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## Impact of COVID-19 on the management and outcomes of ureteric stones in the UK: a multicentre retrospective study

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**Ethical Approval:** We followed NHS Health Research Authority guidance and the study did not require ethical approval. Each participating site obtained local audit approval.

**Study type:** Retrospective cohort study

**Running Title:** COVID Stones study

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## ABSTRACT

**Objectives:** To determine if management of ureteric stones in the United Kingdom changed during the COVID-19 pandemic and whether this affected patient outcomes.

**Patients and methods:** We conducted a multicentre retrospective study of adults with CT-proven ureteric stone disease at 39 UK hospitals during a pre-pandemic period (23/3/19 to 22/6/19) and a period during the pandemic (the 3-month period after the first SARS-CoV-2 case at individual sites). The primary outcome was success of primary treatment modality, defined as no further treatment required for the index ureteric stone. Our study protocol was published prior to data collection.

**Results:** A total of 3735 patients were included (pre-pandemic=1956 patients; pandemic=1779 patients). Stone size was similar between groups ( $p>0.05$ ). During the pandemic, patients had lower hospital admission rates (pre-pandemic=54.0% vs pandemic=46.5%,  $p<0.001$ ), shorter length of stay (mean=4.1 vs. 3.3 days,  $p=0.02$ ), and higher rates of use of medical expulsive therapy (17.4% vs. 25.4%,  $p<0.001$ ). In patients who received interventional management (pre-pandemic  $n=787$  vs. pandemic  $n=685$ ), rates of ESWL (22.7% vs. 34.1%,  $p<0.001$ ) and nephrostomy were higher (7.1% vs. 10.5%,  $p=0.03$ ); and rates of ureteroscopy (57.2% vs. 47.5%,  $p<0.001$ ), stent insertion (68.4% vs. 54.6%,  $p<0.001$ ), and general anaesthetic (92.2% vs. 76.2%,  $p<0.001$ ) were lower.

There was no difference in success of primary treatment modality between patient cohorts (pre-pandemic=73.8% vs. pandemic=76.1%,  $P=0.11$ ), nor when patients

were stratified by treatment modality or stone size. Rates of operative complications, 30-day mortality, and readmission and renal function at 6 months did not differ between the data collection periods.

**Conclusions:** During the COVID-19 pandemic, there were lower admission rates and fewer invasive procedures performed. Despite this, there were no differences in treatment success or outcomes. Our findings indicate that clinicians can safely adopt management strategies developed during the pandemic to treat more patients conservatively and in the community.

## INTRODUCTION

Nephrolithiasis is a major clinical and economic health challenge. Up to 20% of men and 10% of women are affected by stone disease <sup>1,2</sup>. It is responsible for over 85,000 hospital episodes in the UK and costs the UK National Health Service (NHS) an estimated £190-324 million per year <sup>3</sup>.

The management of ureteric stones can be conservative, as most stones smaller than 5mm pass spontaneously <sup>4</sup>. However, interventions such as extracorporeal shockwave lithotripsy (ESWL) or ureteroscopic (URS) laser lithotripsy may be required. Untreated stone disease can result in refractory pain, sepsis, renal failure, and death <sup>5</sup>. The UK National Institute for Health and Care Excellence (NICE) guidelines published in 2019 recommend that adults with ureteric stones measuring less than 10mm should be treated with ESWL and URS is recommended as a second line alternative. For ureteric stones measuring between 10 and 20mm, URS should be offered as first line treatment, and ESWL can be considered if local facilities will allow stone clearance to be achieved within 4 weeks <sup>6</sup>. Similarly, when active management is required, European Association of Urology (EAU) guidelines recommend ESWL or URS for stones <10mm, and URS as first line and ESWL as second line for stones >10mm <sup>7</sup>.

In March 2020, COVID-19 was declared a pandemic by the World Health Organisation (WHO), and measures were introduced across the world to mitigate the spread of infection <sup>8</sup>. There was worldwide disruption to healthcare provision, including increased pressures on healthcare services and the cancellation of elective procedures <sup>9</sup>. The multicentre, international COVIDSurg study demonstrated that

perioperative infection with the SARS-CoV-2 virus was associated with an unadjusted 30-day mortality of 23.8% <sup>10</sup>. In light of this, and as a result of reduced access to operating theatres, recommendations were made to favour non-operative management strategies <sup>9,11-13</sup>. Furthermore, during the peak of the pandemic in the UK, non-COVID-19 related Emergency Department attendances fell dramatically as patients delayed or avoided presentation to hospital due to fear of infection <sup>14</sup>.

