THE VALUE OF PREOPERATIVE AND OPERATIVE FEATURES IN PREDICTING ELECTROLYTE DERANGEMENTS AFTER TRANSURETHRAL RESECTION OF PROSTATE; A RECEIVER OPERATOR CHARACTERISTIC CURVE ANALYSIS

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ABSTRACT

Background: Transurethral resection of prostate (TURP) is one of the commonest urological procedure. Despite tremendous advancements in the technique itself, electrolyte derangements are common, where as much as one third of patients develop the TUR-syndrome, resulting in significant morbidity and mortality.

Objective: Our aim was to analyse the predictive value of preoperative and operative features which could be used to develop a model for estimating the risk of electrolyte derangements following TURP.

Methods: This is a prospective case series study conducted at Urology Unit LRH where we included patients admitted for TURP between January 2014 and December 2015 (24-months). Record was made of patient age, comorbids, preoperative electrolytes (sodium/potassium), renal functions (urea/creatinine), procedure time (in minutes) and the volume of irrigation solution used. All patients were followed postoperatively by determining their electrolytes, renal functions, symptoms related to electrolytes derangement, early complications related to electrolytes derangements and mortality attributable to it.

Results: 93 patients were operated during the study period with an overall mean age of 65.16 years ± 5.49 SD. Comorbidities were present in 31 (33.3%) patients. Hypertension was the commonest comorbidity which was present in 18 (19.4%) patients. The overall preoperative mean serum sodium was 137.57 mmol/L ± 3.94 SD and mean serum potassium was 4.26 mmol/L ± 0.44 SD. Overall mean postoperative serum sodium was 134.63 mmol/L ± 4.45 SD, mean potassium was 4.17 mmol/L ± 0.41 SD. Overall length of stay was 2.59 days ± 0.92 SD with a mortality rate of 1.1%. In multivariate logistic regression analysis, the overall predictive value of comorbids, preop serum Na^+, K^+ and procedure length was determined. Sensitivity was 84.0%, specificity was 92.6%, positive predictive value was 80.7% and negative predictive value was 94.02%.

Conclusions: Preoperative presence of comorbids, preop serum Na^+ & K^+ and intraoperative procedure time and total volume of irrigating solution used are highly predictive of postoperative electrolyte derangements. Significant morbidity and mortality can be prevented if these factors are considered, particularly in a combined model.

Key Words: Benign prostatic hyperplasia, Transurethral resection of prostate, TUR-syndrome, preoperative prediction.

INTRODUCTION

Bladder outlet obstruction (BOO) is a common occurrence in the elderly male population, primarily related to benign prostate hyperplasia (BPH), approaching to 90% by the age of 85 years.[1] A diverse variety of treatment methods have been introduced over the last 20 to 30 years, ranging from medical management to open prostatectomy to laser vaporisation of the adenomatous prostate tissue.[2,3] The diagnostic tools involve clinical evaluation including a digital rectal examination (DRE), ultrasonography for residual volume and prostate size assessment, and the relatively newer methods of uroflowmetry and detrusor activity estimation.[4,5]

Despite tremendous advancements in urological techniques regarding management of BPH, TURP is still the gold standard surgical procedure and one of the most commonly performed.[6] Regional anaesthesia techniques, good intraoperative and postoperative monitoring and swiftness of the surgical technique all contribute to good surgical outcome.[7] However, regardless of advancement in TURP technique, some complications remain high in occurrence, namely, bleeding, postop urinary retention and electrolyte derangements.[8] The later of these complications, electrolyte derangements, have been notoriously associated with the development of the condition called TUR syndrome, which is defined as clinical manifestation of deranged serum electrolytes, particularly sodium which is found to be below 125 mmol/L.[9] Studies have suggested a multifactorial aetiology of TUR syndrome, where clinical features, comorbidities, preoperative fluid and electrolyte status,

