Is non-operative management the best first-line option for high-grade renal trauma? A systematic review.

AUTHORS / COLLABORATORS (Trauma EAU GUIDELINE PANEL):

Arunan Sujenthiran, Department of Urology, St George's Healthcare NHS Trust, London, UK.

Elshout Pieter Jan, Department of Urology, Ghent University Hospital, Ghent, Belgium.

Erik Veskimae, Department of Urology, Tampere University Hospital, Tampere, Finland.

Steven MacLennan, Academic Urology Unit, University of Aberdeen, Scotland, United Kingdom.

Yuhong Yuan, Department of Medicine, Health Science Centre, McMaster University, Hamilton, Ontario, Canada.

Efraim Serafetinidis Department of Urology, Asklipieion General Hospital, Athens, Greece.

D.M.Sharma Department of Urology, St George's Healthcare NHS Trust, London, UK.

N.D. Kitrey Department of Urology, Chaim Sheba Medical Centre, Tel-Hashomer, Israel

N. Djakovic, Department of Urology, Muhldorf General Hospital, Muhldorf am Inn, Germany

N.Lumen, Department of Urology, Ghent University Hospital, Ghent, Belgium

FE.Kuehhas, London Andrology Institute, London, UK

D.J. Summerton, University Hospitals of Leicester NHS Trust, Leicester, UK

Abstract

Context:

The management of high-grade (grade IV-V) renal injuries remains controversial. There has been an increase in the use of non-operative management (NOM) but limited data exists comparing outcomes to open surgical exploration.

Objective: To conduct a systematic review to determine if NOM is the best first-line option for high-grade renal trauma in terms of safety and effectiveness.

Evidence acquisition:

Medline, Embase and Cochrane Library were searched for all relevant publications, without time or language limitations. The primary harm outcome was overall mortality and the primary benefit outcome was renal preservation rate. Secondary outcomes included length of hospital stay and complication rate. Single-arm studies were included as there were few comparative studies. Only studies with more than fifty patients were included. Data were narratively synthesised in light of methodological and clinical heterogeneity.

Evidence synthesis:

Seven non-randomized comparative and four single-arm studies were selected for data-extraction. 787 patients were included from the comparative studies with 535 patients in the NOM group and 252 in the open surgical exploration group. A further 825 patients were included from single-arm studies. Results from comparative studies: Overall mortality: NOM (0-3%), open surgical exploration (0-29%); renal preservation rate: NOM (84-100%), open surgical exploration (0-82%); complication rate: NOM (5-32%), open surgical exploration (10-76%). Overall mortality and renal preservation rate were significantly better in the NOM group whereas there was no statistical difference with regard to complication rate. Length of hospital stay was found be significantly reduced in the NOM group. Patients in the open surgical exploration group were more likely to have grade V injuries, have a lower systolic blood pressure and higher injury severity score on admission.

Conclusion:

No randomized controlled trials were identified and significant heterogeneity existed with regard to outcome reporting. However, NOM appeared to be safe and effective in a stable patient with a higher renal preservation rate, a shorter length of stay and a comparable complication rate to open surgical exploration. Overall mortality was higher in the open surgical exploration group though this was likely due to selection bias.

Patient summary:

The data of this systematic review suggest NOM continues to be favoured to surgical exploration in the management of high-grade renal trauma whenever possible. However, comparisons between both interventions are difficult as patients who have surgery are often more seriously injured than those managed non-operatively, and existing studies do not report on outcomes consistently.

Keywords:

High-grade renal injury, surgical exploration, conservative, non-operative management

Total Word count: 3956

1. INTRODUCTION

The kidney is the most commonly injured genito-urinary organ and occurs in approximately 1-5% of all trauma cases (1, 2). Renal injury can be classified as blunt or penetrating according to mechanism and by grade according to the American Association for the Surgery of Trauma (AAST) organ injury severity scale (Table 1) (3). Most cases of blunt renal trauma are low-grade injuries (grade I-III) and can be managed conservatively (4). There appears to be a trend towards the management of high-grade (IV-V) blunt renal trauma non-operatively, however strong comparative evidence is lacking in this cohort. Penetrating renal injuries have traditionally been managed with open surgical exploration though some studies have reported favourable outcomes with non-operative management (NOM), even in high-grade penetrating injuries (5, 6).

This shift towards NOM has been driven by rapid uptake of minimally-invasive techniques such as angioembolisation; improved clinical pathways; enhanced critical care treatment for trauma patients; readily accessible CT-imaging and a validated renal injury scoring system. Despite these advances, the optimal management of high-grade renal trauma still remains controversial with those supporting open surgical exploration reporting fewer complications (7-10) whereas advocates of NOM highlighting that conservative and minimally-invasive techniques reduce the inherent risk of nephrectomy and subsequent deterioration of renal function (11-16).

Current guidelines on management of high-grade renal trauma are based on retrospective comparative studies and single-arm case series' (17, 18). Existing reviews have not focused on high-grade injury and most were not conducted systematically (19) (4, 20). A systematic review of current evidence is required to establish whether the outcomes of open surgical exploration and NOM are comparable.

The objective of this systematic review was to compare NOM which encompasses angioembolisation, ureteric stenting and conservative management against open surgical exploration, in the management of high-grade renal injuries.

2. EVIDENCE ACQUISITION

The systematic review protocol was registered with PROSPERO. (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016035255)

2.1 Search strategy and selection criteria

The review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA)(21). Studies (January 1, 1946, to June 1, 2016) were identified by highly sensitive searches of electronic databases (Medline, Medline In–Process, Embase, Cochrane library databases). The initial literature search was performed in April 24 2015 and an updated search performed in June 03 2016. The search strategy is described in detail in Supplementary File 1. Animal studies, children, case reports and letters were excluded.

2.2 Types of study design included

There was no restriction on types of study design. Single-arm studies were included as there were only a small number of non-randomized comparative studies. All studies required a minimum of 50 patients and there were no restrictions on language or date of publication.

2.3 Types of participants

The study population was adults (≥18 years) with high-grade (grade IV to V according to AAST classification) CT-confirmed blunt and penetrating injuries.

