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IMPACT OF RETURNING FIRST-TIME RENAL STONE FORMERS TO DUTY ON UNITED STATES NAVY SUBMARINES

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SUMMARY

Until 1991 most submariners were automatically disqualified from submarine service after their first kidney stone. The basis for disqualification was the belief that these individuals would be at risk for recurrent episodes, which could result in mission compromising hazardous medical evacuations from deployed submarines. The purpose of this study is to examine the ramifications of returning submariners back to submarine duty following diagnosis of a renal stone.

We evaluated 190 first-time stone formers and prospectively followed them annually by interval history, urine, and radiologic studies. Seventeen (8.9%) study subjects had a recurrent stone. Average recurrence rate was 2.1 submariners per year. Time of follow-up was 776 man-years resulting in one disqualification per 46 man-years. One of these recurrences resulted in medical evacuation from a deployed submarine. Five of the recurrent stone formers had a history of lithotripsy (using ultrasound to disrupt kidney stones). Thirty-five percent (6/17) of the stone recurrences were found on annual follow-up studies and were asymptomatic at the time. Non-recurrent stone study subjects (n=173) had no statistically significant differences in urinalysis when compared to study subjects with stone recurrence. Upon comparison to reference values all subjects had elevated relative urine supersaturation (saturation relative to normal value) of calcium oxalate, brushite, monosodium urate and uric acid, as well as decreased urine vol-

ume, all of which increase the risk for renal stone occurrence (13, 15).

Results indicate that it is reasonable to return submariners to duty with a low expectation of complications and medical evacuations (MEDEVAC's). The current waiver policy is justified and appropriate. Those with a history of lithotripsy should not be granted waivers and all submariners should be encouraged to increase fluid intake. To further minimize the chances of a stone recurrence at sea, annual radiologic studies (KUB or renal tomograms without contrast) should be continued. This is supported by the high number (35%) of asymptomatic stones discovered at the annual follow-up.

INTRODUCTION

Until 1994 submariners with nephrolithiasis (kidney stones) were disqualified from submarine duty in the United States Navy (USN). The reason for this policy was a concern that these individuals were at a high risk for recurrent stone formation. Recurrences that occur at sea would compromise a submarine mission by necessitating medical evacuation (MEDEVAC). MEDEVACs are disruptive, compromise mission stealth, and are hazardous to conduct (14). Unfortunately, this policy resulted in the disqualification of approximately 40-60 submariners per year (12), a significant loss of experienced personnel, and disruption of the individual submariner's career. In addition, the policy incurred costs associated with training their replacements. It has been estimated that re-training costs amounted to approximately ten million dollars per year (Postma GN, Quinn AD. Point paper regarding the disposition of submariners with the diagnosis of urolithiasis. Letter from COMSUBGRU TWO to Chief of Naval Operations (OP-093), ltr

6000, Ser 004/1209 of 30 May 1989). In order to combat the loss of experienced personnel at a time when submarine retention rates were low, the Naval Submarine Medical Research Laboratory drafted a waiver policy that would allow submariners with renal stones to return to submarine duty. This policy was then accepted and can be found in the Standard Submarine Medical Procedures Manual revised in JUL 1994. Approval of the waiver was initially contingent upon subsequent validation by scientific study. An investigation to determine if there were any metabolic, anatomical, or physiological differences between those submariners with renal stone recurrence and those without was requested.

It is accepted that metabolic and environmental factors contribute to the risk of renal stone formation (13, 15). Metabolic changes that enhance the formation of stones include hypercalciuria, hypocitraturia, hyperuricosuria, and hyperoxaluria (elevated urine calcium, citrate, uric acid, and oxalate)(13). Environmental risk factors include low urine volume and high levels of urinary sodium, sulfate, and phosphorus (15). Several of these predisposing conditions can be modified by drug therapy, changes in dietary composition, and fluid intake (3, 22, 23). The USN currently evaluates, via urine and radiologic studies, all submariners who have a kidney stone for the above risk factors before returning them to duty (7, 8, 13, 15).

This study had the following objectives:

(1) To determine stone recurrence rates and medical evacuation rates in submariners returned to duty following a single renal stone.

(2) Determine if there are any differences in metabolic risk factors between recurrent and non-recurrent stone-formers.

(3) Determine if any predictive characteristics existed for recurrent renal stones in the submarine population.

