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Factors Influencing the Outcome of Extracorporeal Shock Wave Lithotripsy in the Management of Salivary Calculi

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Objectives/Hypothesis: To identify the factors that affect outcome (stone clearance, partial clearance without symptoms, and residual stone with symptoms unchanged) of extracorporeal shock wave lithotripsy (ESWL). To develop and validate a predictive model for outcome of treatment.

Study Design: Prospective controlled trial.

Methods: There were 142 salivary calculi (78 submandibular, 64 parotid) entered into a prospective clinical trial of ESWL. The results were analyzed and a predictive model generated, which was validated using a second group of patients treated by the same technique.

Results: ESWL achieved complete success (stone and symptom free) in 67 (47.15%) of cases (submandibular 28/78, 35.9%; parotid 39/64, 60.9%). Partial success (residual stone and symptom free) was obtained in a further 49 (34.5%) (submandibular 29/78, 37.2%; parotid 20/64, 31.3%). Failure occurred in 26 (18.3%) of cases (submandibular 21/78, 26.9%; parotid 5/64, 7.8%).

Conclusions: ESWL can eradicate salivary calculi but its effectiveness is dependant mainly on size of the stone. Using a regression analysis model stone clearance can be reliably predicted based on stone size. A less important factor is the radiodensity of the stone, whereas a greater proportion of parotid calculi are eliminated by ESWL than submandibular calculi.

Key Words: Salivary, calculi, lithotripsy, outcome.

Level of Evidence: 2b

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INTRODUCTION

Renal lithotripsy rapidly became an established technique following early reports of a 90% stone-free rate, and by 1989 <5% of cases required surgical intervention. The high success rate coupled with a two orders of magnitude reduction in the risk of a major complication or death relative to surgery remain major advantages of the technique.

The technique was later successfully applied to biliary calculi with minimal morbidity and stone free rates of up to 91%. It also had the advantage of being performed on an outpatient basis with only intravenous analgesia. A further use was in pancreatic stones with fragmentation rates of 54% to 100% and complete duct clearance in 46% to 73%.

The first use of a lithotripter for the management of salivary calculi utilized a renal lithotripter (Piezolith 2300; Wolf Ltd., Knittlingen, Germany) and reported a 50% cure rate.[1] The subsequent development of dedicated sialolithotripters, such as the Minilith (Storz Minilith SL-1; Storz Medical, Kreuzlingen, Switzerland) with improved sonographic targeting, mobile therapy heads, and small shock wave foci has reduced morbidity and provided ease of use. In the last 10 years several large studies have shown extracorporeal shock wave lithotripsy (ESWL) to be effective in the management of salivary calculi.[2–7] However, it is unclear as to the relative importance of various factors (e.g., affected gland, stone size, duration of symptoms) on outcome.

One factor that appears important is the gland in which the stone is situated (Table I). A recent multicenter study of 2,102 cases reported a stone clearance rate for parotid calculi of 69.8% as compared to 40.8% for submandibular calculi.[7] Possible explanations for this variation relate to the anatomical configuration of the duct, constitution of saliva, and practical issues, such as the ease with which the parotid stone can be identified

TABLE I.
Summary of Studies That Identified One or More Factors Predictive of the Outcome of Extracorporeal Shock Wave Lithotripsy Using Dedicated Sialolithotripters.

Author	Year	Age	Sex	Gland	Side	Duration of Symptoms	Stone Size, mm	Site	No. of Shock Waves	No. of Treatments
Iro et al.[1]	1992	—	—	P	—	—	—	—	—	—
Hessling et al.[12]	1993	—	—	P	—	—	—	—	—	—
Kater et al.[3]	1994	—	—	P	—	—	<7	—	—	—
Gutman et al.[11]	1995	—	—	—	—	—	—	—	Y*	—
Yoshizaki et al.[13]	1996	—	—	—	—	—	<7	—	—	—
Ottaviani et al.[2]	1996	—	—	P	—	—	<7	—	—	—
Ottaviani et al.[8]	1997	—	—	P	—	—	<7	ID	—	—
Iro et al.[10]	1998	—	—	P	—	—	—	—	—	—
Reimers et al.[14]	2000	—	—	P	—	—	—	—	—	—
Kulkens et al.[15]	2001	—	—	—	—	—	<10	ID	—	—
Schlegel et al.[16]	2001	—	—	P	—	—	<10	ID	—	—
Escudier et al.[4]	2003	—	—	P	—	—	<7	—	—	—
Zenk et al.[5]	2004	—	—	P	—	—	N	—	N	R
Capaccio et al.[9]	2004	≤46	N	P	N	N	<7	ID	<2000	<6
Eggers et al.[17]	2005	N	N	P	—	—	N	N	—	R
Schmitz et al.[6]	2008	—	N	P	—	—	N	—	—	—

