Urol Res (2005) 33: 223–230
DOI 10.1007/s00240-005-0463-9

ORIGINAL PAPER

Yair Lotan · Jeffrey A. Cadeddu · Margaret S. Pearle

International comparison of cost effectiveness of medical management strategies for nephrolithiasis

Received: 20 October 2004 / Accepted: 24 December 2004 / Published online: 28 May 2005

Abstract Although medical therapy is known to reduce the risk of kidney stone recurrence, the cost effectiveness of medical prophylaxis is controversial. We evaluated medical treatment strategies including dietary measures (conservative), empiric medical therapy (empiric) or directed medical therapy (directed) based on comprehensive metabolic evaluation (CME) for patients with recurrent kidney stones, and compared the costs of these strategies using cost data from ten different countries. We previously established rates of stone formation in recurrent stone-formers, risk reduction of medical therapy, sensitivity of CME and rates of spontaneous stone passage from a comprehensive literature search (Lotan et al. 2004 J Urol 172: 2275). The costs of medication, surgical therapy, emergency room visits and CME for ten different countries were obtained from a published report of an international cost survey (Chandhoke 2002 J Urol 168: 937) as well as from our own county hospital in the US. Medication costs in the US were obtained from two national pharmacy chains. A decision tree model was created to compare the costs of different treatment strategies assuming cost accrual for metabolic evaluation, medical therapy and surgery or emergency room visits. For medical therapy, we assumed the distribution of medication use described in the published report, consisting of potassium citrate (60%), thiazide (30%) and allopurinol (10%). A nearly 20-fold difference in the costs of shock-wave lithotripsy, ureteroscopy and medication was found among different countries. From the model (US dollars/patient/year), conservative therapy alone was the most cost effective approach followed by empiric and directed medical therapy in all countries except in the UK. In the UK, the cost of drug therapy (estimated at $29/patient/year) resulted in empiric therapy being the most cost effective strategy for recurrent stone formers. The low likelihood of surgical intervention, as well as the low relative cost of surgery to medication, contributed to the higher cost of empiric and directed medical therapy strategies. Of note, despite the higher cost, drug treatment strategies were associated with significantly lower stone recurrence rates. We found that drug treatment strategies are more costly than conservative treatment but produce good control of stone formation. In all but one country (UK), dietary therapy was the most cost effective approach due to the relatively low cost of surgery compared with medication. The differential resource allocation to different components of a healthcare system (i.e. subsidized medication versus surgical treatment) in different countries determines the cost effectiveness of various treatment strategies.

Keywords Medical evaluation · Nephrolithiasis · Health economics · International comparison

Y. Lotan (✉) · J. A. Cadeddu · M. S. Pearle
Department of Urology,
The University of Texas Southwestern Medical Center,
5323 Harry Hines Blvd., Dallas, TX 75390, USA
E-mail: Yair.lotan@utsouthwestern.edu
Tel.: +1-214-648-0389
Fax: +1-214-648-8786

Introduction

Nephrolithiasis is a common disorder, with an approximate incidence of 0.4–1% and a prevalence of 10–12%. As such, the economic impact of the disease is substantial. Indeed, in 2000, the total annual direct cost of urolithiasis in the US alone, including diagnosis, emergency and surgical management as well as medical prevention, was estimated at nearly $2.1 billion [1]. While medical therapy has been shown to reduce the rate of stone recurrence [2], few studies have evaluated the cost effectiveness of medical evaluation and prophylaxis. Although most authors have concluded that medical therapy for nephrolithiasis is cost effective, their conclusions rely on key assumptions regarding stone recurrence rates and medication risk reduction [3–6].

Chandhoke used a cost model specifically to determine the stone recurrence rate at which medical prophylaxis becomes cost effective. At a recurrence rate of 0.3–4.0 stones/year, he calculated that the cost of medical evaluation and treatment became equivalent to conservative therapy (no drug) [7].

