

# WHAT'S NEW IN THE DIAGNOSIS AND TREATMENT OF URINARY LITHIASIS?

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## ABSTRACT

**OBJECTIVE.** To review developments in the diagnosis and treatment of urinary lithiasis.

**METHODS.** A review of the most important articles on the subject published in Medline indexed periodicals between 1979 and 2009.

**RESULTS.** Stones occur with greater frequency among people with BMI > 30. Computerized tomography without contrast provides the correct diagnosis in up to 98% of cases. Alpha-adrenergic blockers increase elimination of ureteral calculi smaller than 8 mm by 29%. The proportion of patients free from calculi after ESWL varies from 35% to 91%, depending on size and location. In between 60% and 100% of cases, renal calculi larger than 2 cm are eliminated with PCNL. Calculi of the distal ureter are successfully treated in up to 94% of cases using semi-rigid ureteroscopy, compared to 74% using ESWL. For calculi of the upper ureter success rates are around 77% and 91% for ureteroscopy and 41% and 82% for ESWL.

**CONCLUSION.** The association between urinary lithiasis and *Diabetes mellitus*, is well-established. Computerized tomography without contrast is currently the gold standard for diagnosis of urinary lithiasis. In Brazil, ESWL is the method of choice for treating renal calculi smaller than 2 cm and with tomographic density < 1000 HU, except those of the lower pole, where the ideal limit for treatment is 1 cm. Percutaneous nephrolithotripsy is the best method of treating renal calculi larger than 2 cm and semi-rigid ureteroscopy is the best treatment for calculi of the distal ureter. Flexible ureteroscopy is an option for calculi of the upper ureter and renal calculi smaller than 1.5 cm that do not respond to ESWL or where PCNL is contraindicated.

KEY WORDS: Lithiasis. Diagnosis. Lithotripsy. Ureteroscopy.

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## INTRODUCTION

Urolithiasis is one of the first diseases ever described by man. The first reports of lithotomy, performed in Greece, date from around 2500 ago.<sup>1</sup> Over the last 30 years, great advances have been made in understanding the epidemiology, pathophysiology, diagnosis and treatment of urolithiasis.

The objective of this article is to review and report on the most important features of the epidemiology, diagnosis and treatment of urinary lithiasis.

## METHODS

The most important articles published in periodicals indexed on Medline between 1979 and 2009 were reviewed. Some articles not published within this period have also been included for their historical interest.

## RESULTS

Urolithiasis has a worldwide distribution, although it is more common in countries with hot climates. The risk of urinary calculi is 6% in women and 12% in men, including patients with incidental diagnoses.<sup>2,3</sup> Prevalence is increasing and varies according to age, race and the region studied; prevalence among black men is around 1%, while among white men it is 10%.<sup>2,4,5,6,7</sup> Incidence among children is low (around 3% of all cases);<sup>8</sup> begins to increase among men at around 20 years of age and peaks between 40 and 60; among women incidence peaks around 30 years of age and decreases from 50 onwards.<sup>2,4,5</sup> This is a disease prone to relapses: it is estimated that 50% of patients who are not treated clinically will relapse within 5 and 10 years, while clinical treatment can reduce the relapse rate by half.<sup>2,9,10,11</sup> There are well-established relationships between urinary calculi and several different systemic diseases. More recently, it was confirmed that

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diabetes mellitus type 2 patients are more prone to lithiasis because of uric acid.<sup>12</sup> An association has also been demonstrated between obesity and metabolic syndrome and calculi caused by calcium oxalate and uric acid. The incidence of calculi is 30% greater among men with a body mass index (BMI) greater than 30 and double among women with BMI over 30, when compared with normal people.<sup>13,14,15,16</sup>