MATERIALS & METHODS

SUBJECTS

Subjects were consenting active duty submariners with a single renal stone episode, no history of retained stones, and an administrative waiver to return to sea duty. The local Squadron Undersea Medical Officer recruited subjects after initial stone presentation. The minimum criteria for the initial diagnosis of a renal stone in subjects included: 1) a characteristic kidney stone pain pattern, such as unilateral flank pain radiating to the groin, 2) microscopic hematuria (at least 5 red blood cells per high power field), and 3) diagnosis of a renal stone by a Medical Officer. All three criteria had to be present to diagnose a renal stone. Actual stone passage or radiological evidence of a stone was not required as stones are frequently passed prior to medical evaluation (1).

Individuals excluded from the study included: those with retained

stones or multiple stones at initial evaluation. Females were not included in the study as they are not authorized for submarine duty.

Between January 1991 and July 1998, 322 submariners on active duty in the USN submarine force were granted waivers to return to duty. From this group, 190 consented to participate in the study. See Figure 1 for a diagrammatic explanation of how subjects entered the study and their subsequent disposition.

All procedures were reviewed and approved by the Committee to Protect Human Subjects of the Naval Submarine Medical Research Laboratory and of the Naval Medical Research and Development Command in compliance with Federal and Military regulations. Informed consent was obtained from each subject prior to enrollment into the study.

Figure 1: Disposition Of Renal Stone Study Subjects and Waivered Submariners

METHOD

Initial evaluation was conducted by the submariners' squadron medical officer. All eligible and consenting submariners with an administrative waiver to return to duty were given a brief medical assessment including: a history and physical examination, urine laboratory analysis, radiologic studies, and appropriate treatment for their stone. A standardized 24 hour urine test was collected from the study subjects and subjected to the Mission Pharmacal "Stone Risk Profile Test" in which the samples were analyzed for the metabolic, environmental, and physiochemical risk factors listed in Table 1 (8, 9, 13, 15). The test was a commercially available and scientifically validated kit from Mission Pharmacal, San Antonio, TX (9).

Table 1. Urinary risk factors and values for risk of renal stone formation

Metabolic (lower stone risk)	Environmental (lower stone risk)	Physiochemical (lower stone risk)
Calcium - (<250mg/d)	Volume - (>2 l/d)	Calcium Oxalate saturation (<2)
Oxalate - (<45mg/d)	Sodium - (<200mEq/d)	Brushite saturation - (<2)
Uric Acid - (<700mg/d)	Sulfate - (<30mM/d)	Monosodium Urate saturation (<2)
Citrate - (>320mg/d)	Phosphorus - (<1100mg/d)	Struvite saturation - (<75)
pH - (>5.5)	Magnesium - (>60mg/d)	Uric Acid saturation - (<2)

Abbreviations: mg/d, milligrams per day; l/d, liters per day; mEq/d, milliequivalent per day; mM/d, millimole per day

Study subjects received an intravenous pyelogram (IVP) to rule out the presence of structural abnormalities or retained stones (1). If no IVP was available, a non-contrast, computed renal tomogram and/or plain film roentgenogram (Kidney-Ureter-Bladder, KUB) with renal tomograms were considered an acceptable alternative. Correction of metabolic abnormalities and all medical care regarding the study subjects was left to the squadron physician.

Acceptance criteria for admission into the study was documented normal renal function (as evidenced by blood urea nitrogen and creatinine), no evidence of urinary tract infection (as evidenced by sterile urine culture), correction of all urinary metabolic abnormalities (i.e., low urine volume, hypercalciuria, hypocitraturia), and a normal radiologic study.

Subjects were then re-evaluated annually by the local squadron physician and the results forwarded to the study investigators. This

evaluation included: a history (inquiring whether any flank pain, hematuria, or renal stone passage had occurred in the past year), a standardized 24 hour urine test, (Mission Pharmacal "Stone Track Monitoring Test," for pH, total volume, sodium, potassium, creatinine, calcium, oxalate, uric acid, citrate) and a radiologic study (noncontrast renal computed tomogram (CT) or kidney-ureter-bladder (KUB) with tomograms) to identify retained stones. Military operational obligations such as deployment of up to 6 months made annual follow-up evaluations inconsistent. For this reason we did not statistically analyze any follow-up urine data. Annual evaluations continued until subjects were separated or retired from the Navy or they developed a stone recurrence.