While stone recurrence rates and the costs associated with medication, medical evaluation and surgical therapy of stone recurrences are important factors in determining the cost effectiveness of medical evaluation and therapy, several key points have not been adequately addressed in previous studies. First, dietary modification alone is effective in reducing stone formation rates, and most medical management regimens include dietary measures in addition to medications [8]. Second, only a fraction of patients (10–20%) actually become symptomatic from a new stone and only half of symptomatic patients ultimately require surgical intervention [9, 10, 11]. Furthermore, empiric medical therapy without metabolic evaluation has been shown in some randomized trials to reduce the risk of stone recurrence in unselected recurrent calcium stone formers [12]. Thus, previous evaluations have suffered from inherent biases against conservative therapy and in favor of metabolic evaluation and medical treatment. We created a decision analysis model taking these factors into consideration [13]. This study found that for first-time stone formers, conservative therapy is cost effective and efficacious. For recurrent stone formers, however, conservative therapy is unsatisfactory despite the low cost, because of a relatively high rate of stone recurrence. Drug treatment strategies are much more costly than conservative treatment but yield better control of stone formation.

In light of these findings, we sought to evaluate the cost of medical treatment strategies including dietary measures alone, empiric medical therapy or directed medical therapy based on comprehensive metabolic evaluation in ten different countries to determine if world-wide differences in cost components result in differences in the cost effectiveness of various treatment strategies.

Materials and methods

Decision tree model

A decision analysis model (TreeAge [DATA] 3.5 software with linear success rate assumptions) was constructed to estimate the cost of treatment and follow-up in patients with nephrolithiasis. The decision tree was based on cost accrual for the initial physician visit, medical evaluation, medication and emergency room visits and/or surgery for stone recurrences (Fig. 1).

The following treatment strategies, as previously reported [13], were tested in the model:

1. Conservative therapy (conservative) comprised dietary modification, without drug treatment or metabolic evaluation.
2. Empiric medical therapy (empiric). Both drug and dietary treatment were initiated without metabolic evaluation in all patients. This strategy is based on studies demonstrating that medications such as potassium citrate [12] and thiazide diuretics [14, 15, 16, 17] have resulted in a reduction in stone recurrence rates compared with placebo in recurrent calcium stone formers treated non-selectively.
3. Directed medical therapy based on comprehensive metabolic evaluation (CME) (directed). All patients underwent a detailed metabolic evaluation for which directed dietary and drug therapy was initiated. In 10% of patients with no demonstrable metabolic abnormality, no drug treatment was initiated. Evaluation consisted of an initial office visit and two 24-h urine collections for stone risk analysis, and follow-up included an office visit and 24-h urine collection every 6 months, along with a plain radiograph of the kidneys, ureters and bladder yearly.

Baseline assumptions

We previously reported the assumptions used to construct our decision tree model evaluating medical strategies for management of urolithiasis [13]. The assumptions used in the current study are based on these previous assumptions with a few modifications.

Assumption 1. Only patients with idiopathic calcium oxalate nephrolithiasis were considered for analysis.

Assumption 2. With dietary measures alone, stone recurrence rates are 0.07 stones/patient/year and 0.3 stones/patient/year for first time and repeated stone formers, respectively [13].

Assumption 3. Medical treatments evaluated in this model included a potassium-sparing diuretic (50 mg hydrochlorothiazide and 5 mg amiloride) twice a day, allopurinol (300 mg once daily) and potassium citrate (30 meq twice daily) [7]. The distribution of medications administered was derived from previous studies reporting use of potassium citrate in 60%, a potassium-sparing diuretic containing thiazide in 30% and allopurinol in 10% of stone formers, based on the distribution of underlying metabolic abnormalities [3, 7]. This combination of medications yields a reported risk reduction of 80% [7].

Assumption 4. We assumed that 15% of recurrent stones formers have a symptomatic stone episode each year, and that 55% of symptomatic patients require surgical intervention annually, if medical drug treatment is denied, based on the combined results of published reports [9, 10, 11, 18].

Assumption 5. Among patients who require surgical intervention, half undergo shockwave lithotripsy (SWL) and half ureteroscopy (URS).