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length of the procedure and the use of irrigation fluid have been cited a few of the causative factors.[1] Recently, Hahn RG[10,11] has developed a checklist to properly classify TUR syndrome postoperatively. Additionally, Fujiwara A et al[1] have used some operative features in order to predict the development of TUR syndrome, primarily using the prostate weight as is estimated on preop ultrasonography. It is a well-known fact that about 80% of patients undergoing TURP suffer from significant comorbidities.[12,13]

We aimed to evaluate the predictive value of combining preoperative clinical features and operative parameters in order to estimate the occurrence of electrolyte abnormalities, which could eventually lead to the development of TUR syndrome. Our secondary aim is to estimate the early postoperative complications including early mortality, which could be prevented by correctly identifying patients who will be at risk of developing TUR syndrome. Consequently, this would lead to reduction in significant morbidity and mortality.

METHODS

This is a prospective case series study conducted at Urology Unit LRH where we included patients admitted for TURP between January 2014 and December 2015 (24 months). The study was commenced after obtaining permission of the institutes ethical review committee. Informed consent was obtained from all patients included in the study.

Inclusion Criteria

- All patients between the ages of 50 and 85 years were included.
- Patients with American society of anaesthesiologists (ASA) grade I and IV.

Exclusion Criteria

- Patients with significant electrolyte or renal function derangement.
- Patients with prostate or bladder cancer.
- Patients with complicated BPH.
- Recurrent cases listed for reoperation.
- Patients with ASA grade V.

PROCEDURES

All procedures were performed under spinal anaesthesia. Glycine 1.5% was used as the irrigation solution at a height of 60 cm. A monopolar resectoscope of 22 or 24 French was used with continuous irrigation. A maximum procedure time of 60 minutes was used as the cut-off limit before which to end the procedure, as studies have shown that a procedure time of more than 60-minutes lead to a definitively higher incidence of postoperative complications.[1,14] At the end of the procedure, a three-way 20-French Foley's Catheter was used with constant normal saline irrigation for bladder washout for the initial 6-hours postoperatively.

Data Collection

Data was collected about patient demographics, such as age and symptoms duration. Clinical features recorded were the presence or absence of comorbidities. All comorbidities were also recorded separately under separate category such cardiovascular, endocrine, respiratory etc. Patient with simultaneous multiple comorbidities were also categorised separately. A preoperative serum sodium, potassium, serum creatinine and urea were determined one night before surgery. Those patients who had significant electrolytes or renal functional impairments were treated in consultation with a nephrologist. Intraoperatively, procedure time and the volume of irrigation fluid used were recorded. A postoperative serum sodium, potassium, creatinine and urea were determined at the 1st hour postoperatively, and if needed treatment for electrolyte derangements, were managed appropriately using intravenous mannitol and hypertonic saline (3%). Postoperative complications such the development of nausea and vomiting, headaches, confusion, seizures or cardiovascular complications such as ischemic changes and/or hypertension were appropriately managed and recorded.

A deranged electrolyte range was defined as serum sodium below 130 mmol/L or above 145 mmol/L, or, a serum potassium level of less than 3.5 mmol/L or above 5.5 mmol/L.

Data Analysis

Data was imported to and analysed using SPSS statistics version 22.0. Descriptive statistics are presented in mean ± standard deviations unless otherwise stated. An independent t-test was used to determine the significance of mean difference between various continuous variables for the absence/occurrence of electrolyte derangements. Finally, a receiver operator characteristic curve analysis was performed after conducting a binary logistic regression model using the occurrence of electrolytes derangements as the outcome variable. Sensitivity, specificity, positive predictive value and negative predictive values of the said variables were calculated.

RESULTS

Overall Patient Characteristics

93 patients were operated during the study period with an overall mean age of 65.16 years ± 5.49 SD. A mean duration of symptoms was recorded to be 32.40 months ± 14.76 SD. The overall mean procedure time was 36.70 minutes ± 8.02 SD and a mean average volume of irrigation solution used was 15.09 litres ± 4.62 SD.

