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Original Article

Comparison of Renal Function before and After Construction of Arterio-Venous Fistula in CKD Patients before Starting Hemodialysis

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Mohammad Ali Rumee[1], HN Sarker[2]

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ABSTRACT

Background: *Arterio-Venous Fistula (AVF) formation is associated with significant changes in haemodynamics, left ventricular ejection fraction, systemic haemodynamics, left ventricular function, glomerular filtration rate, renal blood flow, renal venous pressure, sodium and water retention and overall renal functions. These changes are persistent even after AVF maturation.* ***Objective:*** *Evaluation of renal function in Chronic Kidney Disease patient after construction of Arterio-Venous fistula before starting Hemodialysis.* ***Methods:*** *This prospective observational study was carried out in 24 CKD patients underwent Arterio-Venous Fistula attended in the in department of Nephrology BSMMU, NIKDU, BIRDEM, Dhaka. during July 2015 and June 2016. Male and female patients aged more than 18 years and patient with CKD 5 who were clinically stable, including; AVF pending, any cause of renal failure, any co-morbid factors were enrolled in this study. Statistical analysis of the results was obtained by using windows computer software with Statistical Packages for Social Sciences (SPSS-version 22).* ***Result:*** *The mean age was found 48.5±10.44 years and male to female ratio was 2.43:1. Almost two third (62.5%) patients had radio cephalic fistula. The mean difference of Serum Creatinine level, blood urea and eGFR between before 4 months of AV fistula construction with at the time of AV fistula construction were statistically significant ($p<0.05$) however, at the time of AV fistula construction with after 4 months of AV fistula construction were almost alike with before 4 months of AV fistula construction, no significant ($p>0.05$) difference was found.* ***Conclusion:*** *This study demonstrated that rate of progression of CKD is decreased after construction of AV fistula.*

Keywords: *Renal, Function, Arterio-Venous Fistula, Hemodialysis.*

1. *Assistant professor, Nephrology, Sher-e-Bangla medical college, Barishal*
2. *Professor (ex), Sher-e-Bangla medical college, Barishal*

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INTRODUCTION

Chronic Kidney Disease (CKD) is a major public health problem worldwide with increasing incidence and prevalence. World Health Report 2002 and Global Burden of Disease project pointed out that diseases of the kidney and urinary tract contribute to the global burden of diseases, with approximately 850,000 deaths every year and 15,010,167 disability-adjusted life years. They are the 12th cause of death and the 17th cause of disability respectively [1]. A systemic review into 26 population based studies reported that the median prevalence of CKD was 7.2% in persons aged 30 years or older and in persons aged 64 years or older prevalence of CKD varied from 23.4% to 35.8% [2]. Associated with this increase in prevalence, is the disproportionate consumption of health care resources. The total cost of care for End Stage Renal Disease (ESRD) patients in the US was around $22.7 billion in 2006 [3].

Among patients initiating chronic hemodialysis, use of a catheter rather than a more permanent form of vascular access such as a graft or fistula, is associated with excess morbidity, mortality, and cost. In order to reduce catheter use among incident dialysis patients, it is generally agreed that patients with chronic kidney disease (CKD) who are expected to begin chronic dialysis should be referred beforehand for surgery to create a permanent access. Ideally, this referral should occur in enough time to allow for fistula maturation and repeat attempts at fistula creation (if necessary) before initiation of dialysis. The preference for the arteriovenous fistula (AVF) access has been based on its potentially smaller surgery, durability, longevity, less need for interventions, maintenance of the skin as a protective barrier against infection, absence of a foreign body and ease of accessibility. Systemic physiologic effects follow the creation of an arteriovenous fistula. Patients with a compressible fistula between peripheral artery and vein provide a unique opportunity to study the reactions of the body to certain abrupt changes in the circulation. Opening or closing a fistula causes an immediate and marked change in peripheral resistance and a shift in the distribution of blood inside the vascular tree. This in turn elicits numerous compensatory adjustments. Creation of an arterio venous (AV) fistula for hemodialysis therapy is a technique that provides convenient access to the circulation in patients with end-stage renal disease. A number of studies showed that cardiac failure could be induced by creation of an AV fistula for dialysis. The contribution of an AV fistula to cardiac performance has been studied using different methods. In many of these studies, patients were already on dialysis therapy, and at some stage, cardiac function was studied while a short manual compression over the fistula attempted to eliminate the effect of the fistula itself. Only a few prospective evaluations comparing cardiac performance before and after creation of an AV fistula have been performed in humans. However, in most of those studies, considerable time 2 weeks had passed after the creation of the fistula. Therefore, the short-term effect of AV fistula creation on cardiac function remains to be elucidated. Chronic volume overload by the AV fistula surely is involved in cardiac structural and functional changes, including left ventricular (LV) remodeling in patients with end-stage renal disease on hemodialysis therapy. However, it also is important to examine serial changes in cardiac function during the early phase in time after fistula creation, apart from its long-term