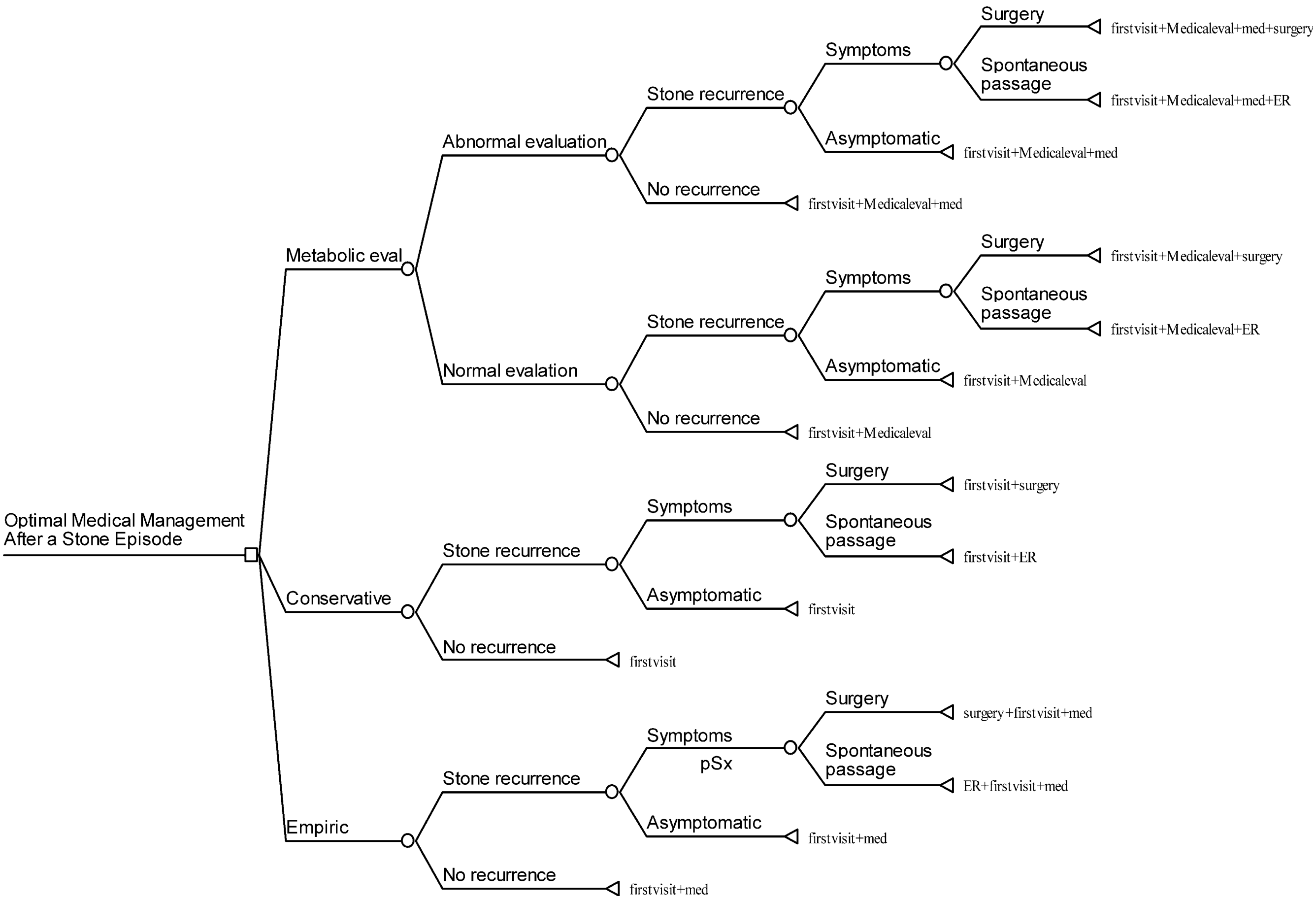

Fig. 1 Decision analysis model

Assumption 6. Comprehensive metabolic evaluations identify specific metabolic defects in 90% of cases, excluding low urine volume [19].

Assumption 7. All patients treated with empiric medical therapy derive maximum benefit from treatment, even though some may have no metabolic defect.

Assumption 8. Patients with no metabolic abnormality detected by CME who receive no medical treatment carry the same risk of stone recurrence as those maintained on conservative therapy.