Until recently, diagnosis of calculi of the urinary tract was based on three imaging exams: abdominal X-ray, ultrasound and intravenous pyelography. Intravenous pyelography is inconvenient because of the ionizing radiation and the need to use iodinated contrast, which causes allergic reactions in around 10% of cases.<sup>17</sup> Ultrasound is a noninvasive, low-cost method available at almost all emergency services, but it is operator dependent and has limitations with obese patients and when calculi are located in the middle third of the ureter. Nevertheless, in experienced hands it can offer sensitivity of up to 96%, and this rate can be improved further if combined with abdominal X-ray.<sup>17</sup> In 1995, Smith introduced helical computerized tomography (CT) as an alternative to intravenous pyelography and it has now become the gold standard for diagnosing both renal and urinary calculi, thanks to its high sensitivity (95%) and specificity (98%).<sup>18,19,20</sup> A CT scan is fast, does not require iodinated contrast, allows the density of the calculi to be calculated, which has implications for treatment, and, in 13% of cases, it makes it possible to diagnose other clinically significant diseases in patients with an initial diagnosis of urinary calculi.<sup>19,20,21</sup> Disadvantages include the cost, which is falling, and the fact that it is not available at many emergency services, and this is especially true in public hospitals in Brazil. In this context, helical CT without contrast is the first choice option and, when this is unavailable, ultrasound combined with simple X-ray of the abdomen are the tests to request.

Ureteral colic was described by Hippocrates,<sup>22</sup> and the traditional treatment is to initiate with analgesics and antispasmodics, such as hyoscine, combined or not with nonsteroidal anti-inflammatories. Central acting analgesics, such as opiates and their sub-products are reserved for cases in which pain control is more difficult. Hyperhydration is controversial, since it does not appear to contribute to eliminating calculi and may even increase the patient's pain.<sup>23,24</sup>

A new clinical approach to treating urethral calculi, known as expulsive therapy, consists of administering drugs to relax the urethral musculature in order to reduce peristalsis and increase the functional caliber of the ureter, thereby aiding elimination of calculi. Calcium channel blockers (nifedipine) and alpha-adrenergic blockers (doxazosin, terazosin, tamsulosin), which are also used to treat benign cases prostate hypertrophy, are among the main drugs used. Some protocols also combine corticoids with these drugs in an attempt to reduce urethral edema and facilitate elimination further still.<sup>25,26</sup> The 4-week elimination rate of urethral calculi of up to 8 mm increased by up to 65%, although a meta-analysis undertaken by the American Urological Association reported a 29% increase

in elimination rate.<sup>25-30</sup> Furthermore, patients who receive this treatment suffer a reduced number of episodes of pain and the time taken to eliminate calculi is also reduced.<sup>26-30</sup> Expulsive therapy needs continuous control of the patient, with clinical and imaging examinations every week or fortnight. If there is no clinical response and the calculi continue to develop, there are signs of infection or uretero-hydronephrosis worsens, interventionist treatment should be initiated. Adverse effects such as hypotension and palpitations are observed in around 4% of patients, while treatment is suspended due to adverse drug effects in just 1% of cases.<sup>28</sup> The addition of corticoids improves results, but the cost-benefit is questionable because of the potential adverse effects.<sup>27,29</sup> There is currently a tendency, which we ourselves follow, to give alpha blockers to patients with urethral calculi smaller than 1 cm, with pain under control, no infection or significant dilatation of the excretory tract, free from angina and with no history of cerebral vascular accident during the previous 6 months; the use of corticoids is questionable because of their potential adverse effects.

Interventional treatment of urinary calculi has also undergone countless changes over the last 3 decades. Pain, infection and dilatation of the excretory tract account for 90% of indications for removing calculi; untreatable pain is responsible for 70% of these indications. The primary factors that affect the type of surgical treatment that will be used are factors relating to the calculi: their size and location within the urinary tract; and factors related to the patient: age and the presence of comorbidities (obesity, DM, heart disease, skeletal deformities, coagulopathies, infection). Nowadays, extracorporeal lithotripsy, percutaneous nephrolithotripsy and endoscopic ureterolithotripsy are the most widely used of the main interventionist methods for the treatment of calculi. Open surgery is the exception to the rule, but has not been completely abandoned.