The existing body of literature around COVID-19 and endourology discusses alterations required of clinical care to accommodate the widespread disruption to healthcare services due to COVID-19. However, these articles were written at the start of the COVID-19 pandemic and do not discuss whether these suggested changes to treatment algorithms manifested during the pandemic or what their impact on outcomes were <sup>12,13,15</sup>.

We hypothesised that during COVID-19 there were delays in patient presentation resulting in higher rates of AKI and sepsis and that non-invasive management options such as observation, ESWL, and alternatives to general anaesthesia were used more frequently, resulting in higher rates of failed index management and subsequent change in treatment modality and/or re-presentation to hospital. We sought to test this hypothesis by undertaking a multicentre, retrospective study to determine how management of ureteric stones changed during the COVID-19 pandemic in the United Kingdom and define how changes in management affected patient outcomes.

## **METHODS**

### **Study design**

We conducted a multicentre, retrospective cohort study of the management and outcomes of patients presenting with ureteric stones before and during the COVID-19 pandemic at 39 hospitals in the United Kingdom.

Our protocol was published prior to data collection <sup>16</sup>. We followed principles of the trainee-led collaborative research model <sup>17</sup>, coordinated by the COVID Stones Collaborative; and the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines <sup>18</sup> (Appendix B). NHS Health Research Authority guidance was followed, and each participating site obtained local audit approval.

Patients aged  $\geq 18$  years with ureteric stone disease confirmed on contrast or non-contrast computed tomography (CT) imaging were identified via retrospective review of all abdominal CT scans undertaken during relevant data collection periods.

Patients with non-ureteric stone disease were excluded.

### **Data collection**

Data was collected during two time periods: a pre-pandemic period from 23/3/19 to 22/6/19; and a period during the pandemic, which was defined as the 3-month period after the first SARS-CoV-2 case at each individual site. This time point was approximately equivalent to the start of the first UK lockdown due to Covid-19 on 23/3/20. Data was collected by local collaborators, and entered and stored on the Research Electronic Data Capture (REDCap) server managed and hosted by the University of Oxford, UK <sup>19,20</sup>. Data collected included demographics, management and outcomes at 6 months follow-up.



## **Outcomes**

Our primary objective was to assess success of primary treatment modality, defined as no additional treatment required for the index ureteric stone. Our secondary objectives were to assess rates of non-operative management, ESWL, stent insertion, ureteroscopy, and nephrostomy insertion; type of anaesthesia for operative management options; operative complications; hospital admission and length of stay; 30-day and 6-month mortality; readmission, and impact of stone on renal function.

## **Statistical analysis**

Statistical analysis was performed using R (version 4.1.0) <sup>21</sup>. Patients in the pre-pandemic cohort were compared to patients in the pandemic cohort. Two-sided unpaired t-tests, and Chi-squared tests were used to analyse the data. Data is presented as mean  $\pm$  standard deviation (SD) or as raw number and percentage. A p-value  $<0.05$  was deemed significant.

## RESULTS

### Demographics

Data were collected from a total of 3735 patients from 39 centres. In the pre-pandemic period data were entered for 1956 patients, and in pandemic period data was entered for 1779 patients. Baseline patient characteristics were broadly similar (Table 1). Although, there was a significant difference in age between cohorts, the median age group for both cohorts was 50-59 years.

Stone site and size were similar between cohorts (Table 1). Unexpectedly, patients from the pre-pandemic cohort were reported to have significantly higher rates of active infection and acute kidney injury on admission, and fever at any point during index admission. However, mean C-reactive protein, white cell count, positive microbiology cultures (urine or blood), and creatinine were not significantly different (Table 1).