2.4 Types of Intervention

The control group was open surgical exploration. The experimental group consisted of patients who received NOM which included conservative (supportive management only); minimally invasive intervention (angioembolisation, ureteric stent insertion, percutaneous drainage); “Package of care” involving step-wise approach (i.e. starting with conservative, followed by minimally invasive and/or surgical exploration if necessary).

2.5 Types of outcome measures

The primary harm outcome was mortality (overall and renal trauma-related). The primary benefit outcome was renal preservation (i.e. kidney removal or complete embolization versus preservation). Secondary outcomes included complications and length of hospital stay. Identified confounders included systolic blood pressure, injury severity score, renal function, blood loss, re-intervention rate and development of hypertension.

2.6 Data collection and data extraction

Following de-duplication of abstracts, two reviewers (A.S. and P.JE.) screened all abstracts and full-text articles independently. Disagreement was resolved by a third party (E.V.). References cited in all full-text articles were also assessed for additional relevant articles. A standardized data-extraction form was developed a priori to collect information on study design, renal injury details, patient characteristics and outcomes measures.

2.7 Risk of bias in individual studies

Two reviewers (A.S. and P.JE.) assessed the "risk of bias" of each included study independently. Any disagreements were resolved by discussion or by consulting a third review author.

Risk of bias in non-randomized comparative studies was evaluated using a modified version of a recommended tool used in the Cochrane Handbook for Systematic Reviews of Interventions. This was a pragmatic approach based on methodological literature (22, 23) and included an additional domain to assess the risk of confounding bias. A list of the 5 most important potential confounders for harm and benefit outcomes was developed a priori with clinical content experts (European Association Urology (EAU) Trauma guideline panel). The confounding factors were: Type of injury (blunt/penetrating), associated injuries, haemodynamic stability of patient, patient fitness and available interventions. This approach is detailed in our study protocol(24)

For single-arm studies, risk of attrition bias, whether an a priori protocol was available (indicating prospective design) and selective outcome reporting were assessed. External validity was also addressed by assessing whether study participants were selected consecutively or representative of a wider patient population. This too is a pragmatic approach informed by methodological literature (25, 26).

2.8 Statistical analysis

Meta-analysis could not be performed due to methodological and clinical heterogeneity of the included studies. Therefore a narrative synthesis was performed instead (https://www.york.ac.uk/crd/guidance/). Forest plots of risk difference were constructed for comparative studies for three outcome measures (mortality, complications and renal preservation). This was not done for length of stay since standard deviations were not consistently reported in the included studies. Statistical methods of assessing heterogeneity were not feasible therefore potential reasons for heterogeneity were explored in relation to population differences between, outcome definitions as well as the methods used to report outcomes. Planned formal subgroup analyses were not possible due to inclusion of non-randomized controlled studies. Therefore, any subgroup differences were discussed narratively to explore potential effect size differences. The 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 also not performed due to the inclusion of non-randomized comparative studies.

3. EVIDENCE SYNTHESIS

3.1. Quality of the studies

A total of 1,375 studies were identified by the literature search and two reviewers screened all study abstracts independently. Of these, 54 articles were selected for full-text screening and 11 studies (7 non-randomized comparative studies, 4 single-arm studies) were eligible for inclusion (Figure 1). The quality of studies was assessed as described above. Risk of bias is summarized for comparative studies in Figure 2 and for single-arm studies in Figure 3. Overall there was a high risk of bias across both comparative and single-arm studies. Study design was retrospective for all studies. Although some studies prospectively inputted data into database, they were still retrospective in study design (27-31).

3.2 Study details

Three of the comparative studies included penetrating and blunt injuries and four only reported on blunt injuries. All single-arm studies reported on patients who had received NOM for blunt injuries. The recruitment period ranged from 1981-2015 and studies were published from 2006-2015. Most studies were performed at trauma centres although three were from a general hospital (29, 32, 33). Most studies were performed in a single-centre. One study was performed across two centres, another across 12 and a multi-centre study used data from 331 units (National Trauma Database Bank).

3.2.1 Participants

In total, 787 patients were included from the comparative studies with 535 patients in the NOM group and 252 in the open surgical exploration group. Four studies included both grade IV and V injuries (28, 30, 32, 34) and two studies only included grade IV injuries (29, 35). Sarani et al. classified grade III to V as high-grade injuries with a mean grade injury of 4 and 3.9 in the NOM and open surgical exploration group, respectively. Apart from grade, there was no strict exclusion criteria stated in most selected studies. One study excluded patients below fifteen years old and those who died before arrival to the hospital. Sarani et al. excluded patients who had a laparotomy without pre-operative CT.

Allocation to the different treatment groups was not randomized in any of the studies. Six studies opted for open surgical exploration if the patient was haemodynamically unstable at presentation and/or was not responding to resuscitation (28-30, 32, 34, 35). Other indications for open surgical exploration in these studies included peritonitis, failed embolization, persistent bleeding, an expanding or pulsatile haematoma, and polytrauma patients in haemorrhagic shock. One study did not specify indications for open surgical exploration (36). Three studies followed an institutional first-line NOM protocol (28, 30, 31) with one study explicitly stating that even unstable patients should receive angioembolisation as first line therapy (30).

825 patients were included from single-arm studies with blunt injuries and received NOM. Three studies included only grade IV injuries (31, 37, 38) and one study included grade III-V studies (33). Of these studies only Long et al. stated the use of a first line non-operative protocol whereby NOM, including angioembolisation in haemodynamically unstable patients, was preferred and open surgical exploration was only performed if immediate resuscitation failed (31). There was a lack of consistency with regard to which outcomes were reported and how they were measured in comparative and single-arm studies. Only three of the comparative studies reported on all four study outcome measures (29, 32, 34)

3.3. Outcomes

3.3.1. Mortality

Five comparative studies reported on overall mortality (29, 30, 32, 34, 36). A significant difference in overall mortality existed in favour of NOM in two studies (34, 36) (Table 4). Van der Wilden et al. reported 3 (2%) patients with renal-related deaths but did not compare rates between NOM and open surgical exploration. Buckley and Shoobridge both reported that both deaths in the NOM group were not renal trauma–related therefore there was no difference found between groups in these two studies with regard to renal-trauma related mortality. Only one case series reported overall mortality and it was 21% in the NOM group (37). No included studies reported the specific time-to-death following renal injury. 4 out of the 5 studies that reported on overall mortality, used in-hospital mortality (30, 32, 34, 36).