effects, because most of the increase in fistula blood flow occurs within the first 2 weeks of surgery. LV systolic function frequently is preserved in patients with congestive heart failure. Previous studies reported that diastolic dysfunction should be considered in patients presenting with heart failure symptoms, but normal systolic function. Diastolic dysfunction precedes LV systolic impairment and, alone, accounts for approximately 30% to 40% of patients with heart failure. Thus, it is essential to evaluate LV diastolic dysfunction as a primary cause of cardiac failure in patients with chronic renal failure [4]. The short term effect of AVAs on cardiac performance in predialysis patients. Fourteen days after creation of an AVA, cardiac output (CO), stroke volume (SV), and ejection fraction (EF) increased, whereas systemic vascular resistance (SVR) decreased. These were associated with an increase in plasma atrial natriuretic polypeptide (ANP) levels and decrease in plasma renin activity (PRA) The prevalence of left ventricular hypertrophy (LVH) is approximately 70% in the predialysis population. LVH is associated with increased mortality. It is assumed that an AVA, along with anemia, may contribute to left ventricular dilatation and LVH (eccentric hypertrophy), whereas hypertension and hypervolemia may contribute to the development of concentric LVH [5].

In mechanical terms, the arteriovenous fistula adds a low resistance, high-compliance venous compartment to the central arterial system. In long-term hypertensive patients with established arterial hypertrophy and reduced vessel compliance, the application of an arteriovenous shunt attenuates arterial stiffness and reduces arterial pressure [6]. Implantation of an arteriovenous coupler (with a flow similar to that in haemodialysis patients) produced a marked reduction in average 24-h ambulatory systolic pressure (−15 mmHg), in a recent randomized trial in patients with resistant hypertension [7]. Similarly, in a previous uncontrolled series of patients with advanced CKD, the creation of an arteriovenous fistula reduced both arterial stiffness and blood pressure [8]. Apart from its mechanical action on the arterial system, the arteriovenous fistula has complex cardiovascular effects. The increase in venous return augments pulmonary flow, which in turn may recruit under perfused lung areas and increased arterial oxygen content. This phenomenon may in turn raise the oxygen delivery to peripheral organs. Due to severe vasoconstriction, the kidney is under perfused in patients with resistant hypertension, and the resulting ischaemia may trigger a chemoreflex driving central sympathetic over activity [9]. Thus, increased oxygen delivery to the kidney may in theory reduce arterial pressure also by mitigating the chemoreflex incited by organ under perfusion [6]. As to the kidney, the acute effect of femoral arteriovenous fistula creation in the anaesthetized dog includes renal vasoconstriction and a reduction in the glomerular filtration rate (GFR) and in water and sodium excretion [10]. On the other hand, peripheral fistula compression in Korean War veterans with long-standing traumatic arteriovenous shunts in the leg, the arm or in the neck caused a dramatic increase in sodium excretion but did not modify the GFR, renal blood flow and renal venous pressure [11]. Of note, these renal haemodynamic parameters did not change even after the compression was withheld. Overall, such findings point to important long term haemodynamic adaptations of the renal