### Management

Overall, patients in the pandemic period had significantly lower rates of admission to hospital (pre-pandemic 54.0% vs. pandemic 46.5%,  $p<0.001$ ) and shorter length of stay in hospital (mean length of stay in days, pre-pandemic=4.1 (SD=8.0) vs. pandemic=3.3 (SD=5.9),  $p=0.02$ ) compared to the pre-pandemic period. The use of alpha blockers was significantly higher during the pandemic (pre-pandemic=17.4% vs. pandemic=25.4%,  $p<0.001$ ). Despite the higher rates of active infection and fever, antibiotic usage was similar between cohorts (Table 2).

### *Interventional management*

There were no differences in rates of interventional management between the cohorts (pre-pandemic, n=787 [40.2%] vs. pandemic, n=685 [38.5%], p=0.30), or ASA grade (p=0.50) and WHO/ECOG Performance status (p=0.21) in patients who received operative management (Table S1). However, there were significantly higher rates of ESWL and nephrostomy insertion, and significantly lower rates of general anaesthetic, ureteroscopy and stent insertion during the pandemic compared to pre-pandemic (Figure 1, Table 2). During the pandemic, planned interventions were delayed due to COVID-19 status in 63 out of 1580 patients (4.0%).

### **Outcomes**

#### *30-day outcomes*

The 30-day operative complication rate among those who received operative management was similar between the pre-pandemic and pandemic cohort (Table 2), as was the 30-day mortality rate (any cause) across the whole of each cohort (pre-pandemic=8 of 1800 [0.4%] vs. pandemic=9 of 1637 [0.6%], p=0.85).

#### *6-month outcomes*

The success rate of primary treatment (i.e. no further treatment required for the index stone after primary treatment modality) was similar between cohorts (pre-pandemic=73.8% vs. pandemic=76.1%, p=0.11). There was no significant difference in success of primary treatment modality when stratified by treatment modality or stone size.

In patients who did require further intervention, the rates of ESWL, ureteroscopy, retrograde stent insertion, and nephrostomy were similar between each cohort (Table 3).

The mean number of unplanned admissions (pre-pandemic=0.17 (SD=0.52) vs. pandemic=0.18 (SD=0.50),  $p=0.83$ ), mean creatinine (pre-pandemic=87.3 (SD=36.9) vs. pandemic=89.4 (SD=51.9)  $\mu\text{mol/L}$ ,  $p=0.31$ ), and chronic kidney disease stage 1 to 5 (pre-pandemic=17.1% vs. pandemic=17.9%,  $p=0.99$ ) were similar between cohorts. There was a higher mortality rate in the pre-pandemic cohort group (pre-pandemic=42 of 1871 [2.3%] vs. pandemic=21 of 1719 [1.2%],  $p=0.02$ ).

## DISCUSSION

In response to the COVID-19 pandemic, strategies to prioritise and triage patients with urological pathology were developed<sup>13</sup>. These included conservative treatment whenever possible<sup>13</sup>, and use of local-anaesthesia to minimise ventilator use and reduce risk of COVID-19 exposure<sup>12,13,15</sup>. If operative management was deemed necessary, recommendations were made to select patients according to surgical priority using patient factors (symptoms, comorbidities, and renal tract abnormalities) and stone factors (obstruction, infection, and conservative management failure)<sup>12,13</sup>. In cases where there was an infected, obstructed system, multiple sources recommended insertion of a ureteric stent under local anaesthetic as first line treatment, with nephrostomy as second line option<sup>13,15</sup>.

In this study, we demonstrate that the management of ureteric stones changed across the UK during at the onset of the COVID-19 pandemic, with fewer invasive procedures and increased rates of ESWL and medical expulsive management. We also found that rates of nephrostomy were higher, despite lower rates of AKI and active infection.

Other studies have reported a decrease in urological presentations during the COVID-19 pandemic<sup>22-25</sup>. We therefore predicted that during the pandemic patients with ureteric colic would have delayed presenting to hospital and therefore have been a more unwell cohort. However, in our data, rates of AKI and active infection were lower in the pandemic patient cohort suggesting that these patients did not delay their presentation long enough to impact their clinical condition. These findings contrast with other urolithiasis datasets. Castellani et al. compared ureteric stone

disease outcomes of 298 patients prior to the pandemic with 218 patients during the pandemic, reporting reduced admissions and higher rates of infected-obstructed systems, hospitalisation, and intervention during the COVID-19 pandemic<sup>26</sup>.