*Positive correlation with protein content >20%.
P = parotid; ID = intraductal (only in relation to submandibular calculi; N = no relationship; R = reducing chance of cure.

and targeted sonographically.[7] The parotid duct has no sharp bends and follows a descending path so that the flow of saliva is assisted by gravity, unlike the submandibular duct. Finally, the submandibular secretions are rich in mucus and more viscous than the serous parotid saliva.

To date exogenous factors have been cited as being more important to outcome than the composition of the calculi[5] in view of the lower cure rates for submandibular when compared to parotid calculi. The rationale for this view is that the combination of the ascending duct and viscous (seromucous) saliva in the submandibular gland promote the impaction of the calculus in the duct wall. A similar situation is encountered in renal calculi where ESWL of renal pelvic stones is more successful than that of ureteral calculi. Stones in the ureter were often impacted and the shock waves were not able to detach them into the lumen.

Attention has been drawn to the size of the stone as a prognostic factor for successful lithotripsy[4,8] as well as the age of the patient, intraductal (as opposed to hilar or intraglandular) location, number of therapeutic sessions, and number of shock waves delivered.[9] The only factor to have been cited by more than one author is the size of the stone, but these findings have been disputed.[5,10]

Similarly, whereas Gutmann et al.[11] demonstrated a positive correlation between a high protein composition (>20%) as demonstrated by infrared spectroscopy and the number of shock waves needed for successful therapy, these findings are in contrast to those of Iro et al.[1,10] where no statistically significant correlation was noted.

The aim of this study was to assess both biological (age and gender of patient, site, duration of symptoms, size, and radiodensity of the stone) and treatment factors (power and number of shock waves) on the outcome of salivary lithotripsy in both the submandibular and parotid glands.

MATERIALS AND METHODS

In the period of 1996 to 2004 a total of 142 patients were recruited for the study as agreed to by the local ethics committee. This included 42 patients who had previously been analyzed as part of an assessment of the efficacy of the technique.[4] The selection criteria applied are shown in Table II.

The test group consisted of 78 submandibular and 64 parotid patients with salivary stones. If treated conventionally these patients would have undergone gland removal. The diagnosis was established by ultrasound and sialographic examination. The characteristics of the study group with respect to age, duration of symptoms, size of calculus, and radiodensity is summarized in Table III. Most patients (95%) complained of painful swelling of the gland (mealtime syndrome).

Patients with submandibular stones were randomly assigned to one of four groups that received either 15,000 or 30,000 shock waves at a shock wave pressure setting of either 4 (25 MPa) or 6 (36 MPa).

TABLE II.
Selection Criteria for Extracorporeal Shock Wave Lithotripsy.*

Inclusion Criteria	Exclusion Criteria
Symptomatic disease	Stones amenable to simple intraoral surgery
Exact sonographic location of concretions	Stones amenable to radiologically guided basket retrieval
	Calculi not readily identifiable by ultrasound
	Patients with blood dyscrasias or hemostatic abnormalities
	Patients who are pregnant
	Patients who have undergone stapedectomy or ossicular repair
	Patients with cardiac pacemakers

*Escudier et al. (2003).

TABLE III.
Characteristics of Study Groups by Gland, Mean, and Range.

Characteristic	Submandibular	Parotid
Number of calculi	78	64
Mean age, yr (range)	45 (10–78)	47 (30–72)
Mean duration of symptoms, yr (range)	4.6 (0.25–50)	4.2 (0.25–22)
Mean size, mm (range)	8.5 (2.5–30)	6.16 (3–11)
No. of radiopaque stones (%)	74 (94.8)	33 (51.6)

TABLE IV.
Overview of Treatment Outcome for Extracorporeal Shock Wave Lithotripsy in 142 Cases.

		Site of Stone	
Outcome	Overall (%), n=142	Submandibular (%), n=78	Parotid (%), n=64
Cured	67 (47.2)	28 (35.9)	39 (60.9)
Partial success	49 (34.5)	29 (37.2)	20 (31.3)
Failure	26 (18.3)	21 (26.9)	5 (7.8)

The number of cases required to demonstrate a statistically significant result at the 5% level was 20 per group. Patients with parotid stones received maximal treatment in the form of 30,000 shock waves delivered at a pressure setting of 6 (36 MPa). Each patient was followed up clinically and outcome determined at 3 months after treatment by ultrasound and sialographic evaluation.