3.3.2. Renal Preservation

Four comparative studies provided data on renal preservation (28, 29, 32, 34). In all four studies, renal preservation rate was higher in NOM (range 84%- 100%) compared to open surgical exploration (range 0%-82%) and in three of these studies there was a significant risk difference in favour of NOM (Table 4).

3.3.3 Complications

Six comparative studies provided data on complications. In terms of absolute rates, four studies found a higher complication rate in NOM groups and two studies found patients who underwent open surgical exploration had a higher complication rate. However, only two studies reported a significant difference between groups and showed a lower rate in NOM (30) (Table 4). The 3 studies that reported lower complication rates in the open surgical exploration cohort showed no statistical difference compared to NOM.

Although all studies specifically reported on renal-related complications, there was a large amount of heterogeneity in their classification and reporting. Only one study used a recognized grading system (Clavien-Dindo) (30). Common complications in the NOM group included fever, haematuria, acute kidney injury and non-resolving urinomas requiring either ureteric stenting or percutaneous drainage. In the open surgical exploration group, complications included wound infection, urinary tract infection and perinephric abscess requiring drainage.

No included studies reported on exact time-to-event for complications, though 4 out of 5 comparative studies (30, 32, 34-36) and 3 out of 4 single-arm studies (31, 33, 38) which reported on complications used short-term in-hospital complications.

3.3.4 Length of Stay

Six studies reported on length of stay and across these studies it was longer in open surgical exploration group (24 days) compared to NOM group (17 days). This was the trend in all the studies and two studies found there to be a statistically significant difference between the two interventions (32, 35).

Confounders

Some confounders developed a priori including patient fitness and available interventions were not consistently reported in studies. Data was available on grade of injury, systolic blood pressure on admission and ISS in two or more studies (Table 5). There was a higher proportion of grade IV injuries in the NOM group and a higher proportion of grade V injuries in the open surgical exploration group. Two studies both found the mean systolic blood pressure to be significantly lower in the open surgical exploration group than NOM group. ISS was available in two studies and was also found to be significantly higher in the open surgical exploration group than NOM group.

Subgroup analysis:

Blunt versus penetrating

Three studies included penetrating high-grade injuries in their population cohort. One study found that three injuries were managed successfully using conservative measures and the one patient who underwent open surgical exploration survived but required a nephrectomy (30). Two studies further divided penetrating injuries into stab and gun-shot injuries (29, 35). Both studies found that patients with gunshot injuries were the most likely to undergo surgical exploration and subsequent nephrectomy compared to stab and blunt injuries.

Isolated Renal Injuries

One study (29) reported on the outcomes of 43 patients who sustained isolated grade IV renal injuries. Surgical exploration was performed in 18 of 43 patients with a renal salvage rate of 83%. The remaining 25 patients were managed non-operatively with a renal salvage rate of 88%. Average hospital stay was similar in both groups and transfusion rates were higher in the surgical exploration group.

3.4. Discussion

This is the first systematic review to use transparent and rigorous methodology to compare NOM and open surgical exploration in the management of high-grade renal trauma. In many units, first-line non-operative protocols have been implemented ahead of acquiring objective evidence due to the difficulty in conducting adequately powered randomized controlled trials. Nonetheless, this study focuses on the best available studies with population sizes greater than fifty patients, and appraises the risk of bias in a transparent way, to assess important outcomes that may not be apparent when reviewed in isolation.

3.4.1 Principal Findings

Mortality

Overall mortality was found to be worse in the open surgical exploration group compared to NOM group albeit in three out of 5 comparative studies with small sample sizes and low event rates. Patients in the open surgical exploration group had higher rate of grade V injuries, higher ISS scores and lower systolic blood-pressure values on admission. Both ISS scores and lower systolic blood pressure values on admission have been shown to be predictors of increased mortality following trauma (39, 40). Therefore, this finding, together with selection bias present in most included studies whereby the most ‘unstable’ patients underwent open surgical exploration, could explain the difference in overall mortality between both groups. There was no evidence of a difference in renal-trauma related mortality between the two interventions in two studies (29, 30).

Complications

Included studies rarely defined and reported complications in a consistent manner. Comparisons can still be made between interventions in the same study. Although three studies reported increasing complication rates in the NOM group, these were not statistically different. Only one study showed a statistical difference and graded complications according to the Clavien-Dindo classification (30). Given the substantial heterogeneity it is difficult to conclude that a higher complication rate exists. This is contrary to many other studies that reported a weakness of NOM to be the high frequency of short-term complications (7-9).

Renal Preservation

Previous studies have shown that open surgical exploration can lead to higher nephrectomy rates (5, 41-43). Our data showed 84-100% of patients had preserved renal units following NOM compared to a 0-82% renal-preservation rate following open surgical exploration. This finding confirms the greater risk of nephrectomy once a decision for open surgical exploration is undertaken.

A weakness of many studies related to renal trauma is a lack of long-term follow-up to measure residual renal function. Only one study (28) reported on relative post-operative renal function six months post-trauma using dimercapto-succinic acid renal scinitigraphy (DMSA) and found poorer long-term renal function was related to percentage of devitalized parenchyma and associated visceral lesions. Studies comparing radical nephrectomy versus partial nephrectomy, although performed on a different population, provide an insight into the potential long-term negative impact of trauma nephrectomy. In selected patients, radical nephrectomy was shown to be associated with poorer survival and the development of chronic kidney disease compared to partial nephrectomy (44-46).

Comparison with Current Guidelines

Current guidelines recommend immediate intervention (open surgical exploration or angioembolisation) for haemodynamically unstable patients (18, 27). The AUA guidelines state that angioembolisation is an option only in experienced centres and surgical exploration should be used in other units. The EAU guidelines state angioembolisation is a first-line option in patients with active bleeding and no other indications for immediate open surgery. For those who do not meet the criteria for immediate intervention, AUA guidelines state that injury grade should not influence whether a patient receives surgical exploration or NOM and the EAU recommends surgical exploration only for grade V vascular injuries. These guidelines highlight the importance of clinical as well as institutional factors (angioembolisation facilities, availability of minimally invasive techniques, and level of critical care support) in deciding on the appropriate management. The current study classified angioembolisation as a non-operative intervention therefore directs comparisons to the guidelines are difficult. However, the benefits of a conservative approach to high-grade renal injury are evident.