Furthermore, Flammia et al. found that serum creatinine was significantly higher in 36 patients with urinary stone emergencies during the pandemic compared to 44 patients with urinary stone emergencies prior to the pandemic, which the authors posited was due to delayed presentation <sup>27</sup>. Similarly, Gul et al. demonstrated an increase in creatinine, white cell count, hospital admissions, antibiotic treatment, and emergency nephrostomy insertion in 35 patients with urolithiasis during the pandemic compared to 114 patients with urolithiasis prior to the pandemic <sup>28</sup>.

Our findings are consistent with those reported by Anderson et al. and Nourian et al. who identified no difference in markers of infection or AKI between pre-pandemic and post-pandemic cohorts of patients presenting with urolithiasis <sup>29, 30</sup>. Our study represents the largest cohort to date investigating ureteric stone outcomes during the pandemic, has a multicentre design and had a pre-defined protocol. Thus, we predict our findings are representative of true outcomes in the UK during the COVID-19 pandemic.

Steinberg et al. suggested that we can use the COVID-19 pandemic as an opportunity to reassess ureteric stone management strategies, and establish whether conservative management strategies have been under-used <sup>31</sup>. Our study is the first to evaluate the impact of changes in the management of ureteric stones during the COVID-19 pandemic on patient outcomes at long term follow up

<sup>27,29,30,32,33</sup>.

We demonstrate that increased use of conservative management strategies did not have a detrimental effect on primary treatment success or patient outcomes at 6-month follow up. Our data supports increased use of less-invasive options recommended by NICE and EAU guidance <sup>6,7</sup>, including watchful waiting with medical expulsive therapy and ESWL as first line – there was an approximately 10% shift from URS to ESWL during the pandemic with non-inferior outcomes. Our data also support a reduction in admission rates and earlier discharge. It is unclear whether these changes will revert once the pandemic stabilises and patient backlog is tackled or if practice will change permanently. Evidence such as this should drive a more permanent change to less-invasive management, as the change in practice during the pandemic has shown that this is safe and as effective.

This study is the first of its kind to be conducted across multiple sites with 6-month follow-up. However, the study is limited by its retrospective design, and missing data. Our study was conducted across 39 centres and the number of cases entered by each centre varied considerably. This may be due to differences in local patient populations; however, it may be that not all patients within each time period were captured. This increases the risk of selection bias within our study and therefore no comment can be made on whether there was a change in the number of presentations with ureteric stone disease during each time period. Unexpectedly, we found there was a significant decrease in the mortality during the pandemic. It is difficult to explain this, particularly when demographic data such as age and other comorbidities was broadly similar. We hypothesise that some patients may have died due to Covid-19 before their stone disease was symptomatic enough to present to hospital, and this may have caused a sampling bias. While we demonstrated no

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difference in clinical outcomes, we did not collect data on quality-of-life outcomes, and this is a limitation. We made the assumption that if a patient's quality of life deteriorated significantly they would re-present to hospital for additional management. We did not collect data on location of ureteric stone, as we felt this data would not have been accurate due to heterogeneity in subjective location between different radiologists. Therefore, there may be differences in the ureteric stone locations between our cohort that we were unable to detect. As parts of the UK were affected by Covid-19 at different times, we sought to mitigate local differences by defining the start of the pandemic period as the first SARS-CoV-2 case at each individual site. We assumed that changes to urological care occurred at each site around this time, although these may have occurred later. As such, there may have been a difference in response over time at each site and this may have underestimated the difference in treatment change during the pandemic period.



## **CONCLUSIONS**

As a result of the COVID-19 pandemic patients in the UK with ureteric stones were less likely to be treated invasively and more likely to be managed without admission. However, this change in practice did not result in inferior outcomes for patients. The pandemic has given the urological community an opportunity to re-evaluate management of ureteric stones; our findings indicate that a greater proportion of ureteric stones can be managed safely and effectively with non-invasive ambulatory options.