Table 1: Comparative representation of descriptive variables for those with and without electrolyte disturbance after TURP

Clinical variable	No Electrolytes Derangements	Electrolyte Derangements (n = 25)
(n = 68)	Electrolyte Derangements	65.40 years ± 4.87
(n = 25)	32.41 months ± 15.00	32.36 months ± 14.38
Preop Na^+	139 mmol/L ± 2.95	133.68 mmol/L ± 3.71
Preop K^+	4.36 mmol/L ± 0.44	3.98 mmol/L ± 0.32
Procedure time	33.35 minutes ± 6.56	45.80 minutes ± 2.85
Volume of solution	13.21 litres ± 3.77	20.20 litres ± 2.26
Length of stay	2.15 days ± 0.47	3.80 days ± 0.76
Postop Na+	136.91 mmol/L ± 2.63	128.44 mmol/L ± 1.42
Postop K+	4.28 mmol/L ± 0.38	3.84 mmol/L ± 0.30

Table 2: Complications distribution

	No electrolyte disturbance (n=68)		Electrolyte disturbance (n=25)	
	Frequency	Percent	Frequency	Percent
Headache	—	—	15	60.0%
Nausea/Vomiting/ Abdominal pain	1	1.5%	16	64.0%
Confusion	1	1.5%	8	32.0%
Seizures	—	—	4	16%
Cardiovascular event (MI/CHF)	1	1.5%	1	4.0%
Mortality	—	—	1	4.0%

Table 3: Logistic regression predicting likelihood of electrolyte derangements based on the shown predictors

	B	S.E.	Wald	df	p	Odds Ratio	95% C.I. for Odds Ratio	
							Lower	Upper
Comorbids	-2.69	0.566	22.631	1	<0.0001	0.068	0.022	0.205
Procedure time	-0.302	0.063	22.985	1	<0.0001	0.740	0.654	0.837
Symptoms duration	0.000	0.016	0.000	1	0.988	1.000	0.969	1.032
Age	-0.060	0.046	1.722	1	0.189	0.942	0.861	1.030
Preop Na	0.434	0.089	23.552	1	<0.0001	1.544	1.295	1.840
Preop K	3.021	0.904	11.174	1	0.001	20.506	3.489	120.529
Preop Creatinine	0.179	1.071	0.028	1	0.867	1.196	0.147	9.762
Preop Urea	0.053	0.093	0.328	1	0.567	1.055	0.879	1.265
Volume of solution	-0.470	0.096	24.084	1	<0.0001	0.625	0.518	0.754
Constant	-27.016	27.50	0.965	1	0.326	0.000		

Comorbidities

Comorbidities were present in 31 (33.3%) patients. Hypertension was the commonest comorbidity which was present in 18 (19.4%) patients, followed in frequency by osteoarthritis in 15 (16.1%) patients, diabetes in 14 (15.1%), ischemic heart disease in 12 (12.9%) patients and COPD in 10 (10.8%) patients. Overall cardiovascular diseases were the commonest comorbidities. 24 (25.8%) patients suffered from 2 or more comorbidities.

Among those who developed electrolyte disturbances postoperatively, 19 (76.0%) cases were with comorbidities, with all of them having two or more comorbidities. Similarly, patients who did not develop electrolyte disturbances postoperatively, only 12 (17.6%) patients had comorbidities and only 5 (7.4%)

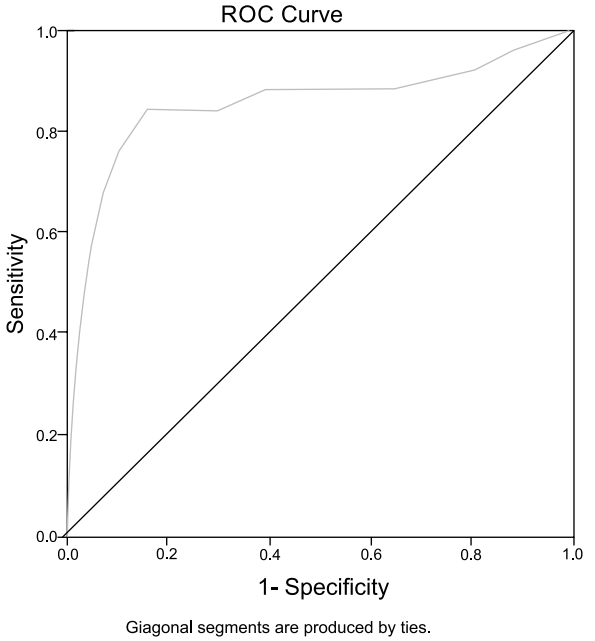

Fig 1: ROC curve for preoperative sodium levels and the development of electrolyte disturbance after TURP (AUC: 0.852, 95% CI: 0.743 to 0.961)