Extracorporeal shock wave lithotripsy (ESWL) was developed in Germany by Chaussy et al. and introduced into clinical practice in 1981.<sup>31</sup> Fragmentation of calculi by shock waves applied externally to the patient rapidly became the principal treatment method used, thanks to the good results, low invasiveness and low incidence of adverse effects.<sup>32,33,34</sup> Despite being the interventionist method that is most used to treat renal and urethral calculi all over the world, ESWL has one major drawback, which is that its results are directly dependent on the size of the calculus being treated. Stone-free rates vary from 14,<sup>22,35,36,37</sup> depending on the size of calculus being treated, its position within the urinary tract, factors related to the patients and the criteria used to assess success, which varies greatly from center to center. The best results are achieved with pelvic stones and calculi of the upper and mid poles that are smaller than 2 cm, with success rates varying from 71 to 91%.<sup>22,35,37,38</sup> As lithotripsy equipment has developed, machines have become less powerful and their use less painful, making anesthesia unnecessary and making it possible for patients to be treated with deep analgesia, or sedated but conscious. These changes mean that the rate of calculus fragmentation achieved by modern machines is

inferior to that of the first generation equipment, which can no longer be purchased.<sup>22,35</sup> Several adaptations to the treatment technique and patient selection have been introduced in order to improve results. With relation to patient selection, currently the helical tomography is used to evaluate the density of the stone and as a predictor of the success of the lithotripsy. The greater the density of the calculus, measured in Hounsfield Units (HU), the more difficult it will be to fragment. Thus, around 100% fragmentation is achieved when calculi have a density of up to 500UH, 85.7% from 500 to 1000UH and 54.5% fragmentation above 1000UH<sup>39,40</sup> Also regarding patient selection, it is well-known that the method has reduced efficacy for removing calculi located in lower pole, where the rate of stone-free patients is approximately 35%,<sup>22,37,41,42,43,44</sup> and also among the obese. The distance between the skin and the calculus is a second predictive factor of lithotripsy success; distances greater than 10 cm are associated with worse results.<sup>45,46</sup> Among the elderly, ESWL has proven to be an effective method, achieving up to 78% of patients free from calculi and with no additional complications related to age.<sup>47</sup> Also with the aim of improving results, technical changes are being introduced to the method of administration; some of the most cited are the reduction in the number of impulses from 120 to 60 per minute and the use of increasing power rather than steady power during administration.<sup>47,48,49</sup> Currently, the indications for ESWL are treatment of non-obese patients (BMI < 30 or weight < 120 kg), patients with pelvic calculi and calculi of the upper or mid poles < 2 cm or lower pole calculi < 1 cm, with a CT-measured density of less than 1000UH and a skin-calculus distance of less than 10 cm. Pregnancy and uncorrected coagulopathies absolutely contraindicate this method.

It was observed that there was increased occurrence of arterial hypertension and DM type II in patients given ESWL. These effects were observed with patients treated using first-generation equipment, which are no longer commercially available, and were not reproduced with more modern machines.<sup>34,51</sup>

In the United States, ESWL is losing ground to percutaneous surgery and ureteroscopy. This is due to the fact that in the United States the costs are similar for all of these procedures, but ESWL resolves fewer cases, in contrast with the situation in Brazil, where the cost of ESWL is much lower. Therefore, ESWL remains the first-line treatment for small renal calculi in our country.

Percutaneous nephrolithotripsy (PCNL) was introduced in 1976 by Fernström and Johansson and has substituted open surgery in the treatment of renal calculi, in particular those larger than 2 cm.<sup>52</sup> Percutaneous nephrolithotripsy consists of the removal of stones, whole or in fragments, using a nephroscope introduced into the excretory tract via an orifice opened in the skin, measuring approximately 2.5 cm. In contrast with ESWL, where results worsen to the extent that the size of the calculus increases, in renal percutaneous surgery the results are less influenced by the mass of the calculus. Percutaneous surgery offers several advantages over open surgery: 1. the lumbar incision is