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**FIGURE CAPTIONS**

*Figure 1: Change in interventional management during the pandemic*



## **TABLES**

*Table 1: baseline characteristics between the pre-pandemic patient cohort and the pandemic patient cohort. AKI = acute kidney injury CFU = colony forming units; CRP = C reactive protein; IQR = interquartile range; SD = standard deviation; WCC = white cell count.*

*Table 2: Management and complications*

*Table 3: Outcomes and additional operative management required at 6 months follow-up.*

## SUPPLEMENTARY TABLES

Table S1: ASA Grade and WHO/ECOG Performance status

Table F: baseline characteristics between the pre-pandemic patient cohort and the pandemic patient cohort. AKI = acute kidney injury CFU = colony forming units; CRP = C reactive protein; IQR = interquartile range; SD = standard deviation; WCC = white cell count.

	Pre-pandemic period (N=1956)	Pandemic period (N=1779)	p-value
<b>Age group</b>			0.02
18-19 years	11 (0.6%)	17 (1.0%)	
20-29 years	198 (10.1%)	164 (9.2%)	
30-39 years	340 (17.4%)	346 (19.4%)	
40-49 years	361 (18.5%)	359 (20.2%)	
50-59 years	409 (20.9%)	405 (22.8%)	
60-69 years	336 (17.2%)	267 (15.0%)	
70-79 years	210 (10.7%)	149 (8.4%)	
80+ years	90 (4.6%)	72 (4.1%)	
<b>Gender</b>			0.823
Female	576 (29.4%)	517 (29.1%)	
Male	1380 (70.6%)	1262 (70.9%)	
<b>BMI</b>			
Mean (SD)	28.8 (6.3)	29.6 (7.4)	0.074
Median [IQR]	28.0 [24.4-32.1]	28.7 [24.7-32.9]	
<b>Non-urological comorbidities</b>			0.075
Yes	538 (36.2%)	453 (32.9%)	
No	950 (63.8%)	923 (67.1%)	
<b>Urological comorbidities</b>			0.662
Yes	56 (3.8%)	46 (3.4%)	
No	1429 (96.2%)	1309 (96.6%)	
<b>Ureteric stone location?</b>			0.52
Left	1014 (51.8%)	929 (52.2%)	
Right	873 (44.6%)	799 (44.9%)	

	Pre-pandemic period (N=1956)	Pandemic period (N=1779)	p-value
Bilateral	69 (3.53%)	51 (2.87%)	
<b>Maximum stone size (mm)</b>			0.687
≤5	1026 (57.5%)	926 (56.9%)	
6-10	633 (35.5%)	598 (36.8%)	
11-19	108 (6.1%)	85 (5.2%)	
≥20	18 (1.0%)	17 (1.1%)	
<b>Active infection at time of presentation</b>			0.032
Yes	258 (13.2%)	193 (10.8%)	
No	1697 (86.8%)	1586 (89.2%)	
<b>Fever (Temperature &gt;38 degree C) at any stage in index admission</b>			0.031
Yes	151 (9.3%)	107 (7.1%)	
No	1482 (90.8%)	1406 (92.9%)	
<b>Admission blood tests CRP (mg/L)</b>			0.562
Mean (SD)	27.7 (64.6)	26.4 (68.7)	
Median [IQR]	4.0 [1.0-17.0]	3.0 [1.0-13.0]	
<b>Admission blood tests WCC (x10<sup>9</sup>/L)</b>			0.725
Mean (SD)	11.0 (6.2)	11.0 (4.2)	
Median [IQR]	10.3 [8.1-12.9]	10.7 [8.1-13.1]	
<b>Positive blood culture</b>			0.749
Yes	51 (38.1%)	41 (41.0%)	
No	83 (61.9%)	59 (59.0%)	
<b>Positive urine culture (&gt;10<sup>5</sup> cfu)</b>			0.796
Yes	97 (21.8%)	78 (20.9%)	
No	347 (78.2%)	296 (79.1%)	
<b>Admission blood tests Creatinine (umol/L)</b>			0.765
Mean (SD)	105 (70.8)	106 (75.9)	
Median [IQR]	94.0 [77.0-113.0]	93.0 [78.0-113.0]	
<b>AKI</b>			0.041
Yes	340 (21.9%)	290 (18.9%)	
No	1211 (78.1%)	1245 (81.1%)	
AKI Grade (KGIDO)			
Grade 1	226 (74.1%)	202 (74.8%)	
Grade 2	55 (18.0%)	44 (16.3%)	
Grade 3	24 (7.9%)	24 (8.9%)	