circulation abolishing the acute renal vasoconstrictive effect of the peripheral arteriovenous fistula. If superimposed to a renal microcirculatory setting, characterized by efferent vasoconstriction and glomerular hypertension, the typical setting of progressive nephropathies, such an adaption may in theory help reduce glomerular hypertension and preserve residual function. Mitigation of a renal chemoreflex triggered by renal under perfusion (see above) may be a relevant mechanism contributing to the putative protective effect of fistula on CKD progression. Golper et al [12]. now move the issue into the clinical arena and report pilot observations testing the 'arteriovenous fistula hypothesis' in a series of 123 patients, with at least two estimated glomerular filtration rate (eGFR) determinations for 2 years before and up to 2 years after functioning fistula creation [12]. Before the intervention, the rate of GFR loss was 5.9 mL/min/year, which dramatically reduced to 0.5 mL/min/year following the same intervention [8]. The aim of this study is to prospectively investigate the long term effects of AVF on systemic haemodynamics, glomerular filtration rate and overall renal function, as these factors are crucial in the pathophysiology of chronic Kidney Disease patients.

MATERIALS AND METHODS

This prospective observational study was carried out in 24 CKD patients who underwent Arterio-Venous Fistula in the Department of Nephrology, BSMMU, NIKDU, BIRDEM, Dhaka, during July 2015 to June 2016. Male and female patients aged more than 18 years and patient with CKD 5 who were clinically stable, including; AVF pending, any cause of renal failure, any co-morbid factors awaiting AV Fistula construction were enrolled in this study. Recent acute illness that required treatment, without full recovery, Medically unstable patient, Cardiac transplantation and CKD stage 5 patients on maintenance hemodialysis/CAPD were excluded from the study. Ethical clearance was taken from the local Ethical Committee to perform the study. All the patients/legal guardians of participants were properly explained about the objectives of the study along with its procedure, risk and benefits to be derived from the study in easily understandable local language and then informed consent was taken from them. It was assured that all records would be kept confidential and would not be disclosed anyway except for the purpose of study. It was assured that the procedure was helpful for both the physician and patients in making rational approach regarding management of the case.

STUDY PROCEDURE

AV fistula formation procedures were done but not started maintenance Hemodialysis. Vascular surgeons require thorough pre-fistula assessment and vascular mapping before surgery to ensure feasibility for AVF. The patients were followed 4 months before, at the time and 4 months after Arterio Venous fistula creation. Renal function assessments with associated laboratory test were repeated. Any complications that occurred throughout the study with fistulae of patients (thrombotic occlusion, infection, failure to mature etc.) were recorded. Those patients that suffered AVF failure, as a result, exit the main study but monitoring continued. Re-entry to the study occurred if a new AVF will to be created.

STATISTICAL ANALYSIS

Statistical analyses were carried out by using the statistical package for social

sciences version 20.0 for windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Data was presented in graph, pie chart & tabulated form. The comparison of level of blood urea and serum creatinine was done between 4 months before and at the time of AV fistula creation. In addition to that the comparison also performed between at the time of AV fistula creation and after 4 months by paired t-test. The comparison of eGFR also done between before 4 months and at the time of AV fistula creation. In addition to that the comparison also performed between at the time of AV fistula creation and after 4 months by paired t-test. A "p" value <0.05 was considered as significant after different statistical tests.

RESULTS

Majority (41.7%) patients age belonged to 41-50 years and 51-60 years varied from 26 to 68 years. Almost three fourth (70.8%) patients were male and 7(29.2%) female. Nearly a half (45.8%) of the patients had HTN in cause of CKD, 10(41.7%) had GN, 3(12.5%) had DN and most of the patients suffering from HTN (55.0%) as co morbid condition followed by 6(30.0%) DM and 3(12.5%) IHD. The mean pulse was 85.33±8.88 bpm varied from 72 - 100 bpm. Mean Blood pressure systolic and diastolic was 143.8±15.2 mmHg varied from 100 – 160 mmHg and 86.25±7.7 mmHg varied from 70 – 100 mmHg respectively. Mean size of the right and left kidney was 7.46±0.56 cm and 7.98±0.62 cm with the range of 6.5 to 8.5cm and 7 to 9 cm respectively.

