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New and contemporary markers of prognosis in nonmuscle invasive urothelial cancer

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Doctor! Will I be dry? Factors determining recurrence after vesicovaginal fistula repair

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Abstract

Objective: To evaluate various prognostic factors which determine outcome after surgical repair of vesicovaginal fistula.

Methods: The retrospective study was conducted at Koohi Goth Fistula Hospital, Karachi, and comprised data related to patients having undergone vesicovaginal fistula repair from January 2007 to June 2012. Multivariate analysis of the record was done using SPSS 19 software determining odds ratio with 95% confidence interval.

Results: Record of 640 patients were analysed with an overall success in 558(87.2%) cases. Multivariate analysis determined that the recurrence of vesicovaginal fistula was significantly related to multiplicity (9-fold recurrence risk), pre-operative size (10-fold recurrence risk for fistula >2cm compared to <1cm), secondary repair (5-fold risk) and duration of the fistula (3-fold risk). Interposition of flap and delayed reconstruction (between 6 weeks and 1 year) was related to successful surgical outcome. Age, parity, aetiology, route of repair and location of fistula were not significant ($p>0.05$ each) prognostic factors for recurrence.

Conclusion: Successful surgical repair of vesicovaginal fistula require careful evaluation of various factors, including number, size, previous attempts to surgical repair and duration of fistula.

Keywords: Prognostic factors, Recurrence, Surgical repair, Vesicovaginal fistula. (JPMA 65: 954; 2015)

Introduction

Vesicovaginal fistula (VVF), the most common among urogenital fistulas, is considered an obstetric morbidity estimated to affect more than two million women worldwide.¹ In industrialised countries, the incidence of VVF is very low where it arises mainly as a complication of pelvic surgeries or radiation therapy.^{2,3} On the other hand, in developing countries, VVF is a major problem that occurs as a consequence of neglected, prolonged or obstructed childbirth.⁴

Surgical repair is the only definitive treatment of VVF with a success rate as high as 85% to 95% with first surgical repair.⁵ Although open surgical repair is considered the gold standard treatment of VVF, its role has been challenged by recent studies which show that similar results (around 90% success rate) can be achieved by laparoscopic repair of VVF with the added advantage of minimum incision, less surgical trauma and early recovery in postoperative period.⁶⁻⁸ The same outcome has been achieved by robotic repair of VVF.⁹ However, due to lack of availability of expertise and long-term results of VVF repair by these minimally invasive techniques, open

surgical repair remains the treatment of choice for VVF.

VVF has significant impact on the patients not only physically but also socially and psychologically.¹⁰ Moreover, patients with VVF are poor and surgical repair of VVF poses significant economic burden on them. Due to these factors, patients undergoing surgical repair are anxious and concerned about the outcome. Therefore, pre- and post-operative counselling of the patients about the possible chances of successful VVF repair is very important.¹¹

In spite of large-scale research on VVF, there are very few studies addressing the factors which predict the possible outcome of surgical repair. The current study was planned to review characteristics of the patients, fistula and the surgical procedures in order to identify the factors helpful in determining the prognosis of surgical repair of VVF.

Patients and Methods

The retrospective study was conducted at Koohi Goth Fistula Hospital, Karachi, and comprised data related to patients having undergone VVF repair from January 2007 to June 2012. In the absence of ethical review board in the hospital at the time of the study's commencement, permission was obtained from the directors of the hospital. All the patients who had their VVF repaired for the first time at the hospital were included in the study. Patients who had either additional surgical procedures

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performed or incomplete records were excluded. The patients were identified from the Microsoft Excel datasheets of the hospital database. Individual case charts were reviewed and data was collected regarding patients' age, parity, aetiology of VVF (obstetric versus non-obstetric causes). Duration, size, location and number of fistula were also noted. In relation to surgical procedure, we considered the route of repair, use of flaps and number of attempts. Outcome of fistula repair was also documented. We did not review intra- and peri-operative complications due to lack of documentation.

History of all the patients had been taken, followed by physical examination, complete blood count (CBC), serum biochemistry and urine analysis. Patients with positive urine cultures were treated according to the sensitivity before undergoing surgery.