Technique

ESWL was usually undertaken on an outpatient basis, normally with a rest period of at least 1 week between treatment sessions.[4] However, if the patient lived far from the treatment center, then treatment was given on alternate days despite increased morbidity.[4] Treatment was undertaken with the patient semireclined in a dental chair (Fig. 1) and lasted about 1 hour with no analgesia required. The shock wave focus of the sialolithotripter is 2.4-mm wide by 25-mm long, and ultrasound jelly is applied between the therapy head and the skin to prevent energy loss during transduction of the shock waves. An in-line ultrasound transducer (7.5 MHz, Sigma 1AC; Kontron Instruments, St. Quentin en Yvelines, France) provides continuous sonographic monitoring during treatment. Cotton wool is placed in the buccal sulcus to protect teeth in the line of the shock wave. Shock waves were delivered at a frequency of 2 Hz per second and the number of shocks provided per session was up to 5,000.

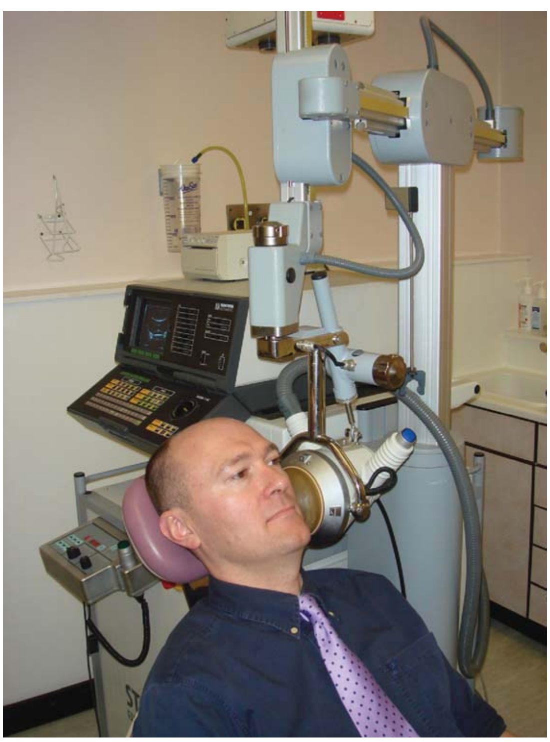

Fig. 1. Patient positioned for extracorporeal shock wave lithotripsy. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Statistical Analysis

Outcome (test variable) was categorized as cured (stone free and symptom free), partial success (residual fragments but no symptoms), and failed treatment (retained fragments and continuing symptoms). Analytical variables included age, gender, site (parotid/submandibular), duration of symptoms, size, radiodensity of stone, and number and pressure of shock waves. Data were analyzed by logistic regression with statistically significant results at the 5% level and a trend to significance at the 10% level.

To validate the results of the test group, a second cohort of patients treated with an identical lithotripsy machine, by a single operator at the University of Milan, were used for comparison. The cohort consisted of 238 patients (173 submandibular, 65 parotid) of whom 114 (64 submandibular, 50 parotid) were cured (rendered stone and symptom free) based on ultrasonographic evidence. Published results for this center (including this group of patients) indicates an overall cure rate (parotid and submandibular) of 45%.[9] The comparative group were used to validate a predictive model developed from the study group using the Hosmer and Lemeshow Goodness-of-Fit Test.

RESULTS

The overall results for the test group were cure 47.2% (67/142), partial success 34.5% (49/142), and failure 18.3% (26/142). However, the results were generally inferior in the submandibular gland (Table IV). The cure rate for each of the submandibular treatment groups (1, 2, 3, and 4) was 40.9%, 31.6%, 36.0%, and 33.3%, respectively (Table V). In contrast, 60.9% (n = 39) of parotid stones were cured, whereas 31.3% (n = 20) showed partial success, and in 7.8% (n = 5) of cases ESWL failed (Table IV).

In a univariate analysis factors predictive for cure were reducing stone size, radiolucency, and a stone in the parotid gland ($P < .05$). A weaker relationship (10%

TABLE V.
Outcome for Submandibular Gland Calculi by Treatment Group.