STATISTICS

Recurrences were expressed as disqualifications per man-year involved in the study. Man-years for a subject is defined as the length of time between entry into the study and stone recurrence or until leaving submarine service or study termination. Urine labora-

Table 2. General characteristics of kidney stone subjects

Characteristic	Number (%)	Number (%)	Number (%)
	All Subjects	Non-recurrent stone subjects	Recurrent stone subjects
Enlisted	154 (81.1)	137 (79.2)	17 (100)
Officer	36 (18.9)	36 (20.8)	0 (0)
Average age at first stone (years)	30.2 ± 5.8	30.2 ± 5.9	30.3 ± 5.8
Average time in service (years)	13.6 ± 0.4	12.3 ± 6.9	13.6 ± 0.4 (n=11)
Mean duration of follow-up (years)	4.2 ± 1.8	4.3 ± 1.8	3.8 ± 2.0
Caucasian	181 (95.3)	166 (95.9)	15 (88.2)
African-American	9 (4.7)	7 (4.1)	2 (11.8)
Total	190 (100)	173 (100)	17 (100)

Table 3

Urine studies of Non-recurrent Stone Study Subjects compared to Recurrence Stone Study Subjects, with reference values

Test	Non-recurrent Stone Study Subjects (SD) (n=173)	Recurrent Stone Subjects (n=17)	Reference Values for decreased stone risk
Calcium (mg/d)	239.55 (114.17)	238.18 (98.96)	<250
Oxalate (mg/d)	36.17 (13.11)	35.47 (20.64)	<45.0
Uric Acid (mg/d)	689.31 (228.28)	692.53 (344.68)	<700
Citrate (mg/d)	516.18 (236.80)	546.06 (373.24)	>320
pH	6.07 (0.42)	5.93 (.41)	>5.5
Volume (l/d)	1.93 (1.02)	1.42 (.92)	>2
Sodium (meq/d)	190.42 (78.10)	156.29 (66.93)	<200
Sulfate (mM/d)	23.02 (8.11)	24.00 (11.28)	<30
Phosphorus (mg/d)	1,061.97 (375.28)	1036.84 (468.58)	<1100
Magnesium (mg/d)	106.73 (39.86)	109.47 (51.54)	>60
Relative Supersaturation:			
Calcium oxalate	2.14 (1.27)	2.93 (1.77)	<2
Brushite	2.23 (1.80)	2.73 (1.85)	<2
Monosodium urate	3.98 (3.30)	4.53 (2.40)	<2
Struvite	25.40 (95.20)	16.50 (21.40)	<75
Uric Acid	2.01 (1.78)	3.25 (2.32)	<2
Creatinine (mg/d)	1,768.34 (450.62)	1871.94 (944.18)	
Potassium (mEq/d)	55.17 (22.26)	55.17 (26.41)	
NH ₄ (meq/d)	38.64 (14.54)	38.64 (18.18)	

Values are the mean and standard deviation for 24-hour urine samples collected from male subjects with kidney stones and those with a kidney stone recurrence. Group differences were analyzed using Student's *t* test. Tests are two-tailed and *p* values < .05 are significant after Bonferroni correction for multiple Student's *t*-test.
* = denotes significance.

tory values were calculated for each variable as means and standard deviations (5). Statistical significance between groups was tested using paired Student's *t* test with a Bonferroni correction to account for multiple *t*-tests. All tests are two-tailed and the alpha level for each was set at < 0.05.

RESULTS

Subjects

Figure 1 and Table 2 present population demographics, length of follow-up, and study characteristics. Seventeen study subjects (17/190 or 8.9%) had recurrent stones during the study period. The mean duration of follow-up for study subjects was calculated as the difference between date of initial stone presentation and time of analysis (July 1998). 35% (6/17) of those disqualified had asymptomatic retained renal stones discovered radiographically.

Urine Studies

Table 3 shows the results of the initial 24-hour urine analysis for recurrent stone subjects and non-recurrent stone subjects with reference values. There was no statistically significant difference between the urinalysis of the recurrent stone study subjects and the non-recurrent stone study subjects.

Recurrence and MEDEVAC Rates

Stone recurrence rates per man-year can be found in Table 4. Annual recurrence rates were determined by dividing the number of recurrent stone formers per year by the number of study subjects followed at that time (i.e. the number at risk for recurrence). There were 17 disqualifications per 776 man-years, or one disqualification per 46 man-years. Only one study subject was MEDEVAC'd over the duration of this study. This was one MEDEVAC per 776 man-years.