VVF was diagnosed on cysto-urethrogram. Concomitant urethro-genital fistulae were ruled out by performing intravenous urography (IVU). Before surgery, all patients underwent examination under anaesthesia (EUA) and cystoscopy in order to identify the characteristics of fistula. We considered VVF to be 'low' when the fistula was below the interureteric ridge, and 'high' when it was above the ridge. Decision about the route of surgery (vaginal or abdominal) was made according to accessibility from the vagina. All surgeries were performed by two surgeons with special interest and experience of more than 10 years in female reconstructive urology.

Vaginal repairs were done in lithotomy position. Fistula tract was identified and marked by inserting a Foley's catheter through vagina. Tract was excised around the catheter and then bladder and vagina were closed separately in layers. Martius flap was considered only in multiple and large fistulae with significant fibrosis.

In abdominal repair, intra-peritoneal approach was used. Bladder was bisected from the dome down to the fistula posteriorly. The fistula was excised. The bladder and vagina were then closed separately. The interposition of omental flap between the repair and the vaginal wall was done whenever it was found to be necessary (due to large or multiple fistulae or excessive fibrosis of surrounding tissue) or feasible.

Post-operatively, all the patients remained catheterised for a period of two weeks. Patients remained hospitalised for the duration of catheterisation and for two additional days after the removal of catheter. Cystourethrogram was performed after two weeks of the surgical repair before removing the Foley's Catheter (which was removed after cystourethrogram if no leakage of contrast material was

seen). If contrast extravasation was found patient was kept catheterised and further management was planned according to degree of leakage. After discharge patients were followed at two weeks, one month and three months. Successful surgical repair was defined as no evidence of urinary leakage on cystourethrogram on 14th postoperative day and clinical evaluation on subsequent followup visits till four months after the surgery.

Data was analysed using SPSS 19. Univariate analysis was done to assess individual variables. Variables significant on univariate analysis were considered in a multivariate analysis. $P < 0.05$ was considered significant, while odds ratio (OR) were determined with 95% confidence interval (CI).

Results

Of the total 1003 surgical repairs during the study period, record of 640(63.8%) patients were analysed, while 363(36.2%) were excluded either due to additional surgical procedures or incomplete records. The mean age of the patients was 32.5 ± 9.488 years (range: 13-66). Mean parity was 3.35 ± 2.745 (range: 0-13). There was a mean duration of 58.4 ± 1302.71 months between VVF development and surgery though minimum delay of 4 days was also documented (range: 4-14600 days). Leading cause of fistula was obstetric procedures in 438(68.4%) patients followed by hysterectomy 109(17%) and Caesarean section 88(13.75%). Overall, 367(57.3%) patients underwent vaginal repair. Short-term success was reported in 558(87.2%) patients (Table-1).

In Univariate analysis, menopause ($p=0.15$) and parity ($p=0.14$) were not statistically significant (Table-2).

There was no statistically significant difference in

Table-1: Descriptive data.

Total number	640
Mean age (years)	32.5 (13-66) \pm 9.488
Mean parity	3.35 (0-13) \pm 2.745
Mean duration (months)	58.4 (4-14600 days) \pm 1302.71
Aetiology	
Obstetric procedures	438(68.4%)
Hysterectomy	109(17%)
Caesarean section	88(13.8%)
Non- gynaecologic pelvic surgeries	1(0.2%)
episiotomy	1(0.2%)
Trauma	3(0.5%)
Route of repair	
Transvaginal route	367(57.3%)
Transabdominal route	273(42.7%)
Outcome of repair	
successful	558(87.2%)
failed	82(12.8%)

Table-2: Univariate analysis.

