



Extended Research Article

Clinical and cost-effectiveness of percutaneous nephrolithotomy, flexible ureterorenoscopy and extracorporeal shockwave lithotripsy for lower pole stones: the PUrE RCTs

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Scientific summary

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Scientific summary

Background

Renal tract stone disease is very common, with a lifetime prevalence of approximately 10% across the world. It mainly affects adults of working age, and the incidence has been increasing over recent decades. Approximately 50% of people with renal tract stones will experience symptoms, typically kidney pain, and about 25% of patients with stones will require active treatment. Many of these stones occur in the lower pole of the kidney and the three standard active intervention options are extracorporeal shockwave lithotripsy (ESWL), flexible ureteroscopic stone treatment (FURS) and keyhole surgery [percutaneous nephrolithotomy (PCNL)].

Objectives

The aim of the PUrE study was to determine which of ESWL, FURS and PCNL offer the best treatment outcomes in terms of health status, clinical-effectiveness, and cost-effectiveness for people with lower pole kidney stones seeking treatment within the UK NHS.

Methods

Design

Two pragmatic multicentre, patient-randomised, open-label superiority randomised controlled trials (RCTs): the first (RCT1) for lower pole stones (LPSs) ≤ 10 mm in maximum dimension and the second (RCT2) for LPSs > 10 and ≤ 25 mm.

Setting

National Health Service secondary care units across the UK, with a high volume of patients presenting with LPSs, and able to deliver all active treatments.

Participants

Adults (16 years or over) with lower pole renal stones judged to require active treatment.

Intervention

Treatment following either the ESWL, FURS or PCNL pathways. Participants that were eligible and consented were randomised within RCT1 to FURS or ESWL, or within RCT2 to FURS or PCNL.

Main outcome measures

Clinical: (1) Health status area under the curve (AUC) measured weekly to 12 weeks post intervention using the EuroQol-5 Dimensions, five-level version (EQ-5D-5L) and (2) stone clearance at 12 weeks.

Economic: Incremental cost per quality-adjusted life-years (QALYs) gained at 12-months from randomisation. QALYs are based on the responses to the EQ-5D-5L.

Results

Main outcome

RCT1: The mean health status AUC was 0.807 [standard deviation (SD) 0.205] in the FURS group ($n = 164$) and 0.826 (SD 0.207) in the ESWL group ($n = 188$). The adjusted effect estimate was 0.024 [confidence interval (CI) -0.004 to 0.053] and this was not significant ($p = 0.097$). Complete stone clearance was higher with FURS (72%) than with ESWL (36%).

RCT2: The mean health status AUC was 0.794 (SD 0.198) in the FURS group ($n = 57$) and was 0.818 (SD 0.217) in the PCNL group ($n = 63$). The adjusted effect estimate was -0.07 (CI -0.11 to -0.02 ; $p = 0.006$). Complete stone clearance was higher with PCNL (71%) than with FURS (48%).

Economic evaluation

RCT1: The mean cost for the NHS were £3362 and £2223 for the intention to treat (ITT) with FURS and ESWL groups, respectively, resulting in an adjusted cost difference of £1138 [95% confidence interval (CI) £646 to £1631]. The mean QALYs per participant were 0.804 and 0.787 for the FURS and ESWL groups, respectively, producing an adjusted QALY difference of 0.017 QALYs (95% CI -0.008 to 0.043) for the 12-month follow-up period. The incremental cost-effectiveness ratio (ICER) between FURS and ESWL was £65,163 per QALY gained by FURS. At a threshold value of £20,000 per QALY, ESWL has a 99.9% chance of being cost-effective.

RCT2: The mean cost for the NHS was £5298 and £4565 for the ITT with FURS and PCNL, respectively; giving an adjusted difference of £733 (95% CI $-£508$ to $£1973$). The mean QALY per participant were 0.773 and 0.775 for FURS and PCNL, respectively, yielding an adjusted difference of -0.001 (95% CI -0.044 to 0.042).

Therefore, ITT with FURS is on average more costly and does not produce additional QALYs compared with ITT with PCNL. PCNL is highly likely to be cost-effective at the usual cost-effectiveness threshold values used for decision-making in the UK NHS (e.g. probability of 0.87 at £20,000 per QALY gained). These results, however, are dependent on the method used to estimate the costs of the initial interventions. Therefore, using costings based on the Health Care Resource Group (HRG) the mean cost for the NHS was £5769 for FURS and £6703 for PCNL; resulting in FURS being £934 less costly than PCNL (95% CI $-£2582$ to $£714$; ICER: £883,375). That is, ITT with FURS would save on average, £883,375 per QALY forgone.

Comparison with similar randomised trials

The health status outcomes and the economic outcomes, as they relate to the UK NHS, have not been evaluated in previous randomised trials.

Conclusions

The PuE study shows in RCT1 that ESWL for lower renal pole stones under 10 mm was more cost-effective than FURS, and there was no meaningful difference in patient health status. Stone-free rates (SFRs) were higher, however with FURS. From an overall NHS perspective, the costs savings of treating all patients with these stones with ESWL would be substantial. In RCT2, for larger stones 10–25 mm, PCNL was more cost-effective than FURS when using micro-costing to cost the interventions. Health status was marginally beneficial and SFRs were higher with PCNL.

Implications for health care

The choice of health status assessment as the primary outcome measure provides important data for patient counselling for decision-making and for resource allocation based on the cost per QALY analysis. RCT1 demonstrated that ESWL was the more cost-effective treatment for LPSs < 10 mm. This complements the recommendation from National Institute for Health and Care Excellence (NICE) Renal Stone Guidelines 2019 that ESWL should be offered as the first-line intervention for renal stones of this size.

In RCT2 the cost-effectiveness for FURS and PCNL is less clear-cut, because of the discrepancy between a micro-costing analysis (which showed PCNL was more cost-effective) and HRG-based analysis (which showed that FURS was more cost-effective). It is unclear to us why the HRG costs differ that much between FURS and PCNL given the resources used do not substantially differ between the two procedures. Greater transparency in the way the HRG are costed would be beneficial to inform decision-making in the NHS.

The consistent drop in health status at week one in both trials, particularly for those in the FURS treatment arms has important implications for practice during consent to treatment. Based on this data it is important for clinicians to emphasise that patients are likely to feel worse before they feel better. While this is true of most surgical interventions, and therefore likely to be expected by most patients, the PUrE study provides detailed information regarding the anticipated post-treatment health status that will help make patients' consent to be more fully informed.

The results from RCT1 show no meaningful difference in health status, while RCT2 indicates marginal benefit for PCNL. However, when considering secondary outcomes, patients should be counselled that for smaller LPSs < 10 mm, FURS leads to a higher stone free rate than ESWL, and for LPSs between 10 and 25 mm, PCNL leads to higher stone free rates than FURS.

Recommendations for research

What effect will suction devices, improvements in laser technology, and intraoperative pressure monitoring have on postoperative pain, QoL, SFRs, complications, and costs of FURS?

What is the effect of minaturisation of PCNL on postoperative pain, length of stay, complications, SFRs, and costs?

What is the clinical and cost-effectiveness of full metabolic assessment compared with standard advice alone, in people who have undergone treatment for LPSs?

Trial registration

This trial is registered as ISRCTN98970319.

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