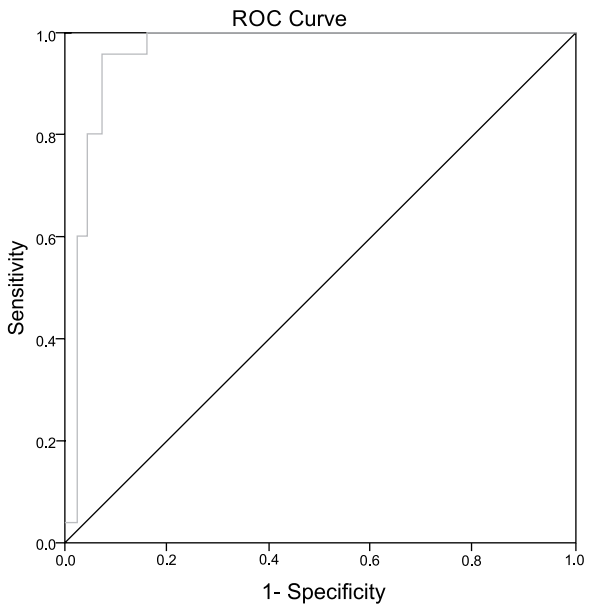

Fig 2: ROC curve for combined model of clinical, laboratory and operative predictors for electrolytes disturbance after TURP (AUC: 0.956, 95% CI: 0.914 to 0.999)

of them had two or more comorbidities concomitantly.

Serum Studies

The overall preoperative mean serum sodium was 137.57 mmol/L ± 3.94 SD, mean serum potassium was 4.26 mmol/L ± 0.44 SD, mean preop creatinine was 0.82 mg/dL ± 0.22 SD and mean preop urea was 10.89 mg/dL ± 2.59 SD.

Overall mean postoperative serum sodium was 134.63 mmol/L ± 4.45 SD, mean potassium was 4.17 mmol/L ± 0.41 SD, mean creatinine 0.88 mg/dL ± 0.22 SD and mean postop urea was 11.12 mg/dL ± 2.72 SD.

Length of stay and Complications

Overall length of stay was 2.59 days ± 0.92 SD with a mortality rate of 1.1% (n =1). There were 25 (26.9%) cases which were identified as suffering from acute electrolyte disturbance, primarily, significant hyponatremia (≤130 mmol/L). Only 1 patient out of these 25 was diagnosed as TUR syndrome according to the definition of a serum sodium ≤125 mmol/L. Table 2

Table 1 shows distribution of patients according to presence or absence of electrolyte disturbance, along with stratified descriptive statistics and complications.

Detailed Analysis

On chi-square analysis it was found that the presence of comorbidities was significantly associated with postoperative electrolytes derangements ($p < 0.0001$). The association was strong on analysis ($\Phi = 0.55$, Cramer's V: 0.55). Furthermore, it was observed that the presence of multiple concomitant comorbidities was significantly and strongly associated with the development of postoperative electrolyte derangements ($p < 0.0001$, Phi: 0.69, Cramer's V: 0.69). Patients with comorbidities, and especially those who were already on diuretics, angiotensin converting enzyme (ACE) inhibitors or those on oral hypoglycemic drugs and non-steroidal anti-inflammatory drugs (NSAIDs) were significantly more likely to have lower serum sodium and potassium levels as compared to those who did not have comorbids.