3.4.2 Clinical Implications

The ultimate goal of conservative or minimally-invasive management is to minimize unnecessary explorations and reduce iatrogenic nephrectomy rates without increasing morbidity or mortality. This study has shown that outcomes following NOM are at the very least non-inferior to those following open surgical exploration, all while avoiding the morbidity associated with surgery. The findings from our study help to strengthen the argument for conservative management taking into account some of the absolute indications for surgical exploration that have been discussed.

The NOM of trauma can be viewed as a “package of care”; a step-wise approach starting with conservative, followed by minimally invasive and/or surgical exploration if necessary. It should be noted that an algorithm for “package of care” will vary in different centres according to available interventions however, the importance of escalation in treatment interventions should be emphasized.

3.4.3 Limitations

High-powered studies on trauma are difficult to conduct due to relatively low incidence and concerns about studies in life-threatening situations. Using retrospective comparative studies is the next best approach but remains a challenge as management has already shifted to NOM in many units. It is our belief that this review provides the first rigorously conducted systematic review on high-grade renal injury and therefore represents a review of current available best evidence.

There was high risk of bias in the included studies predominantly due to the retrospective study design and selection bias. Analysis of study confounders showed that patients in the open surgical exploration group were more likely to have grade V injuries, be more clinically unstable on admission and have a higher ISS compared to those in the NOM group. It is important therefore that certain outcomes heavily influenced by such confounders such as overall mortality are interpreted with caution. Mortality and complication rates were not reported on a time-to-event basis in included studies which together with small sample sizes and low event rates mean findings should be also interpreted cautiously. Although most studies reported mortality and complications that occurred “in-hospital”, the lack of defined time-periods is a key limitation. Included studies which reported on complications did not provide separate data for men in the open surgical exploration group who did not require nephrectomy. Subsequently some of the complications incurred in this group could be related specifically to the nephrectomy. However, given that most patients who underwent exploration did not require nephrectomy and that the spectra of complications with or without nephrectomy will be similar, the degree of over-estimation of complications in the exploration group will be low.

High grade renal injury conventionally encompasses grade IV and V renal injuries according to the AAST classification. Variation may exist across institutions on whether injuries are classified as grade IV or V dependent on reporting radiologists. Caution must be exercised when allocating a defined protocol for high-grade renal injuries when grade IV and V injuries are grouped.

Well-designed trials comparing these two modalities are lacking and the mainstay of reports in the literature remain retrospective case-series. The comparative observational studies identified are limited by selection bias that occurs between interventions and therefore any statistical pooling of data is misleading. Furthermore, consensus is needed regarding which outcomes are reported, how they are defined, as well as how and when they are measured. This will enable more meaningful comparisons in the evidence base in future,

3.4.4 Conclusion

This systematic review has provided evidence that NOM is the most appropriate first-line management option in high-grade renal trauma resulting in a renal preservation rate of approximately 84 - 100%. This systematic review has highlighted the difficulty in comparing NOM and open surgical exploration due to inherent selection bias that will remain an issue unless consensus on outcome definition, measurement and reporting is achieved and adopted for future studies. The use of functional tests such as DMSA or blood parameters such as serum creatinine should be more often reported in comparative studies, if possible beyond six months. We recommend the development of prospective multi-centre trauma registers as well as standardized reporting of outcome measures to assist in making fair comparisons between studies.

Supplementary File 1

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <May 2016>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to June 02, 2016>, Embase <1974 to 2016 June 03>, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1 exp kidney injury/

2 exp Acute Kidney Injury/

3 exp kidney/ and (exp blunt trauma/ or exp penetrating trauma/ or exp laceration/) (

4 exp Kidney/ and (exp "Wounds and Injuries"/ or exp Lacerations/)

5 ((kidney or kidneys or renal) adj5 (trauma* or injur* or lesion* or rupture* or laceration* or avulsion* or contusion* or damage*)).tw,kw.

6 or/1-5

7 ((grade or grades or grading) adj5 ("4" or "5" or four or five or IV or V or "4-5" or "IV-V")).tw.

8 ((high or higher or advance*) adj5 (grade or grades or grading)).tw.

9 (severe adj2 (trauma* or injur* or lesion* or rupture* or laceration* or avulsion* or contusion* or damage*)).tw. (

10 ((subgroup* or sub-group or sub-analysis or sub-analyses or different or groups or categories) adj5 (grade or grading)).tw.

11 exp kidney pelvis/

12 ((renal or kidney*) adj5 (pelvis or pelvic or ureteropelvic or hilar or hilum or collecting system)).tw.

13 ((urinary or urine) adj5 (extravasation or extra-vasation)).tw.

14 exp kidney artery/ or exp renal artery/ (21039)

15 exp Renal Veins/

16 ((renal or kidney*) and (artery orarteries or vein or veins or vascular)).tw.

17 ((segmental adj2 infarction*) or (subcapsular adj2 hematomas) or (ureteropelvic adj2 avulsion*)).tw.

18 ((shattered or devasculariz*or devascularis*) adj5 kidney).tw.

19 ((major or penetrating or blunt) adj2 (trauma* or injur* or lesion* or rupture* or laceration* or avulsion* or contusion* or damage*)).tw.

20 or/7-19

21 6 and 20

22 exp conservative treatment/

23 exp minimally invasive surgery/

24 exp Minimally Invasive Surgical Procedures/

25 exp ureter stent/

26 exp percutaneous drainage/

27 (minimal* adj5 invasive).tw.

28 ((ureter* adj2 stent*) or (percutaneous adj2 drainage)).tw.

29 (((angiograph*or blood vessel or vasculograph*) adj5 (embolization or embolisation or embolism or embolus or occlusion*)) or embolotherap*).tw.