replaced by one or two orifices in the skin, which reduces postoperative pain and recovery time and practically eliminates wound-related complications; 2. the same orifices can be used in any early reoperation if there is residual fragments, reducing morbidity; 3. bilateral calculi can be treated during the same operation, without increasing morbidity; 4. late repeat operations are easier to perform when compared with open surgery.<sup>52</sup> Furthermore, this technique can be used in patients who only have one kidney without compromising renal function.<sup>54</sup> In terms of patients free from stones, the results of PCNL vary from 60 to 100%.<sup>55-58</sup> Percutaneous renal surgery has a complication rate of around 15%, with varying severity.<sup>57</sup> Significant intraoperative bleeding is the most common complication, occurring in 1.4 to 17.5% of cases, with transfusion rates varying from 5% to 10%.<sup>59-63</sup> Hydrothorax occurs in 2 to 12% of cases and is caused by irrigation liquid infiltrating into the pleural cavity in cases when a puncture is made above the 12th or 11th rib. Other, less common, complications are injuries to the colon, liver or spleen, affecting less than 1% of cases.<sup>61,62,64</sup> Percutaneous renal surgery offers good results with obese patients, children and in cases where there are accompanying comorbidities.<sup>65-69</sup> Although PCNL is a significant development, it still involves certain problems: it is considered a technically demanding operation, to the extent that a surgeon must complete 115 procedures before being considered capable of performing the procedure safely;<sup>70</sup> the initial investment in equipment is significant and the cost of each procedure is also elevated due to the large quantities of disposable materials employed. Nevertheless, the operation is constantly gaining in popularity and is currently the first-choice treatment for renal calculi > 2 cm, multiple calculi, particularly hard calculi, such as cystine calculi and also in cases where ESWL fails or is contraindicated.<sup>71</sup>

The interventional treatment for ureteral stones has also undergone changes, in this case due to major development in ureteroscopy, which is a technique for removing calculi from the urinary tract using the ureteroscope, introduced via the urethra. This intervention is indicated for the removal of urethral calculi larger than 5 mm, since calculi of 5 mm or less are eliminated spontaneously<sup>30</sup>. First introduced during the 1970s, ureteroscopy evolved greatly from the 1990s onward, with the development of semirigid ureteroscopes, that were narrower and lighter and had a working canal to allow baskets and laser fibers to be inserted and also thanks to the introduction of flexible ureteroscopes.<sup>72</sup> The method continues to evolve thanks to the advent of digital cameras and advances in calculi fragmentation sources. The availability of these new apparatus resulted in a great increase in the rate of calculi removal and a reduction in morbidity related to the procedure, which in turn led to universal dissemination of the method.<sup>72,73</sup> Semirigid ureteroscopy is the method of choice for the treatment of calculi in the distal ureter, achieving 94% of patients free from calculi, in contrast to 74% achieved using ESWL.<sup>74</sup> For stones located in the mid and upper ureter, these rates are around 77 and 91%, depending on the size of calculus,

which is also better than achieved using ESWL, with which rates vary around 41% and 82.<sup>22,29,30</sup> It is now acknowledged that both ESWL and ureteroscopy are effective treatments for ureteral stones. Ureteroscopy always achieves better rates of calculi-free patients, but demands general anesthetic and a brief hospital stay, whereas ESWL is an outpatient procedure, performed under sedation. In Brazil, ureteroscopy is the more expensive option, but eliminating fragments after ESWL maybe painful and fragments can obstruct the ureter in up to 7% of cases.<sup>75</sup> In general, it is accepted that ESWL is indicated for calculi of the proximal ureter smaller than 10 mm and ureteroscopy is indicated above 10 mm, since ESWL results worsen to the extent that the size of the calculus increases.