Financial assumptions

Assumptions regarding the cost of evaluation, medical treatment and surgical intervention were obtained from two sources. The evaluation, treatment and follow-up costs in the US, excluding outpatient medication, were obtained from a large, metropolitan county hospital. The costs of medical therapy, medical evaluation, office visits, surgical therapy and emergency room costs for nine different countries were obtained directly from a previously published comprehensive economic survey (Table 1) [7].

Assumption 1. Each patient is evaluated with a basic serum electrolyte panel that is routinely performed; as such, this cost was excluded from the analysis.

Assumption 2. The yearly follow-up regimen was identical for all patients and was excluded from the cost evaluation.

Assumption 3. The decision tree always chose the least costly pathway for determining the final cost of treatment.

Assumption 4. The international cost survey did not separate the costs of the initial visit (physician fee) and 24-h urine studies separately. As such, we assumed that the physician fee comprised half of the total cost of the initial evaluation based on relative costs at our own institution in the US. This figure was added to the conservative and empiric arms to provide the cost of physician consultation regarding dietary recommendations and empiric medication when appropriate.

Outcomes

The cost of different management strategies was calculated using the preceding assumptions. Thus, the overall cost of each treatment strategy was determined by: whether or not an evaluation was performed, the type of treatment (conservative or drug), whether treatment was provided to all or only to some patients (empiric vs directed), the rate of stone recurrence associated with different treatments or medications and the need for emergency visits or surgery for recurrent stone episodes.

Table 1 Cost (in US dollars) of various cost centers involved in management of the stone-forming patient based on an international cost survey [7] and local institutional costs (US). Medical treatments included a potassium-sparing thiazide (50 mg hydrochlorothiazide and 5 mg amiloride) twice a day, allopurinol 300 mg once a day or potassium citrate twice a day [7]. It was assumed that recurrent calcium stones were treated with potassium citrate 60% of the time, a potassium-sparing thiazide 30% and allopurinol 10% of the time [7]

Country Payer (US dollars)	Australia National health care	Canada Institutional costs	Germany National health care	Italy National health care	Japan Institutional costs	Sweden Institutional costs	Switzerland Billing costs	Turkey Institutional costs	UK National health care	USA Institutional costs
Emergency room (includes CT scan)	$202	$230	$80	$173	$190	$350	$750	$152	$497	$625
Initial limited evaluation + office visit	$126	$50	$44	$73	$165	$306	$172	$97	$223	$143
Follow-up visit + 24 h urine test twice a year	$164	$60	$53	$114	$172	$412	$192	$114	$355	$181
Drug therapy/year*	$341	$190	$432	$534	$250	$277	$117	$150	$29	$508
Shock wave lithotripsy	$900	$750	$360	$1,685	$2,490	$1,100	$670	$373	$2,740	$6,697
Ureteroscopy and stone fragmentation	$205	$750	$160	$1,685	$1,527	$1,100	$1,900	$491	$926	$4,185

In addition to overall cost, the model also yielded the rate of recurrent stone formation on treatment. Thus, it was possible to weigh cost against efficacy for each treatment strategy.

Sensitivity analysis

A series of one-way sensitivity analyses was performed, which evaluated the effect of different individual probabilities and costs, by varying one parameter while holding the others fixed. As such, it was possible to calculate the "medication cost threshold" at varying levels of "risk reduction" that would achieve cost equivalence with conservative therapy for each strategy. Risk reduction was calculated as 100% minus the ratio (in percent) of stone formation rate on a drug treatment strategy and stone formation rate on conservative treatment.

Results

First time stone formers

The stone recurrence rate on conservative therapy was 0.07 stones/patient/year, or one stone every 14 years. According to the model, conservative therapy (without drug) was the least costly strategy (Table 2) except in the UK where conservative and empiric therapies had nearly identical costs ($127/patient/year versus $136/patient/year, respectively). Indeed, the cost of a conservative strategy was only 5% of the cost of directed medical therapy based on a comprehensive metabolic evaluation alone. Drug treatment strategies were twofold to 20-fold more costly than conservative therapy but also yielded lower stone recurrence rates (by 80%).