An independent samples t-test was run to see if differences exist between patients with or without electrolytes derangements in terms of various preoperative, operative and postoperative clinical parameters. Significant differences were noted between patient with electrolytes derangements and those without electrolytes derangements in terms of preoperative serum Na^+ (mean difference: -5.32, 95% CI: -6.79 to -3.85, $p<0.0001$, $t(91) = -7.18$,) , K^+ (mean difference: -0.38, 95% CI: -0.57 to -0.19, $p<0.0001$, $t(91) = -3.96$), operative procedure time (mean difference: 12.45, 95% CI: 9.75 to 15.15, $p<0.0001$, $t(91) = 9.15$) and volume of the irrigation solution used (mean difference: 6.99, 95% CI: 5.39 to 8.59, $p<0.0001$, $t(91) = 8.71$). No differences were observed for age (mean difference: 1.69, 95% CI: -0.85 to 4.24, $p = 0.19$, $t(91) = 1.32$), duration of symptoms (mean difference: -0.052, 95% CI: -6.95 to 6.84, $p = 0.98$, $t(91) = -0.015$), preoperative serum creatinine (mean difference: -0.008, 95% CI: -0.11 to 0.095, $p = 0.86$, $t(91) = -0.16$) and urea values (mean difference: -0.34, 95% CI: -1.55 to 0.86, $p = 0.57$, $t(91) = -0.56$). These results have shown that patients who developed significant electrolyte derangements had lower mean sodium and potassium values preoperatively as well as postoperatively.

Logistic Regression Analysis

In a multivariate logistic regression model, preoperative clinical features such as the presence of comorbidities, age, symptoms duration, preoperative Na^+, preoperative K^+, serum urea and creatinine and total length of procedure were tested against the development of postoperative electrolytes derangements. The logistic regression model was statistically significant, $\chi 2(9) = 65.35$, $p<0.0005$. The model explained 73.4% (Nagelkerke R2) of the variance in postoperative electrolytes derangements and correctly classified 90.3% of cases. Sensitivity was 84.0%, specificity was 92.6%, positive predictive value was 80.7% and negative predictive value was 94.02%. Of the nine predictor variables only four were statistically significant: comorbids, procedure length, preoperative sodium levels and the volume of irrigation solution used (as shown in Table 3). These predictor variables are of significant prognostic value as is shown in Table 3 with Odds ratio and 95% confidence intervals.

Receiver Operator Characteristic Curve Analysis

An ROC curve analysis as in figure showed that a combination of the above stated predictor variables was of high prognostic value as the area under the curve has reached 95.6% (95% CI: 0.914 to 0.99, $p<0.0001$). Individual ROC curve analyses also showed interesting characteristics of the predictor variables. For example, the presence of comorbids reached sensitivity of 76% and a specificity of 82.4% with an AUC of 79.2% (95% CI: 0.681 to 0.903, $p<0.0001$). Similarly, a cut-off value of preoperative serum sodium of 136.5 mmol/L had a sensitivity of 84.0% and specificity of 83.8% (AUC: 85.2%, 95% CI: 0.743 to 0.961, $p<0.0001$). The length of operative procedure was another variable highly predictive of the development of electrolytes derangements with a cut-off limit of 42.5 minutes with a sensitivity of 92.0% and specificity of 89.7% (AUC: 92.2%, 95% CI: 0.863 to 0.980, $p<0.0001$).

DISCUSSION

Electrolyte derangements and fluid overload following TURP are a common occurrence resulting in significant morbidity.[15] Mortality may result if the derangements are overlooked, as these patients have concomitant comorbidities, especially cardiovascular and respiratory which can lead to rapid decompensation.[16] Numerous pathophysiological mechanisms have been suggested for the development of electrolyte derangements and frank TUR-syndrome, the commonest of these are irrigation fluid absorption via open prostatic venous sinuses, high irrigation fluid pressures, prolonged procedure times, glycine toxicity, cell lysis, bacteraemia, and septicaemia as well as the use of hypotonic irrigation fluids.[11] The presence of concomitant comorbidities especially cardiovascular and respiratory, have been proposed as one of the inciting factors for the development of TUR-syndrome as well as electrolyte derangements.[15]