	Submandibular, n=78			
Outcome	Group 1 (%), n=22	Group 2 (%), n=19	Group 3 (%), n=20	Group 4 (%), n=17
Fully cured	9 (40.9)	6 (31.6)	7 (35.0)	6 (35.4)
Partially cured	9 (40.9)	11 (57.9)	6 (30.0)	3 (17.6)
Failure	4 (18.2)	2 (10.5)	7 (35.0)	8 (47.0)

TABLE VI.
Analysis of Predictors of Outcome for Extracorporeal Shock Wave Lithotripsy.

Variable	Fully Cured		Partially Cured	
	Univariate, OR (95% CI)	Multivariate, OR (95% CI)	Univariate, OR (95% CI)	Multivariate, OR (95% CI)
Age	1.01 (0.99-1.02)	1.02* (1.00-1.03)	1.01 (0.99-1.03)	1.01 (0.98-1.03)
Size	0.82† (0.72-0.93)	0.85† (0.75-0.96)	0.92* (0.83-1.00)	0.95 (0.85-1.05)
No. of shocks	1.04 (0.98-1.08)	0.99 (0.92-1.06)	1.05 (0.98-1.11)	0.98 (0.89-1.09)
Gender	1.05 (0.54-2.05)	1.06 (0.51-2.22)	0.96 (0.37-2.45)	0.99 (0.32-3.00)
Duration	0.99* (0.98-1.00)	0.99 (0.99-1.00)	0.99 (0.99-1.00)	1.00 (0.99-1.00)
Levels	1.39* (0.96-2.02)	1.22 (0.73-2.03)	0.63* (0.36-1.08)	0.39† (0.20-0.76)
Radiodensity	0.37† (0.17-0.82)	0.73 (0.28-1.89)	0.80 (0.22-2.93)	3.52 (0.52-23.49)
Site of stone (gland)	2.78† (1.41-5.51)	1.81 (0.51-6.46)	2.89* (0.94-8.96)	14.62† (1.74-122.43)E

*$P < .10$.
†$P < .05$.
OR = odds ration; CI = confidence interval.

association) existed between the magnitude and number of shocks ($P < .10$) and stone clearance. However, duration of symptoms, age, and gender of the patient were not statistically significant. When positive factors were entered into a multivariate model, only size proved an independent predictor for stone clearance (Table VI).

Factors Predicting for a Partial Success

Cured cases were then excluded from the analysis and the data re-evaluated for partial success (Table IV). Using a univariate analysis, stone size, level of shock wave, and gland involved (parotid) were associated with partial stone clearance when measured at the 10% level of significance ($P < .10$) but not at the 5% level ($P < .05$).

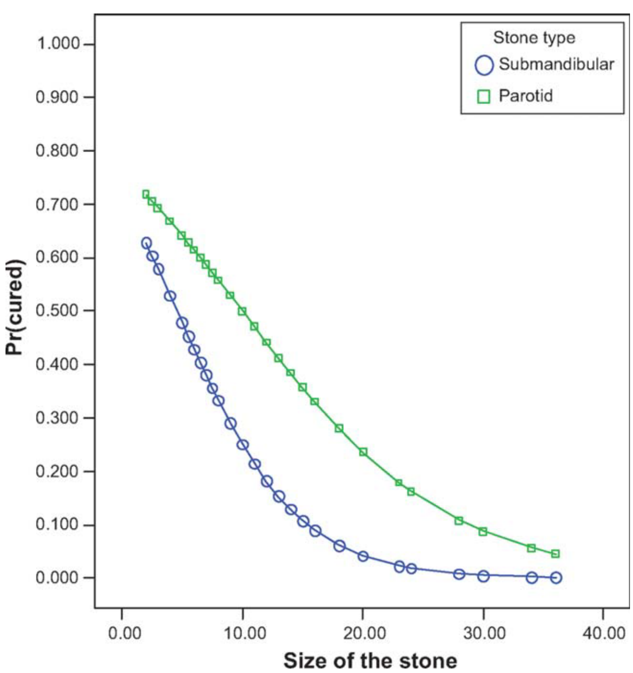

Fig. 2. Predictive model of probability of cure by gland for a given stone size based on London data. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

When positive factors were entered into a multivariate model, the level (power) of the shock wave and the gland type proved to be independent predictors of partial success ($P < .05$).