Recurrent stone formers

For each treatment strategy, the cost of treatment and the rate of recurrent stone formation were higher among recurrent stone formers than first time stone formers (Table 2). Conservative therapy was the least costly strategy in all countries except the UK, but was associated with the highest stone recurrence rate (0.3 stones/patient/year). The relatively large difference in cost between conservative treatment and the strategies involving drugs was largely due to the high cost of medication. However, in the UK where the cost of medication is low ($29/patient/year), empiric therapy is more cost effective than conservative therapy. In other countries with relatively low medication costs such as Switzerland and Turkey ($117 and $150 per patient/year, respectively), only small differences between empiric and conservative therapy were demonstrated. On the other hand, in countries with high medication costs such as the US

($508/patient/year), Germany ($432/patient/year) and Italy ($534/patient/year), conservative therapy offers a significant cost advantage over empiric therapy. Given the added cost of the metabolic evaluation and little demonstrable improvement in stone recurrence rates, strategies involving metabolic evaluation are less cost effective than empiric therapy.

For recurrent stone formers, drug therapy (empiric and directed) was associated with a significantly lower rate of stone recurrence than conservative therapy. However, empiric therapy was minimally more effective than directed therapy because of our assumption that medication is uniformly effective in all treated patients whether or not a metabolic abnormality is present.

Sensitivity analyses

A series of one-way sensitivity analyses was performed to determine the threshold for stone recurrence rates and costs (in US dollars) of medication, surgery and metabolic evaluation at which empiric therapy would be cost equivalent to conservative therapy (Table 3). Because of the cost associated with a CME, but no additional risk reduction compared with empiric therapy, any additional cost for the metabolic evaluation rendered the directed strategy cost inferior to empiric therapy and therefore a cost threshold is not calculable. In most countries, a recurrence rate in excess of one stone per patient per year would be necessary for empiric therapy to be more cost effective than conservative therapy. However, in the UK, where medication cost is exceptionally low, a stone recurrence rate exceeding 0.12 stones/patient/year is associated with a cost benefit for empiric therapy. Likewise, in Switzerland with a similarly low medication cost, empiric therapy is cost advantageous if the stone recurrence rate exceeds 0.67 stones/patient/year. In contrast, in all others countries, empiric therapy reaches cost equivalence with conservative therapy only if medication costs decrease or surgical costs increase substantially.

Discussion

Although economic concerns have recently come to assume a prominent role in healthcare policy and practice and the US, the cost of medical treatments and new technology has long dictated the availability of certain healthcare resources in other industrialized countries. Because of the high cost associated with the management of nephrolithiasis [1], cost effective treatment regimens aimed at reducing the incidence of kidney stones are becoming increasingly important world-wide. The objective of this study was to compare the cost effectiveness of commonly used treatment strategies in the context of their efficacy in stone prevention and to compare costs among a number of industrialized countries.

For first time stone formers, we found that conservative therapy consisting of dietary measures alone was the least costly treatment strategy, although the associated risk of stone recurrence was higher than among the drug treatment strategies. With the exception of the UK where the cost of medication is low, the use of drugs, with or without medical evaluation, increased the overall cost by twofold to 20-fold. Moreover, because of the low likelihood of forming new stones (one stone

Table 2 Outcomes of the model for first-time and repeated stone formers in US dollars

	Stone recurrence rate (stones/patient/year)	Cost according to model									
		Australia	Canada	Germany	Italy	Japan	Sweden	Switzerland	Turkey	UK	USA
First-time stone formers											
Conservative	0.07	$68	$32	$24	$48	$96	$163	$101	$53	$127	$109
Empiric	0.014	$405	$216	$454	$573	$335	$432	$206	$199	$136	$587
Directed	0.02	$598	$283	$486	$671	$566	$970	$474	$347	$601	$852
Recurrent stone formers											
Conservative	0.3	$86	$54	$32	$86	$141	$196	$152	$66	$179	$234
Empiric	0.06	$409	$221	$456	$580	$344	$439	$216	$202	$146	$612
Directed	0.084	$603	$289	$489	$681	$578	$979	$488	$351	$616	$887