30 (conservative or supportive or less aggressive or "not aggressive" or "non aggressive").tw.

31 (nonopera* or non-opera* or non-surgical or nonsurgical or organ sparing or without operation* or nonresect* or non resect*).tw.

32 (package of care or step wise).tw.

33 or/22-32

34 21 and 33

35 ((exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/) not (humans/ or human/)) or ((rats or mice or mouse or cats or dogs or animal* or in vitro or cell lines) not (human* or men or women)).ti. (

36 34 not 35

37 ((child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/) not adult/) or ((child or children or pediatric* or paediatric* or peadiatric* or infant* or new born or adolescent or preschool or pre-school) not (aged or adult* or senior or men or women)).ti.

38 36 not 37

39 (case report/ or case reports/ or case report.ti.) not (cases or case series).tw.

40 38 not 39

41 remove duplicates from 40

List of abbreviations:

AAST: The American Association for the Surgery of Trauma

AE: Angioembolisation

CT: Computerised tomography

EAU: European Association of Urology

NOM: non-operative management

OSE: Open surgical exploration

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Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-analysis flow diagram: search and study selection process for this review

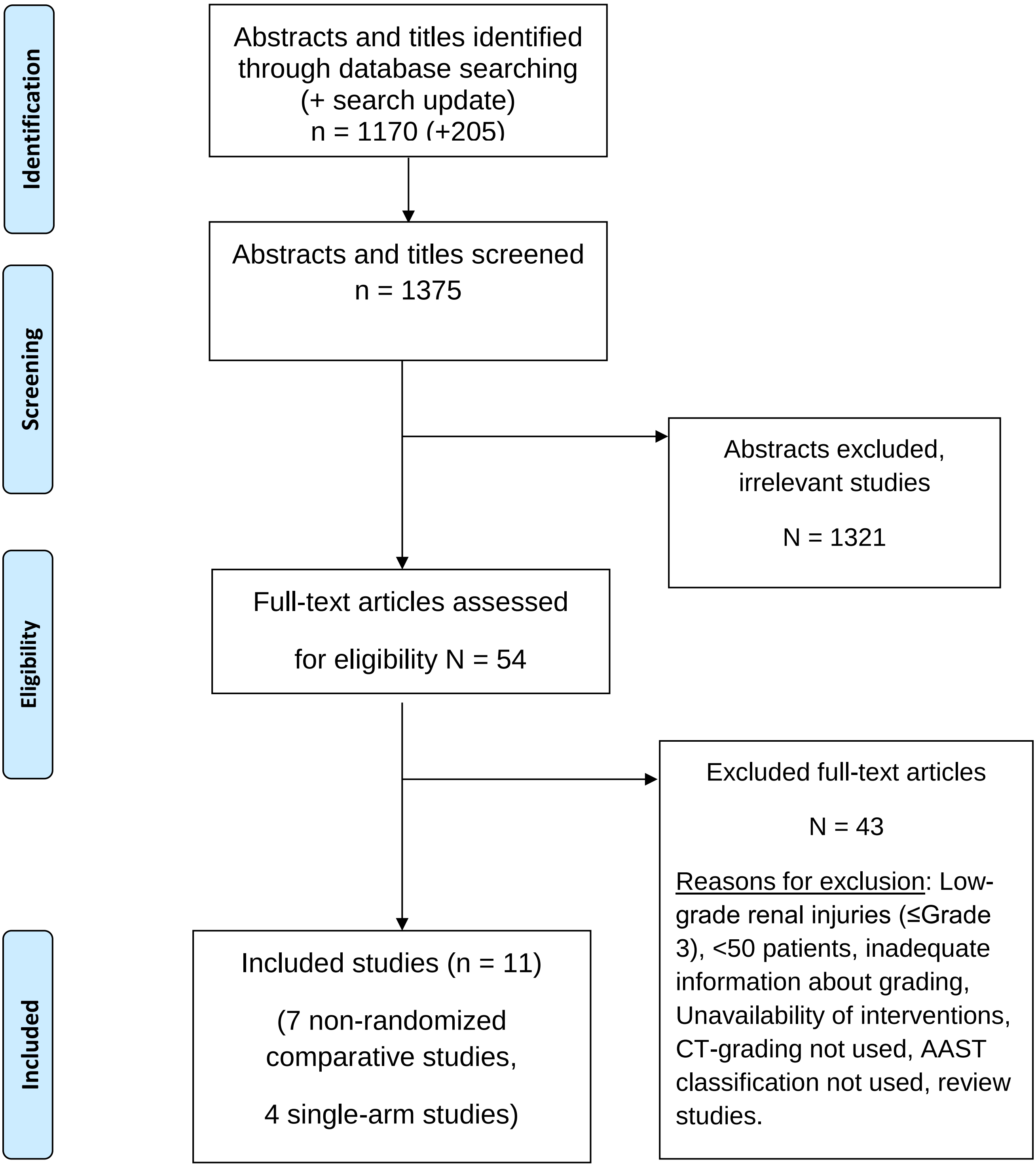


Figure 2: Risk of Bias Table for non-randomised comparative studies

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias): Renal preservation	Blinding of participants and personnel (performance bias): Complications	Blinding of participants and personnel (performance bias): Mortality	Blinding of outcome assessment (detection bias): Renal preservation	Blinding of outcome assessment (detection bias): Complications	Blinding of outcome assessment (detection bias): Mortality	Incomplete outcome data (attrition bias): Renal preservation	Incomplete outcome data (attrition bias): Complications	Incomplete outcome data (attrition bias): Mortality	Selective reporting (reporting bias)	Other bias	Confounder 1: Blunt versus penetrating trauma	Confounder 2: Associated injuries	Confounder 3: Haemodynamic status	Confounder 4: Patient fitness	Confounder 5: Available interventions
Buckley 2006	−	−	−	?	+	−	−	+	+	+	+	?	−	+	+	−	−	?
Elashry 2008	−	−	−	?	+	−	?	+	+	?	+	?	−	+	?	?	−	?
Lanchon 2015	−	−	?	?	?	−	?	?	−	?	?	?	−	+	+	+	−	?
Sarani 2011	−	−	?	?	+	?	?	?	?	?	+	?	−	+	+	+	−	+
Shariat 2008	−	−	−	−	+	−	−	+	?	+	?	?	−	+	+	+	−	?
Shoobridge 2012	−	+	?	?	+	?	?	+	?	+	+	?	−	+	?	?	−	?
van der Wilden 2013	−	−	−	−	+	−	−	+	+	+	+	?	−	+	+	+	−	?