Flexible ureteroscope is a significant development within ureteroscopy and has given rise to a new concept in endourology, which is known as retrograde intrarenal surgery.<sup>74</sup> Thanks to the flexibility, this technique makes it possible to reach the upper ureter, the renal pelvis and the calyces and fragment calculi in these locations or remove them via the ureter, without the need for an orifice or incision. This relatively new resource within urology greatly facilitates work with obese patients or coagulopathy patients, in whom percutaneous surgery is sometimes difficult or contraindicated. The low likelihood of bleeding with ureteroscopy means that patients can be operated without suspending anticoagulants.<sup>76,77</sup> The technique is also extremely useful with patients who have renal and ureteral stones, since both can be removed in a single operation.<sup>78</sup> The major obstacle to wider dissemination of this method is its cost. The flexible ureteroscope does not last very long, around 40 operations, and consumption of disposable materials during the procedure (ureteral catheters, baskets, laser fibers) also increases the cost. As a result, in Brazil flexible ureteroscopy is still restricted to university hospitals and centers of excellence. The technique is very useful for treating calculi of the upper ureter, calyceal stones that do not respond to treatment with ESWL or lower pole calculi with characteristics that make ESWL inappropriate, i.e., tomographic density above 1000UH, cystine calculi or very obese patients.<sup>41,79</sup> Flexible ureteroscopy achieves 50% of patients free from calculi compared to 35% for ESWL.<sup>36</sup> Taking all renal calculi treatments together, this method achieves calculi-free patient rates of around 80%.<sup>80,81</sup> Ureteroscopy is also the method of choice for treating urethral calculi during pregnancy, with rates of success and of complications that are comparable with those for patients who are not pregnant.<sup>82,83,84</sup> In our opinion, flexible ureteroscopy is gaining ground in Brazil and without doubt, as costs reduce, will soon be disseminated throughout the country. Although it is infrequently indicated nowadays, accounting for around 1% of procedures for removal of calculi in the United States,<sup>85</sup> open surgery still has a role in treatment of urinary calculi. Here in Brazil, this percentage is greater because of reduced access to technology. Among the open surgery techniques that are still used, extended pyelolithotomy and anatomic nephrolithotomy are the most common procedures. The first of these consists in removing calculi via a wide incision in the

renal pelvis; the second consists of removal of the calculus via an incision opened along the entire convex surface of the kidney, accessing the collecting system via an incision in the renal parenchyma, after temporary clamping of the renal artery.<sup>86</sup> While it is efficient and results are comparable with those achieved with percutaneous surgery, open surgery requires an incision in the lumbar region, which has the disadvantages of postoperative pain, longer recovery time before the patient is able to return to their day-to-day activities, wound complications (infection and hernia) and aesthetic problems.<sup>85,87</sup> Today the main indications for open surgery are complex stones, occupying all renal poles and with stenosis of the infundibuli; the removal of calculi in patients who would undergo open surgery for treatment of other pathologies anyway; complex urinary malformations<sup>85,87</sup> or when the devices necessary to undertake less invasive surgery are not available, which is rare in developed countries but common in the third world.

## CONCLUSION

The association between urinary lithiasis and *Diabetes mellitus*, metabolic syndrome and obesity is well established. Helical computerized tomography without contrast is currently the gold standard for diagnosis of urinary lithiasis. Expulsive therapy, based on the administration of alpha-adrenergic blockers, has contributed to increasing the elimination rate of urethral calculi smaller than 8 mm and to reducing the number of episodes of pain suffered by patients. Extracorporeal shock wave lithotripsy is the method of choice for treating renal calculi smaller than 2 cm, with the exception of those in the lower pole, where the limit is 1 cm and also for stones in the upper ureter smaller than 1 cm. Percutaneous nephrolithotripsy is the method of choice for the treatment of renal calculi larger than 2 cm and ureteroscopy is preferred for calculi of the lower ureter and upper ureter larger than 1 cm. Flexible ureteroscopy is an option for renal calculi and calculi of the upper ureter smaller than 1.5 cm that don't respond to ESWL or for patients for whom PCNL is contraindicated. There are still certain circumstances in which open surgery is indicated for the treatment of urinary calculi.

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