10 (90.1%)	18 (78.3%)
Shrestha (19)		0		1 (5%)
Abdelsalam (17)		3(7%)		13(32%)
Moudouni (4)		0		4 (13.7%)
El Kady (12)		0		0
Sofer (20)		0		6 (55%)
Leddy (22)		0		4 (21%)
Kim (18)		3(20%)		7(47%)

Table 4: Need for auxiliary procedures

Study ID	NFAP (n,%)			
	SPS + DU		EER	
	endoscopic	open	endoscopic	open
Abdalla (11)	2 (12.5%)	2(12.5%)	8 (50%)	8(50%)
Boulma (21)	2 (20%)	1 (10%)	4 (20%)	3 (15%)
Hadjizacharia (14)	NR	7 (100%)	2 (14.3%)	0 (0%)
Ku (15)	8 (40%)	5 (25%)	15 (42.9%)	6 (17.1%)
Moudouni (16)	4 (40%)	0	7 (23.3%)	1 (3.3%)
Johnsen (13)	0	11(77%)	10(37%)	7(26%)
Shrestha (19)			2 (25%)	0 (0%)
Abdelsalam (17)			15 (36.6%)	8 (19.5%)
Moudouni (4)			10 (34.5%)	2 (6.9%)
El Kady (12)			4 (26.6%)	5(31%)
Sofer (20)			2 (18.2%)	3 (27.3%)
Leddy (22)			3 (15.8%)	11(57.9%)
Kim (18)			6(40%)	?

NRCS: non randomised comparitave studies
NCS: non comparative studies