Figure 3: Risk of Bias Table for single-centre studies

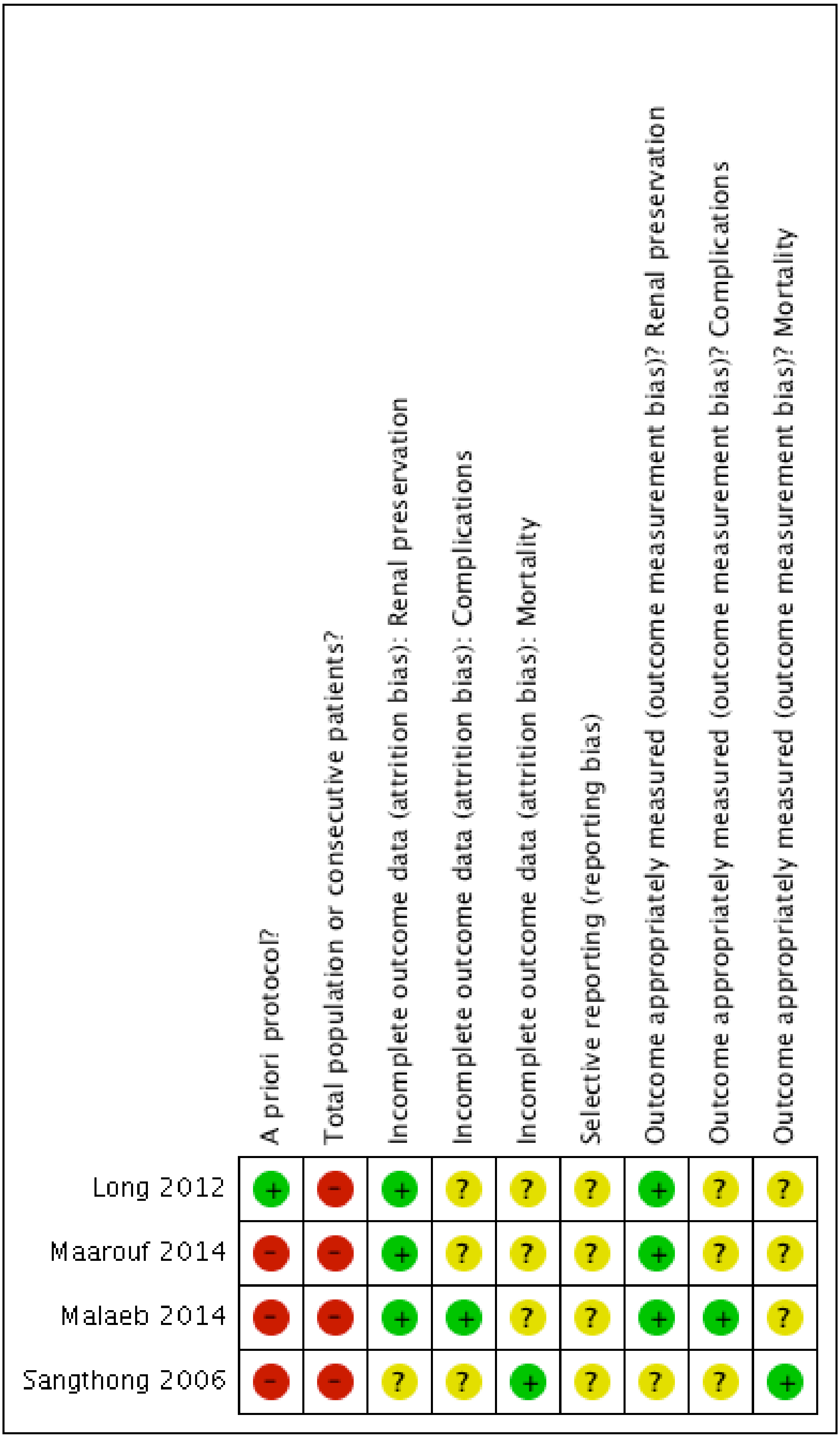


Table 1: The American Association for the Surgery of Trauma (AAST) kidney injury severity scale.

*Grade**	*Description of Injury*
1	*Contusion or non-expanding subcapsular haematoma* *No laceration*
2	*Non-expanding peri-renal haematoma* *Cortical laceration <1cm deep without extravasation*
3	*Cortical laceration >1cm without urinary extravasation*
4	*Laceration: through corticomedullary junction into collecting system* *or* *Vascular: segmental renal artery or vein injury with contained haematoma,* *or partial vessel laceration, or vessel thrombosis*
5	*Laceration: shattered kidney* *or* *Vascular: renal pedicle or avulsion*