Table 2: Management and complications

	Pre-pandemic period (N=1956)	Pandemic period (N=1779)	P-value
<b>Admitted to hospital?</b>			<0.001
Yes	1057 (54.0%)	827 (46.5%)	
No	899 (46.0%)	952 (53.5%)	
<b>Length of stay (days)</b>			0.021
Mean (SD)	4.08 (8.04)	3.29 (5.94)	
<b>Alpha blocker</b>			<0.001
Yes	316 (17.4%)	414 (25.4%)	
No	1501 (82.6%)	1219 (74.6%)	
<b>Antibiotics</b>			
Yes-Oral	171 (8.74%)	148 (8.32%)	0.251
Yes-IV	304 (15.5%)	245 (13.8%)	
No	1481 (75.7%)	1386 (77.9%)	
<b>Interventional management</b>			0.295
Yes	787 (40.2%)	685 (38.5%)	
No	1169 (59.8%)	1094 (61.5%)	
	Pre-pandemic period (N=787)	Pandemic period (N=685)	P-value
<b>Anaesthetic</b>			<0.001
General	390 (92.2%)	173 (76.2%)	
Non-general	33 (7.80%)	54 (23.8%)	
<b>ESWL for index stone</b>			<0.001
Yes	179 (22.7%)	233 (34.1%)	
No	608 (77.3%)	451 (65.9%)	
<b>Ureterscopy for index stone</b>			<0.001

Yes	450 (57.2%)	325 (47.5%)	
No	337 (42.8%)	359 (52.5%)	
<b>Stent insertion for index stone (alone or as part of Ureteroscopy)</b>			<b>&lt;0.001</b>
Yes	538 (68.4%)	374 (54.6%)	
No	249 (31.6%)	311 (45.4%)	
<b>Emergency nephrostomy insertion for index stone</b>			<b>0.027</b>
Yes	56 (7.1%)	72 (10.5%)	
No	731 (92.9%)	613 (89.5%)	
<b>Operative complication</b>			<b>0.616</b>
Yes	87 (11.5%)	68 (10.5%)	
No	671 (88.5%)	580 (89.5%)	
<b>30-day highest Clavien-Dindo grade</b>			
None	671 (88.5%)	580 (89.5%)	
I	44 (5.8%)	28 (4.3%)	
II	29 (3.8%)	15 (2.3%)	
III-A	1 (0.1%)	8 (1.2%)	
III-B	9 (1.2%)	12 (1.9%)	
IV-A	2 (0.3%)	0 (0.0%)	
IV-B	1 (0.1%)	2 (0.3%)	
V (death)	1 (0.1%)	3 (0.5%)	

*Table 3: Outcomes and additional operative management required at 6 months follow-up.*

	<b>Pre-pandemic period (N=1956)</b>	<b>Pandemic period (N=1779)</b>	<b>P-value</b>
<b>Primary treatment success</b>			<b>0.113</b>

Yes	1379 (73.8%)	1308 (76.1%)	
No	490 (26.2%)	410 (23.9%)	
<b>Unplanned readmission for ureteric stone disease</b>			0.826
Mean (SD)	0.173 (0.520)	0.176 (0.500)	
<b>Creatinine (umol/L)</b>			0.305
Mean (SD)	87.3 (36.9)	89.4 (51.9)	
<b>CKD</b>			0.989
Yes	230 (17.2%)	213 (17.1%)	
No	1111 (82.8%)	1036 (82.9%)	
<b>Death</b>			0.021
Yes	43 (2.30%)	21 (1.22%)	
No	1828 (97.7%)	1698 (99.0%)	