Table 3 One-way sensitivity analyses to determine thresholds for stone recurrence rates and costs (US dollars) of medication, surgery and metabolic evaluation. There was no cost of metabolic evaluation low enough to allow this strategy to reach cost equivalence with conservative therapy

	Australia	Canada	Germany	Italy	Japan	Sweden	Switzerland	Turkey	UK	USA
Stone recurrence (stones/patient/year)	> 1	> 1	> 1	> 1	> 1	> 1	0.67	> 1	0.12	> 1
Annual medical cost	$18	$23	$8	$40	$47	$34	$52	$14	$54	$130
Surgical cost	$17,057	$9,408	$21,753	$26,828	$12,471	$13,704	$5,296	$7,451	$654	$25,145

every 14 years) and the infrequent need for surgical intervention (0.06%/year) on conservative treatment, the additional 80% reduction in stone recurrence rate achieved with drug treatment may not justify the cost and side effects of drug treatment.

For recurrent stone formers, conservative therapy was also the least costly strategy in all countries except the UK, because of the high cost of medication compared with the relatively low overall cost of a stone recurrence (emergency visits and surgery). However, the high rate of stone recurrence associated with conservative therapy (one stone every 3 years) may be unacceptable despite the low cost. In countries with low medication costs, such as Switzerland and Turkey, the cost difference between empiric and conservative therapy is small; indeed, in the UK where medication costs are only $29/patient/year, empiric therapy is the most cost effective strategy. Because the likelihood of needing surgical intervention is just over 2% annually, even when the stone recurrence rate is as high as 30%, it is the cost of medication that drives the model because it requires most or all patients to take medication on a daily basis.

One-way sensitivity analyses showed that stone recurrence rates must exceed one stone/patient/year before empiric therapy is cost superior to conservative therapy in all countries except the UK and Switzerland (where stone recurrence rates must exceed only 0.12 or 0.67 stones/patient/year, respectively). Furthermore, the additional cost of the metabolic evaluation prevents a strategy of directed medical therapy from ever becoming more cost effective than conservative therapy. In most countries, medication costs must decrease or surgical costs must increase in order for empiric therapy to reach cost equivalence with conservative therapy.

In contrast to our study, other groups have found drug therapy to be cost effective [3, 4, 5, 6, 7]. Parks and Coe estimated cost savings of $1,162–$3,162/patient/year with medical therapy in the US assuming a remission rate of 83% for medication [4]. Robertson compared the cost of medical therapy with no treatment in the UK and established that a medication regimen associated with a 50% reduction in the risk of stone recurrence and a cost of £8/year in patients with a stone recurrence rate of 0.2 stones/patient/year would result in cost savings of £38/year [5]. Tiselius assumed a baseline stone recurrence rate of 0.3 stones/year, medication costs of $220/year and a cost per stone episode of $2,500 in the Swedish healthcare system, and determined that initiation of a medication known to produce a 50% reduction in stone recurrence rates would result in cost savings of $375/year [3]. Finally, Strohmaier and Hörmann calculated an annual cost savings of 333.1 million marks in Germany for a prophylactic regimen associated with a 40% risk reduction in patients with an annual stone recurrence rate of 40% [6].

Chandhoke used a cost model to determine the stone recurrence rate at which medical prophylaxis becomes cost effective. At a recurrence rate of 0.3–4.0 stones/year, he calculated that the cost of medical evaluation and treatment became equivalent to conservative therapy (no drug) [7].