**Advance one grade for bilateral injuries up to grade III*

Table 2: Characteristics of Included Studies

Author	Year	Study Design	Country	Number of centres	Type of centre(s)	Recruitment period	No. of patients NOM	No. of patients open surgical exploration	Blunt / Penetrating	Outcomes reported
Comparative										
Buckley (29)	**2006**	**retrospective**	**USA**	**1**	**General Hospital**	**25 y (1981-2006)**	50	103	Both	Mortality, Comps, RP, LOS
Elashry (32)	**2009**	**retrospective**	**Saudi Arabia**	**1**	**General Hospital**	**10 y (1999–2008)**	51	21	Blunt only	Mortality, Comps, LOS, RP
Lanchon (28)	**2015**	**retrospective**	**France**	**1**	**Trauma centre**	**11y (2004-2015)**	148	3	Blunt only	RP
Sarani (36)	**2011**	**retrospective**	**USA**	**2**	**Trauma centre**	**10 y (1998-2008)**	20	17	Blunt only	Mortality, Comps, LOS
Shariat (35)	**2008**	**retrospective**	**USA**	**1**	**Trauma centre**	**9 y (1997-2006)**	45	32	Both	Comps, LOS
Shoobridge (30)	**2013**	**retrospective**	**Australia**	**1**	**Trauma centre**	**9 y (2001-2010)**	67	24	Both	Mortality, Comps, LOS
VanderWilden (34)	**2013**	**retrospective**	**USA**	**12**	**Trauma centres**	**11 y (2000-2011)**	154	52	Blunt only	Mortality, Comps, RP, LOS
Total							535	252		
Case series										
Long (31)	**2012**	**retrospective**	**France**	**1**	**Trauma centre**	**7 y (2004-2011)**	99	NA	Blunt only	Mortality, RP, LOS
Maarouf (33)	**2015**	**retrospective**	**Saudi Arabia**	**3**	**General Hospitals**	**7y (2007-2014)**	206	NA	Blunt only	RP
Malaeb (38)	**2014**	**retrospective**	**USA**	**1**	**Trauma centre**	**7y (2003-2010)**	144	NA	Blunt only	Comps, RP
Sangthong (37)	**2006**	**retrospective**	**USA**	**331**	**Trauma centres**	**13 y (1991-2003)**	376	NA	Blunt only	Mortality
Total							825			

RP: Renal preservation*; Comps:* Complications; *LOS*: Length of Stay

Table 3: Outcomes

Author	**Overall Mortality N (%)**				**Complications N (%)**				**Renal Preservation N (%)**			**Length of Stay Days**		
	NOM	OSE	Time period	p-value	NOM	OSE	p-value	Time period	NOM	OSE	p-value	NOM	OSE	p-value
Comparative Studies														
Buckley (29)	1/50 **(2%)**	0/103 **(0%)**	Not specified	-	3 /50 **(6%)**	10 /103 **(10%)**	-	Not specified	44/50 **(88%)**	84 /103 **(82%)**	-	12^	12	-
Elashry (32)	0 /51 **(0%)**	3/21 **(14%)**	In-hospital	-	11/51 **(22%)**	16 /21 **(76%)**	<0.001	In-hospital	51 /51 **(100%)**	6 /21 **(29%)**		12^	16	0.003
Lanchon (28)	NR	NR	n/a	-	NR	NR	-	n/a	124/148 **(84%)**	0 /3 **(0%)**	-	NR	NR	-
Sarani (36)	0/20 **(0%)**	5/17 **(29%)**	In-hospital	0.01	4 /20 **(20%)**	2 /17 **(12%)**	0.51	In-hospital	NR	NR	-	17^	24	-
Shariat (35)	NR	NR	n/a	-	13 /45 **(28%)**	4/32 **(13%)**	0.2	In-hospital	NR	NR	-	7*	12	0.001
Shoobridge (30)	1/67 **(2%)**	0/24 **(0%)**	In hospital	-	3 /67 **(5%)**	2 /24 **(8%)**	0.004	In-hospital	NR	NR	-	13*(AE), 11* (Cons)	20	-
Van der Wilden (34)	5/154 **(3%)**	12/52 **(23%)**	In-hospital	<0.01	49 /154 **(32%)**	12/52 **(23)**	0.23	In-hospital	139 154 **(90%)**	18 /52 **(35%)**	-	13.1^	23	-
Single-arm Studies														
Long (31)	NR	n/a	n/a	-	27/99 **(27%)**	n/a	-	In-hospital	87/99 **(88%)**	n/a	-	7^	n/a	-
Maarouf (33)	NR	n/a	n/a	-	12/206 **(56%)**	n/a	-	In-hospital	189/206 **(92%)**	n/a	-	NR	n/a	-
Malaeb (38)	NR	n/a	n/a	-	44 /144 **(31%)**	n/a	-	In-hospital	141/144 **(98%)**	n/a	-	NR	n/a	-
Sangthong (37)	79/376 **(21%)**	n/a	Not specified	-	NR	n/a	-	n/a	NR	n/a	-	NR	n/a	-

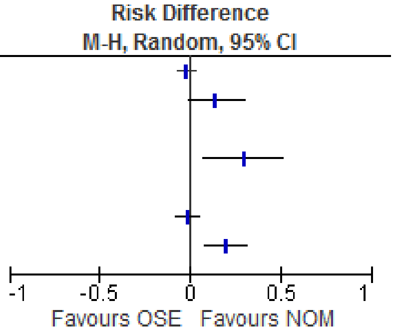
**Median, ^Mean*

AE: Angioembolisation; *Cons:* Conservative management; OSE: Open surgical exploration

Table 4 –Forest plots of risk difference between open surgical exploration (OSE) and NOM in comparative studies:

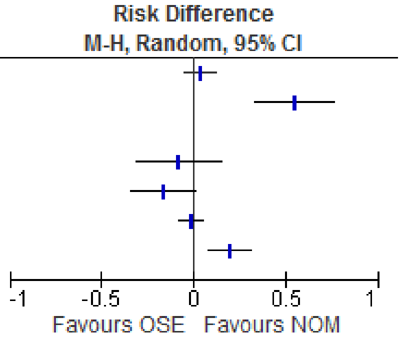
Overall Mortality

	OSE		NOM			Risk Difference
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Buckley 2006	0	103	1	50		-0.02 [-0.07, 0.03]
Elashry 2009	3	21	0	51		0.14 [-0.01, 0.30]
Lanchon 2015	0	0	0	0		Not estimable
Sarani 2011	5	17	0	20		0.29 [0.07, 0.52]
Shariat 2008	0	0	0	0		Not estimable
Shoonbridge 2013	0	24	1	67		-0.01 [-0.08, 0.05]
Van der Wilden 2013	12	52	5	154		0.20 [0.08, 0.32]



Complications

	OSE		NOM			Risk Difference
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Buckley 2006	10	103	3	50		0.04 [-0.05, 0.12]
Elashry 2009	16	21	11	51		0.55 [0.33, 0.76]
Lanchon 2015	0	0	0	0		Not estimable
Sarani 2011	2	17	4	20		-0.08 [-0.32, 0.15]
Shariat 2008	4	32	13	45		-0.16 [-0.34, 0.01]
Shoonbridge 2013	0	24	1	67		-0.01 [-0.08, 0.05]
Van der Wilden 2013	12	52	5	154		0.20 [0.08, 0.32]