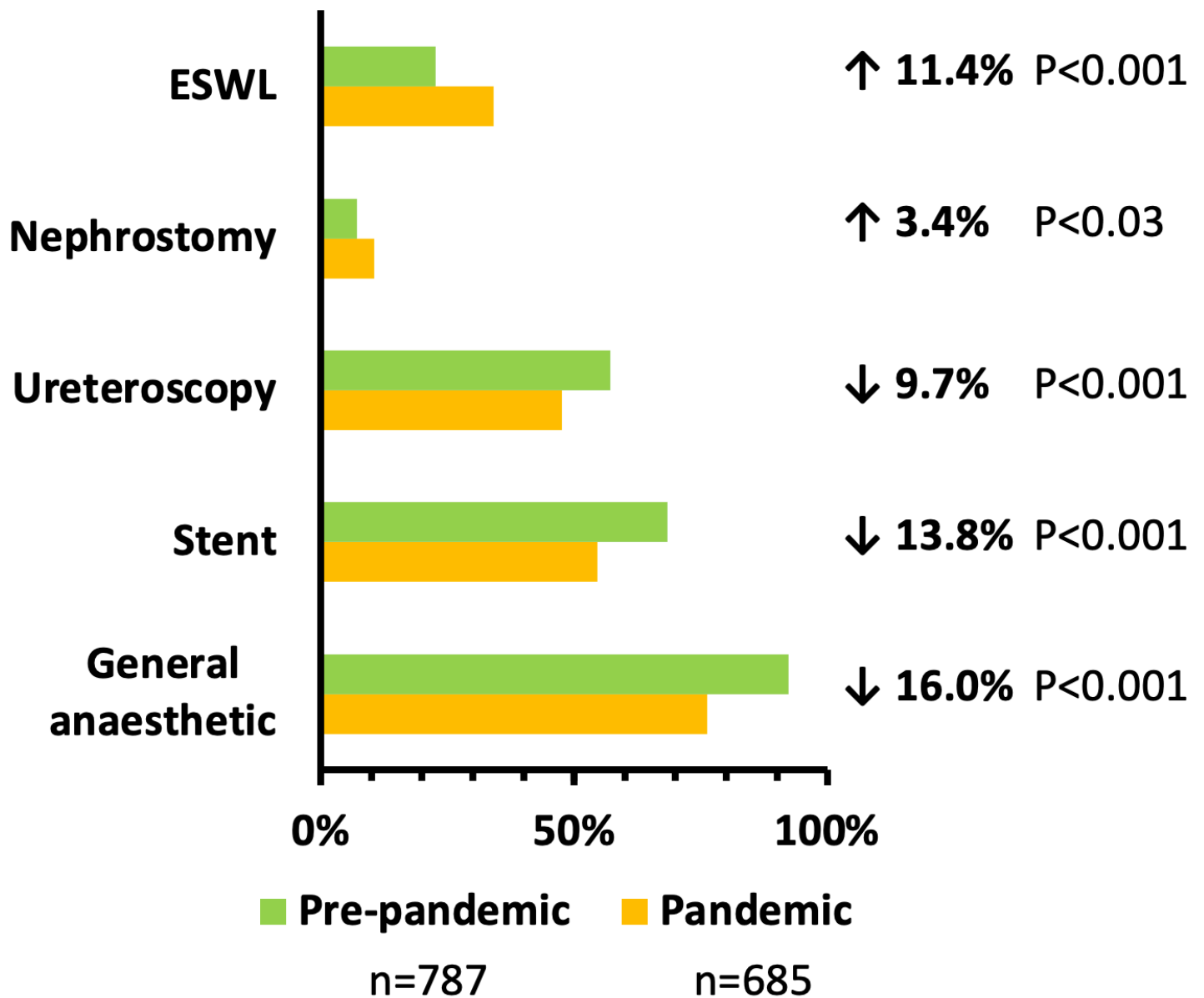
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**Additional interventions**

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<b>ESWL</b>			0.231
Yes	87 (4.9%)	95 (5.8%)	
No	1689 (95.1%)	1519 (94.1%)	
<b>Ureterscopy +/- Laser lithotripsy +/- Stent insertion</b>			0.072
Yes	358 (19.5%)	288 (17.1%)	
No	1481 (80.5%)	1400 (82.9%)	
<b>Stent insertion retrograde</b>			0.62
Yes	84 (4.8%)	69 (4.3%)	
No	1685 (95.3%)	1524 (95.7%)	
<b>Nephrostomy insertion</b>			0.782
Yes	17 (1.0%)	13 (0.8%)	
No	1767 (99.0%)	1602 (99.2%)	

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