In our study the basic demographic features such as age and symptoms duration were comparable to other similar studies. In a study by Pasha MT et al[17] regarding the postoperative complications of irrigation fluids after TURP, it was found that mean age was 67.15 years ± 7.067 SD and electrolytes disturbances were observed in a total of 15.3% cases.[17] In our study electrolyte disturbances were noted in 26.9% of cases with an overall mean age of 65.16. Numerous studies have reported the incidence of electrolyte disturbances after TURP, which ranges from less than 10% to about 30%. Most authors have recommended the use of 1.5% glycine as an irrigation solution due to its relatively better isotonic properties and low load of glycine as well as better lesser diathermy interference, though some authors have also investigated sterile distilled water and found little evidence of benefit.[8,17,18] Despite the recommendations of experts for minimising incidence of electrolytes derangements, the incidence rates are still very high and it seems that merely following these recommendations will not reduce the incidence. It is imperative to state that preoperative clinical and laboratory parameters as well intraoperative features be kept in mind in order to segregate high risk patients in order to strictly monitor them.[8,19]

Hahn RG[20] in a detailed review of the pathophysiology of fluid absorption in endoscopic surgeries has presented a postoperative symptoms checklist with a cumulative score which could be used to predict the likelihood of significant electrolyte derangements and TUR syndrome. In another study by Fujiwara A et al[1], preoperative prostate weight estimation was used to predict postoperative clinical manifestations of significant electrolyte derangements and TUR syndrome.[1] They concluded that a prostate weight of ≥75 g was the cut-off limit with a sensitivity and specificity of 70%.[1] In our study, as is mentioned earlier, we tried to additionally test the predictability of preoperative clinical risk factors, laboratory parameters and intraoperative features. We not only evaluated the inter-relationship of these parameters individually but also developed a combined linear regression model where we tried to test the combined predictability of these factors. As is shown by our results, it is obvious that the presence of major comorbidities, a tendency towards lower levels of preoperative Na^+ and K^+, operative procedure length of more than 45 minutes and higher irrigation fluid volumes (cut-off: 13 litres) are all associated with electrolyte derangements after TURP. Comorbidities preoperatively are particularly important because patients with cardiovascular problems are usually on diuretic or the ACE inhibitors, which though not toxic in therapeutic doses, are frequently associated with lower serum Na^+ & K^+ values.[15,21] Similarly, the sulfonylureas in diabetics and several of the respiratory drugs are also associated with serum electrolyte derangements.[22,23] These characteristics makes an elderly male under an increased threat of a narrow margin for developing the TUR syndrome and other electrolyte abnormalities. Additionally, as is proven in numerous studies, operation length is linearly related to the risk of electrolytes derangements and hence an advice to keep the procedure time below 60 minutes.[15]

These results are comparable to the findings of Aziz W et al[15] study where they found significant differences for the incidence of comorbidities, preoperative laboratory electrolytes values, diuretic use, surgeons experience and volume of irrigation solution between those patients who developed post-TURP electrolytes derangements and those who did not.[15] In our study the major comorbid was hypertension and ischemic heart disease where maximum patients used diuretics for prolonged periods before surgery. Hence these preoperative features should be kept in mind whenever a patient with significant comorbid condition is put on list for TURP. Preoperative serum electrolytes, procedure time and volume of irrigation should be minimised. However, if these risk factors are present or if the intraoperative risk factors get out of hand, then postoperative monitoring should be vigilant and therapy should be initiated as soon as the patient shows symptoms of significant electrolytes abnormality or laboratory evidence of electrolytes disorder is at hand. These measures can significantly reduce the number of these cases and their sequelae.

Larger, randomised controlled trials are required to further elucidate the importance of the stated preoperative clinical, laboratory and intraoperative parameters. Further studies are also encouraged in establishing proper management guidelines.

CONCLUSION

Electrolytes abnormalities are very common following transurethral resection of prostate. Preoperative presence of comorbids, preop serum Na^+ & K^+ and intraoperative procedure time and total volume of irrigating solution used are highly predictive of postoperative electrolyte derangements. Significant morbidity and mortality can be prevented if these factors are considered, particularly in a combined model.

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