Careful analysis of previous studies, however, reveals several assumptions that may bias cost in favor drug treatment. In most cases, the benefit derived from conservative measures alone, which are considerably less costly than drug treatments, was not taken into account. As such, the reduction in stone recurrence rates associated with drug strategies likely included that attributable not only to drugs but to conservative dietary measures as well. Indeed, Hosking and colleagues found no stone growth or new stone formation in 58% of patients treated with dietary modification alone, among patients with mixed metabolic causes (71% with hypercalciuria and 47% with hyperuricosuria), underscoring the benefit of conservative dietary measures only in reducing stone recurrence rates [8]. In addition, some of the studies mentioned above relied on costly medical evaluations to determine drug therapy, thereby further adding cost that was not accounted for in the cost analyses. Furthermore, there is evidence that empiric therapy may be effective in reducing stone formation without the added cost of a metabolic evaluation [12, 14, 15, 16, 17]. On the other hand, with this strategy (empiric therapy), patients without metabolic abnormalities are subjected, perhaps unnecessarily, to drug treatment. Lastly, many of these studies fail to take into account the finding that not all recurrent stones cause symptoms or require surgical intervention. Indeed, our search of the literature suggested that only 10–20% of patients actually become symptomatic from a new stone and only half of the symptomatic patients ultimately require surgical intervention [9, 10, 11]. Thus, the cost of conservative therapy may be overestimated in studies that assume that all stone recurrences require surgical intervention [7].

The most important determinant of cost effectiveness in our model is the relative cost of medication and surgical therapy. In countries where the cost of surgery and physician reimbursement are heavily regulated, such as the U.S., strategies involving drug therapy are not cost effective. Medication cost, however, is unregulated, and therefore costly medications require high out-of-pocket expense by the patients themselves. In contrast, insurers as well as the Centers for Medicare and Medicaid Services (government sponsored insurer) dictate reimbursement rates for services including hospitalization, surgical procedures and physician fees, leading to a disproportionately higher cost for medication than surgery when taking into account the relative frequency of medication use (daily) and the infrequency of surgery (0.6–2.5% annually).

The obvious limitation of any study comparing costs of therapy in different healthcare systems is the variation in the degree of regulation and subsidization of services. As such, "cost effectiveness" of treatment strategies depends on whose point of view is assumed, the patient, the payer or the provider. Differences from country to country in the cost of surgical treatment or medication are primarily the result of differences in the degree of subsidization of services by healthcare systems. The nearly 20-fold difference in the cost of SWL, ureteroscopy and medication among different countries is evidence that subsidization plays a significant role in determining costs of the various strategies for managing nephrolithiasis (Table 1). Any analysis attempting to evaluate the cost effectiveness of stone management has to take into account these artificial differences in cost. Indeed, cost effectiveness is healthcare system-specific, and comparison among different treatment strategies may be best performed within a single healthcare system.

The advantage of our decision tree model for cost effectiveness analysis is that we can apply data from individual institutions, patients and medications in order to determine the cost effectiveness of any treatment strategy in a particular situation. Our model offers a unique opportunity to compare different treatment strategies for medical evaluation and treatment of nephrolithiasis regardless of healthcare system. Indeed, as new medications are developed, the cost effectiveness of treatment regimens that include them can be assessed.

We acknowledge some limitations of our study. In our model, we assumed that the severity of stone disease was comparable among the various trials of stone prevention, a factor that can influence the response to treatment, and may have affected the recurrent stone formation rates from different trials on which the assumption of risk reduction for various treatment strategies was based. Furthermore, we considered only comprehensive metabolic evaluation in conjunction with drug therapy since we had only the individualized costs from each country based on this approach. A simplified metabolic evaluation, at lower cost but similar efficacy, could yield different results. A previous analysis found that simple metabolic evaluation and medical therapy was less costly, but of comparable effectiveness, compared with comprehensive metabolic evaluation and treatment [13]. This analysis, however, found that simple metabolic evaluation was not as cost effective as empiric or conservative therapy. Finally, although cost models provide valuable information to healthcare providers regarding treatment strategies, the decision as to how to manage a patient after a stone event should ultimately be left to the well-informed patient and his/her physician.

Conclusions

In all but one country (UK), drug treatment strategies are much more costly than conservative treatment, although they are associated with good control of stone formation. The relatively low cost of surgery (due to infrequent need for intervention) compared with medication (used daily) accounted for the lower cost of dietary therapy. The differential resource allocation to different components of a healthcare system (i.e. subsidized medication versus surgical treatment) determines the cost effectiveness of various treatment strategies.