The Hosmer and Lemeshow Goodness-of-Fit Test was applied to the study group and the Milanese and showed similar patterns within the two separate cohorts of patients treated in different units (Fig. 2 and Fig. 3). Both the site (affected gland) and size of the stone have an important bearing on outcome. The test statistic was 6.45 at 11 *df* for both submandibular and parotid stones combined with a P value of .8416. Similarly, for submandibular stones alone the values were 14.11 at 12 *df* and for parotid stone were 7.82 at 8 *df*. The corresponding P values were .2940 and .4516, which indicates that the logistic model shows the same predictive levels in the Italian data.

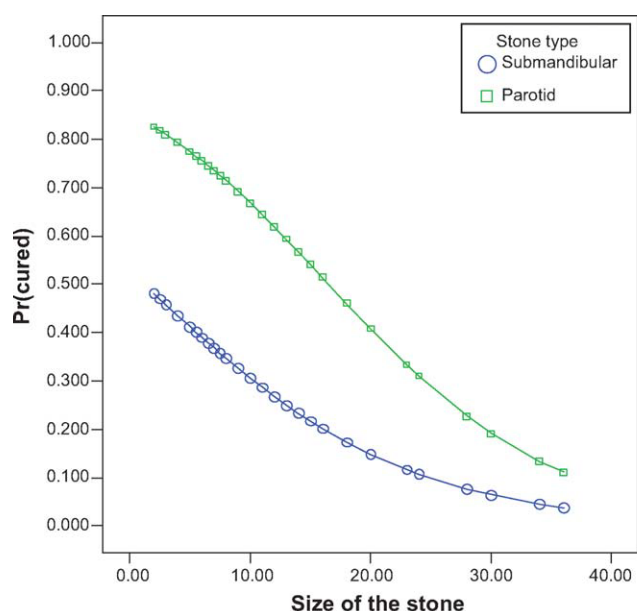

Fig. 3. Predictive model of probability of cure by gland for a given stone size based on Milan data. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

DISCUSSION

This study reinforces the findings of earlier studies (Table I). The stone site (parotid) and size are the main factors predicting for stone clearance, that is the smaller the stone the greater the prospect of cure.

In this study more parotid stones were eliminated than those in the submandibular gland. The parotid gland is a serous secreting gland, and a greater proportion of parotid stones are radiolucent. Although both the site (parotid) and the presence of a radiolucent stone, as in the case of renal and pancreatic calculi, are associated with stone clearance, they are not as important as stone size. The effect of stone size is shown in a number of ways. The higher cure rate in the study group for parotid calculi than for submandibular stones probably largely reflects the difference in mean stone diameter (parotid 6.1 mm vs. submandibular 8.5 mm). Additional factors mitigating for a higher clearance rate might include the greater parotid duct diameter and the fact that the parotid duct runs horizontally rather than uphill. A second example of the effect of stone size is seen in the fact that the mean stone size reduced as the degree of success increased (failure 10.81 mm, partial success 7.77 mm, and cure 6.45 mm). This is analogous to the renal situation where lithotripsy is the first line management for calculi $<$30 mm in diameter, whereas an upper limit of 7 mm has been proposed for salivary calculi.[2,9] In contrast others have found no relationship to stone size in a retrospective study.[5]

In circumstances of partial success, where the stone was broken sufficiently to allow saliva to pass but remained in the ductal system, then the magnitude of the shockwave was important to the outcome for submandibular stones. It is not clear if composition might render some stones more resistant to shock waves than others, as has been shown for renal calculi, or whether the retention of calculi is due to the dynamics of duct salivary flow. Technical issues, such as ease of targeting and the position of the stone within the ductal system, could also play a subsidiary role in determining the outcome for parotid stones, as they are easier to target. A similar finding has been reported in the case of renal calculi. However, all stones in this cohort were reliably identified on ultrasound and could be adequately targeted. Initial follow-up of cases with residual fragments indicates an increased risk of recurrent symptoms and the need for further intervention.

The technique has a very low morbidity as shown previously.[2–7] In this study an acute exacerbation of the infection occurred in 6.3% (9/142) cases.

The much lower success rate for ESWL in the management of submandibular calculi is low in comparison to other low-morbidity, gland-preserving techniques.[7] The technique is therefore best reserved for those submandibular cases that are not suitable for these treatments.[7]

CONCLUSION

ESWL is best suited to the management of fixed parotid calculi. Selection of cases will ensure the best prognosis and should also include consideration of the stone size and to a lesser degree the radiodensity of the calculus. Overall, although there is no maximum size of stone, the smaller the calculus the greater the probability of rendering the patient stone free. In those patients not rendered stone free, the probability of achieving symptomatic relief is related to the magnitude of the applied shock wave.

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