DISCUSSION

The results of this prospective observational study suggest a low renal stone recurrence rate for first-time renal stone forming submariners. Submariners who were returned to active duty in the submarine force following the diagnosis of a presumed renal stone and correction of potential stone-forming risk factors did not significantly impact the submarine force mission. Prior to this study, the U.S. Navy Submarine Force was concerned that allowing these submariners to return to sea would result in an increase in MEDEVACs for recurrent renal stones. MEDEVACS are not only hazardous to the patient and the personnel involved in the transfer, but they may also negatively

Table 4

Renal stone recurrence rates for study subjects by year

YEAR	91	92	93	94	95	96	97	98	TOTAL
Number joining study	25	54	41	33	18	17	2	0	190
Number leaving study (all reasons-see Figure 1 for breakdown)	0	0	1	4	22	24	15	9	75
Recurrent stones	0	0	1	3	3	5	2	3	17
									Mean 2.1/yr
Number followed in study	25	79	119	148	144	137	124	115	
Cumulative Man-years	0	25	104	223	371	515	652	776	776
Annual recurrence rate	0.0%	0.0%	0.8%	2.0%	2.1%	3.6%	1.6%	2.6%	Mean 1.6%/yr

impact a submarine's operational mission.

It appears the incidence of nephrolithiasis in submariners is similar to that of the general civilian population. The Consensus Conference for Prevention and Treatment of Kidney Stones cites annual rates of 7 to 21 renal stones per 10,000 patients (0.07 to 0.21%) (3). Scott (16) states that various southern states have annual rates of 4.3 to 19.25 renal stones per 10,000 patients (0.04 to 0.19%). Another source (6) gives a lifetime prevalence for renal stones at 3-12% and an annual incidence of 10 per year per 10,000 for first-time renal stone formers. It appears that the average stone incidence in civilians is about 0.04 to 0.20% per year. Incidence in the submarine force is 0.14% per year with the assumption that the average size of the entire submarine force is 35,000 with an average of 50 renal stone disqualifications per year. Thus it appears that the baseline incidence of renal stones in the USN submarine force is comparable to that reported in the civilian literature.

One other objective of this study was to identify potential risk factors for renal stone recurrence. Three factors may be predictive of renal stone recurrence in submariners: relative super-saturation of urine metabolites, low urine volume, and lithotripsy. A comparison of non-recurrent stone study subjects with the recurrent stone study subjects did not demonstrate any statistically significant differences in demographics or urine values. However, when each of these two groups are compared to the reference values, one notes low urine volumes, and elevated relative supersaturations of calcium oxalate, brushite, monosodium urate, and uric acid.

Additionally, there was a high rate of recurrence within the subgroup that underwent lithotripsy for their first renal stone. All five stone-forming submariners who had a history of lithotripsy had a recurrence. A number of studies have confirmed that a history of lithotripsy is a risk factor for stone recurrence (2). Fine and Pak (4) noted that more than half of the subjects (N = 26) with clinically insignificant fragments remaining in the urinary tract following lithotripsy who did not continue on medical therapy demonstrated significant stone growth during follow up, suggesting that these fragments were not clinically insignificant. Thus it appears that renal stone occurrence treated with lithotripsy is a strong risk factor for stone recurrence.

The limitations of this study are comparable to those of other follow-up studies. Nonstandardization of laboratory tests (such as urine cultures, radiologic tests, serum blood urea nitrogen and creatinine) used to evaluate study subjects and missing data elements were present. A second weakness in the study design was the lack of control or monitoring for diet and fluid intake. This was unavoidable as the study subjects returned to submarine duty were in the same conditions and environment as other submariners and diet control would have been difficult to implement. A third weakness was the inability to determine if the 32 submariners who declined participation were unique in any way, but as they did not sign consents for study participation we were unable to collect their data. A fourth limitation was subjects lost to follow-up due to retirement or separation from the USN. Lastly, special consideration should be taken whenever urine data are analyzed as there is a wide natural range of normal values for urinary constituents that increases the difficulty of detecting statistically significant differences.

While first-time stone formers in submarine service are at low risk for stone recurrence if urine abnormalities are corrected and can generally be returned safely to active duty, our data suggest that those treated with lithotripsy should be regarded as high risk for renal stone recurrence. Suggestions are as follows: 1) Those with a history of lithotripsy should be regarded as very high risk for renal stone recurrence (as all five stone-forming submariners who had a history of lithotripsy had a recurrence) and if the current trend continues they should be considered for disqualification from submarine service; 2) All submariners with a single renal stone without retained stones should be allowed to return to sea duty; 3) Continued annual follow-up is prudent, as close to one third of those terminated from the study had asymptomatic retained stones discovered by the annual follow-up exam; 4) Yearly radiologic studies (KUB or renal tomograms without contrast) should be continued to further minimize the chances of a recurrence at sea; 5) Additional study into the characteristics of those with renal stone recurrence may demonstrate other urinary abnormalities for use in screening submariners prior to receiving a waiver; and 6) All submariners with renal stones should be encouraged to remain well hydrated to decrease their risk for stone recurrence and all submariners should be encouraged to increase fluid intake to decrease their risk for initial stone formation.

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