	Successful	Failed	p-value
Patient-related factors			
Menopausal status			
Pre-menopausal	446	71	0.15
Post-menopausal	112	11	
Parity			
Nulliparous	45	9	0.14
Uniparous	152	26	
Multiparous	241	38	
Grand multiparous	120	9	
Fistula related factors			
Aetiology			
Obstetric	386	60	0.23
Non-obstetric	172	22	
Duration			
<6weeks	69	16	<0.002
6 weeks – 1 year	317	25	
> 1 year	172	41	
Size			
< 1cm	256	13	<0.002
1cm - 2cm	216	22	
> 2cm	86	47	
Number			
Single	428	23	<0.002
Multiple	130	59	
Surgery related factors			
Route of repair			
Vaginal	323	44	0.47
Abdominal	235	38	
Attempt of repair			
Primary	334	34	0.002
Secondary	224	48	
Flap interposition			
Yes	254	22	0.001
No	304	60	

outcome of obstetric versus non-obstetric causes ($p=0.235$) and route of repair ($p=0.47$). Duration of the fistula ($p < 0.002$), size ($p=0.01$), number ($p < 0.002$) were significant factors. Similarly, attempts of repair classified as Primary vs. Secondary repair ($p=0.002$) and flap interposition ($p=0.001$) were also significant.

Multivariate analysis determined that the recurrence of VVF was significantly related to multiplicity (9-fold recurrence risk), pre-operative size (10-fold recurrence risk for fistula >2cm compared to <1cm), secondary repair (5-fold risk) and duration of the fistula (3-fold risk). Interposition of flap and delayed reconstruction (between 6 weeks and 1 year) was related to successful surgical outcome. Age, parity, aetiology, route of repair and location of fistula were not significant ($p > 0.05$ each) prognostic factors for recurrence (Table-3).

Table-3: Multivariate analysis.

Factor	Odds ratio	95% confidence interval
Duration of fistula		
< 6 weeks	1	
6 weeks to 1 year	1.74	0.87-3.49
> 1 year	0.13	0.18-0.52
Size of fistula		
<1cm	1	
1-2 cm	0.09	0.04-0.18
>2cm	0.18	0.10-0.32
Number of fistula		
Single	1	
Multiple	0.11	0.70-0.19
Attempt of repair		
Primary	1	
Secondary	0.27	0.16-0.45
Flap interposition		
Yes	1	
No	0.43	0.26-0.73

Discussion

Results reflect low literacy, poor health facilities and lack of infrastructure, as is evident from younger age at presentation, high mean parity, and obstetric procedures, being the leading causes and prolonged delay between the occurrence and treatment as the major cause of VVF. Prevention of such fistulae requires improvement in infrastructure like more equipped ambulances and better roads (for swift transportation of the patients), well-equipped mobile maternity centres (to provide care to the patients of remote areas who cannot reach the hospitals on time), better women status (to allow them to seek timely care), improving the healthcare system by producing well-trained nurses and doctors (to provide best possible treatment to the patient) and by bringing the latest technology and better healthcare facilities in hospitals. Measures should be taken to reduce associated factors such as cephalopelvic disproportion which mainly results from malnutrition and pregnancy at an early age.^{12,13} This can be done by public awareness campaigns educating the people about the drawbacks of marriages in childhood, and also telling them how a pregnant lady should be taken care of.

The major problem that we faced during the study was the lack of standardisation of terminologies. Though several classifications have been proposed,¹⁴ there is no gold standard classification of VVF on the basis of which management of VVF may be standardised. Likewise, there is no proper definition of small vs. large fistulae, early vs. late repair,^{15,16} or simple vs. complex fistulae. Standardisation of the terminologies is therefore required

so that VVF could be properly managed.

Ideal timing for surgical intervention for VVF is still controversial.^{16,17} A delay of 3 to 4 months is generally recommended for repair.^{18,19} However, several studies show that, especially for small un-infected fistulae, early repair has better or at least similar success rates compared to delayed repair^{16,20} with additional advantage of reduced suffering and early commencement of normal life.¹⁷ On the other hand, many reports indicate that timing of repair does not affect the outcome.^{21,22} In our study, patients who underwent surgical repair < 6 weeks had more chances of failure probably due to inflamed and immature fistula tract. Similarly, patients undergoing surgery very late i-e after 1 year had high failure rates which could be due to defunctionalisation of detrusor muscle (like pronged indwelling catheterisation) and reduced blood supply leading to impaired bladder function as well as healing.²³ Best results were seen for patients in whom repair was done between 6 weeks and 1 year.