References

1. Pearle MS, Curhan GC, Calhoun EA (2004) Urolithiasis. In: Litwin MS, Saigal CS (eds) Urologic diseases in America. US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, NIH publication no. 04-5512. US Government Publishing Office, Washington, p 3
2. Pearle MS, Roehrborn CG, Pak CY (1999) Meta-analysis of randomized trials for medical prevention of calcium oxalate nephrolithiasis. J Endourol 13: 679
3. Tiselius H-G (2000) Comprehensive metabolic evaluation of stone formers is cost effective. In: Rodgers AL, Hibbert BE, Hess B, Kahn SR, Preminger GM (eds) Urolithiasis 2000, Proceedings of the 9th International Symposium on Urolithiasis, Cape Town, South Africa. University of Cape Town Press Cape Town, p 349
4. Parks JH, Coe FL (1996) The financial effects of kidney stone prevention. Kidney Int 50: 1706
5. Robertson WG (2000) The economic case for the biochemical screening of stone patients. In: Rodgers AL, Hibbert BE, Hess B, Kahn SR, Preminger GM (eds) Urolithiasis 2000, Proceedings of the 9th International Symposium on Urolithiasis, Cape Town, South Africa. University of Cape Town Press Cape Town, p 403
6. Strohmaier WL, Hormann M (2000) Economic aspects of urolithiasis (U) and metaphylaxis (M) in Germany. In: Rodgers AL, Hibbert BE, Hess B, Kahn SR, Preminger GM (eds) Urolithiasis 2000, Proceedings of the 9th International Symposium on Urolithiasis, Cape Town, South Africa. University of Cape Town Press Cape Town, p 406
7. Chandhoke PS (2002) When is medical prophylaxis cost-effective for recurrent calcium stones? J Urol 168: 937
8. Hosking DH, Erickson SB, Van den Berg CJ, Wilson DM, Smith LH (1983) The stone clinic effect in patients with idiopathic calcium urolithiasis. J Urol 130: 1115
9. Keeley FXJr, Tilling K, Elves A, Menezes P, Wills M, Rao N et al. (2001) Preliminary results of a randomized controlled trial of prophylactic shock wave lithotripsy for small asymptomatic renal calyceal stones. BJU Int 87: 1
10. Glowacki LS, Beecroft ML, Cook RJ, Pahl D, Churchill DN (1992) The natural history of asymptomatic urolithiasis. J Urol 147: 319
11. Streem SB, Yost A, Mascha E (1996) Clinical implications of clinically insignificant store fragments after extracorporeal shock wave lithotripsy. J Urol 155: 1186
12. Ettinger B, Pak CY, Citron JT, Thomas C, Adams-Huet B, Vangessel A (1997) Potassium-magnesium citrate is an effective prophylaxis against recurrent calcium oxalate nephrolithiasis. J Urol 158: 2069
13. Lotan Y, Cadeddu JA, Roehrborn CG, Pak CYC, Pearle MS (2004) Cost-effectiveness of medical management strategies of nephrolithiasis. J Urol 172: 2275
14. Ettinger B, Citron JT, Livermore B, Dolman LI (1988) Chlorthalidone reduces calcium oxalate calculous recurrence but magnesium hydroxide does not. J Urol 139: 679
15. Laerum E, Larsen S (215) Thiazide prophylaxis of urolithiasis. A double-blind study in general practice. Acta Med Scand 215: 383
16. Wilson DR, Strauss AL, Manuel MA (1984) Comparison of medical treatments for the prevention of recurrent calcium nephrolithiasis. Urol Res 12: 39
17. Robertson WG, Peacock M, Selby PL et al. (1985) A mulitcentre trial to evaluate three treatments for idiopathic calcium stone disease: a preliminary report. In: Schwille O, Smith L, Robertson WG, Vahlensieck W (eds) Urolithiasis and related clinical research. Plenum Press, New York, p 545

18. Trinchieri A, Ostini F, Nespoli R, Rovera F, Montanari E, Zanetti G (1999) A prospective study of recurrence rate and risk factors for recurrence after a first renal stone. J Urol 162: 27

19. Yagisawa T, Chandhoke PS, Fan J (1999) Comparison of comprehensive and limited metabolic evaluations in the treatment of patients with recurrent calcium urolithiasis. J Urol 161: 1449