Renal Preservation

	OSE		NOM			Risk Difference (Non-event)
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Buckley 2006	84	103	44	50		0.06 [-0.05, 0.18]
Elashry 2009	6	21	51	51		0.71 [0.52, 0.91]
Lanchon 2015	0	3	124	148		0.84 [0.51, 1.17]
Sarani 2011	0	0	0	0		Not estimable
Shariat 2008	0	0	0	0		Not estimable
Shoonbridge 2013	0	0	0	0		Not estimable
Van der Wilden 2013	18	52	139	154		0.56 [0.42, 0.69]

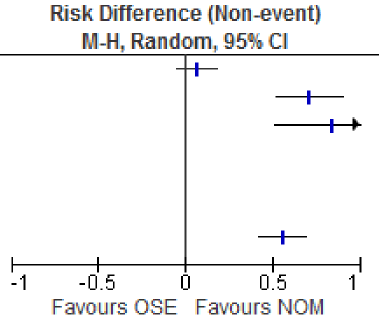


Table 5: Confounders

Author	Grade of Injury (IV/V)		Admission Systolic Blood Pressure Mean		Injury Severity Score (ISS)	
	NOM	open surgical exploration	NOM	open surgical exploration	NOM	open surgical exploration
Comparative Studies						
Buckley (29)	All Grade IV	All Grade IV	NR	NR	NR	NR
Elashry (32)	48 **(94%)** / 3 **(6%)**	9 **(43%)** / 12 **(57%)**	NR	NR	NR	NR
Lanchon (28)	124 **(82%)** / 27 **(18%)**	0 **(0%)** / 3 **(100%)**	NR	NR	NR	NR
Sarani (36)	4.0 (mean grade)	3.9 (mean grade)	**121**	**100***	**24**	**40***
Shariat (35)	All Grade IV	All Grade IV	NR	NR	NR	NR
Shoobridge (30)	53 **(79%)** / 14 **(21%)**	1 **(4%)** / 23 **(96%)**	NR	NR	**25 (AE), 25(Cons)**	**38**
Van der Wilden (34)	128 **(83%)** / 26 **(17%)**	26 **(50%)** / 26 **(50%)**	**121**	**105***	**23**	**34***
Single-arm Studies						
Long (31)	All Grade IV	NA	NR	NA	NR	NA
Maarouf (33)	Grade III-V	NA	NR	NA	NR	NA
Malaeb (38)	All Grade IV	NA	NR	NR	**28(AE), 30 (Cons)**	NA
Sangthong (37)	All Grade IV	NA	NR	NA	**30**	NA

AE: Angioembolisation; *Cons:* Conservative management

Supplementary File 1

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <May 2016>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to June 02, 2016>, Embase <1974 to 2016 June 03>, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1 exp kidney injury/

2 exp Acute Kidney Injury/

3 exp kidney/ and (exp blunt trauma/ or exp penetrating trauma/ or exp laceration/) (

4 exp Kidney/ and (exp "Wounds and Injuries"/ or exp Lacerations/)

5 ((kidney or kidneys or renal) adj5 (trauma* or injur* or lesion* or rupture* or laceration* or avulsion* or contusion* or damage*)).tw,kw.

6 or/1-5

7 ((grade or grades or grading) adj5 ("4" or "5" or four or five or IV or V or "4-5" or "IV-V")).tw.

8 ((high or higher or advance*) adj5 (grade or grades or grading)).tw.

9 (severe adj2 (trauma* or injur* or lesion* or rupture* or laceration* or avulsion* or contusion* or damage*)).tw. (

10 ((subgroup* or sub-group or sub-analysis or sub-analyses or different or groups or categories) adj5 (grade or grading)).tw.

11 exp kidney pelvis/

12 ((renal or kidney*) adj5 (pelvis or pelvic or ureteropelvic or hilar or hilum or collecting system)).tw.

13 ((urinary or urine) adj5 (extravasation or extra-vasation)).tw.

14 exp kidney artery/ or exp renal artery/ (21039)

15 exp Renal Veins/

16 ((renal or kidney*) and (artery orarteries or vein or veins or vascular)).tw.

17 ((segmental adj2 infarction*) or (subcapsular adj2 hematomas) or (ureteropelvic adj2 avulsion*)).tw.

18 ((shattered or devasculariz*or devascularis*) adj5 kidney).tw.

19 ((major or penetrating or blunt) adj2 (trauma* or injur* or lesion* or rupture* or laceration* or avulsion* or contusion* or damage*)).tw.

20 or/7-19

21 6 and 20

22 exp conservative treatment/

23 exp minimally invasive surgery/

24 exp Minimally Invasive Surgical Procedures/

25 exp ureter stent/

26 exp percutaneous drainage/

27 (minimal* adj5 invasive).tw.

28 ((ureter* adj2 stent*) or (percutaneous adj2 drainage)).tw.

29 (((angiograph*or blood vessel or vasculograph*) adj5 (embolization or embolisation or embolism or embolus or occlusion*)) or embolotherap*).tw.

30 (conservative or supportive or less aggressive or "not aggressive" or "non aggressive").tw.

31 (nonopera* or non-opera* or non-surgical or nonsurgical or organ sparing or without operation* or nonresect* or non resect*).tw.

32 (package of care or step wise).tw.

33 or/22-32

34 21 and 33

35 ((exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/) not (humans/ or human/)) or ((rats or mice or mouse or cats or dogs or animal* or in vitro or cell lines) not (human* or men or women)).ti. (

36 34 not 35

37 ((child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/) not adult/) or ((child or children or pediatric* or paediatric* or peadiatric* or infant* or new born or adolescent or preschool or pre-school) not (aged or adult* or senior or men or women)).ti.

38 36 not 37

39 (case report/ or case reports/ or case report.ti.) not (cases or case series).tw.

40 38 not 39

41 remove duplicates from 40

List of abbreviations:

AAST: The American Association for the Surgery of Trauma

AE: Angioembolisation

CT: Computerised tomography

EAU: European Association of Urology

NOM: non-operative management

OSE: Open surgical exploration

References