There is a general consensus that increasing size as well as number of the fistula negatively effects the outcome of surgery^{5,16,24} and use of interpositional flaps is advised for large fistula and also for multiple fistula irrespective of the size.^{16,24-27} In our analysis, we had similar results. Failure of the repair was significantly associated with fistula >2cm and fistula which were multiple, especially with those in which tissue interposition was not done. Some authors suggest routine flap interposition especially when repair is done through transabdominal route.²⁸ We feel that it is a good option and flap interposition with greater omentum should be used in all tranabdominal repairs whether fistula are simple (small and single) or complex (large and multiple). Though it is not easy to do flap interposition during trans-vaginal repair, it should be done at least in fistulae which are either large (>2cm) or multiple or having both the predictors.

Majority of reports suggest that success rate reduces with increasing number of repairs.^{5,22,23,29-31} A series of 2484 patients found 83% success rate with primary repair which dropped to 65% with subsequent repairs.³⁰ On the other hand, another study²⁶ found the number of repair to be an insignificant factor for the outcome. We found that previous repairs were significantly associated with failure. Previous surgical trauma not only altered the local anatomy, but also led to ischaemia and devitalisation of the tissues which resulted in severe adhesions and fibrosis, making subsequent repairs more difficult. It is recommended that secondary repairs should be done only by experienced surgeons and interpositional flaps should be used during the repair.

Route of repair i-e abdominal or vaginal, is probably the most debated factor in VVF repair.

Many surgeons advocate the vaginal route.^{16,25,31,32} Others suggest abdominal route.^{19,23} However, there are several studies which prove that the route of repair does not influence the outcome.^{16,24,29,31} Our analysis found the route of repair to be an insignificant prognostic factor and it should be chosen by the surgeon with which he or she is most comfortable. According to one study³³ that non-obstetric causes are related to better success rates but this factor did not reach statistical significance in our study. Other factors which were statistically insignificant included menopause and parity. No study suggested that these factors are significant for determining the outcome.

Along with all the above factors, one should not forget to follow basic surgical principles including pre-operative optimisation (like correction of nutritional status and anaemia and treatment of any active infection), careful surgical technique (wide exposure of the fistula, excision of fibrous tissues, maintenance of dry, uninfected suture line and tension-free water-tight closure) and proper post-operative follow-up (antimicrobial cover, adequate fluid intake, early mobilisation and vulvovaginal toilet). Avoidance of intercourse at least for 3 months, careful planning of pregnancy and proper antenatal care are very important in maintaining long-term success of repair.³⁴

Equally important is the role of specialised fistula centres. History of previous failed repairs is a very important factor in determining the outcome of surgical repair of VVF. Most of the surgeons are not familiar with VVF repair. Surgeries for VVF repair at such centres which are not specialised fistula centres usually fail and subsequent surgical attempts to repair VVF become even more difficult. So whenever possible these patients should be referred to specialised fistula centres in order to achieve best possible results. Especially those patients who have complex VVF or history of previous failed repairs should always be referred to these specialised fistula centres.

Due to its retrospective nature, our study has certain limitations. Several cases were excluded due to unavailability of proper data. No record was available regarding intra-operative findings like proper location, extent of fibrosis, sutures used and intra-operative complications. Long-term follow-up was missing as well. On the other hand, our study, with a large number of cases, represents an effort to identify the factors which provide the highest chances of successful closure of the fistula with restoration of continence and resuming a normal, healthy respectable life.

Conclusion

Obstetric fistula remains a major problem for women in poor countries. A successful closure of VVF requires careful evaluation of certain prognostic factors. Surgical repair has more chances of success if it is done between 6 weeks and 1 year after development of fistula, flap interposition is done (especially for large and multiple fistulae) and repaired for the first time. Route of repair has insignificant effect on the outcome of repair and should be chosen according to surgeons' choice and accessibility. Prospective studies are required to locate factors significant in determining the outcome of VVF repair.

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