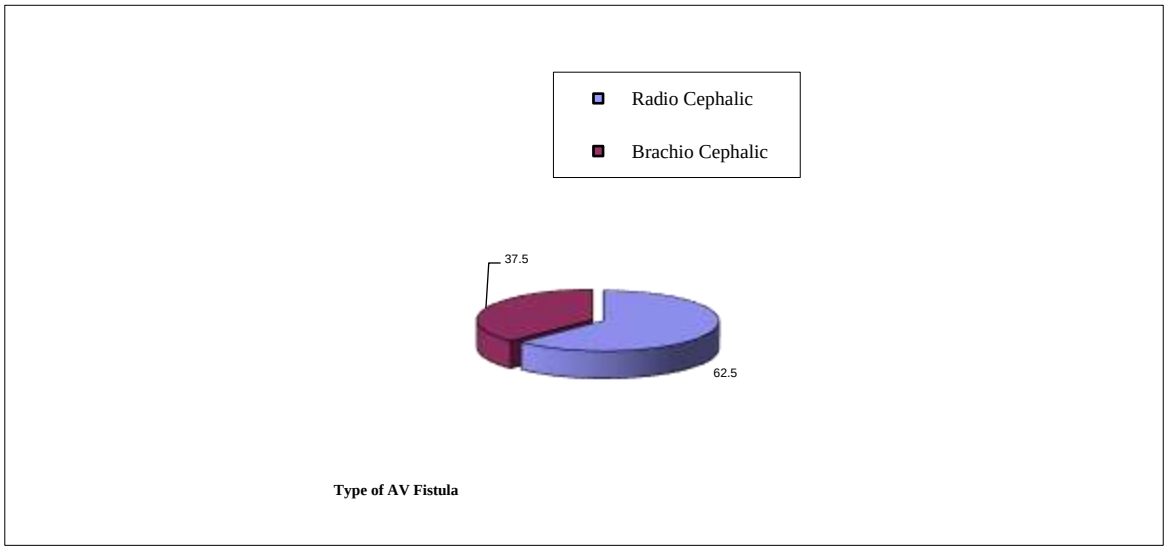

Figure 1: shows AV fistula of the study patients and showed 62.5% patients had Radio Cephalic fistula and 3.5% had Radio Cephalic.

Table I: Distribution of the study patients according to Serum Creatinine (n=24)

Serum Creatinine (mg/dl)	Mean±SD	Range(Min, Max)	P value
Before 4 months of AV Fistula construction (mg/dl)	5.52±1.54	(3,8.5)	

At the time of AV Fistula construction (mg/dl)	7.42±1.58	(4.8,10)	
P value before 4 months vs at the time of AV Fistula construction			0.001 s
After 4 months of AV Fistula construction (mg/dl)	7.35±2.44	(3.21,11)	
P value at the time vs after 4 months of AV Fistula construction			0.733 ns

s= significant, ns= not significant, P value reached from paired t-test.

The difference before 4 months vs at the time of AV Fistula construction was statistically significant ($p<0.05$) and at the time vs after 4 months of AV Fistula construction was not significant ($p>0.05$).

Table II: Distribution of the study patients according to Blood urea (n=24)

Blood urea of AV Fistula construction (mg/dl)	**Mean±SD**	**Range(Min, Max)**	**P value**
Before 4 months of AV Fistula construction (mg/dl)	87.13±21.51	(48,130)	
P value before 4 months vs at the time of AV Fistula construction			0.001[s]
At the time of AV Fistula construction (mg/dl)	111.9±20.09	(75,142)	
After 4 months of AV Fistula construction (mg/dl)	109±30.79	(50,150)	
P value at the time vs after 4 months of AV Fistula construction			0.320[ns]

s= significant
ns= not significant
P value reached from paired t-test.

The difference before 4 months vs at the time of AV Fistula construction was statistically significant ($p<0.05$) and at the time vs after 4 months of AV Fistula construction was not significant ($p>0.05$).

Table VIII: Distribution of the study patients according to eGFR (n=24)

eGFR(ml/min/1.73 m2 BSA)	**Mean±SD**	**Range(Min, Max)**	**P value**
eGFR(ml/min/1.73 m2 BSA) before 4 months of AV Fistula construction	12.78±3.85	(7.27,22.8)	
P value before 4 months vs at the time of AV Fistula construction			0.001[s]
eGFR(ml/min/1.73 m2 BSA) at the time of AV Fistula construction	8.81±2.17	(5.68,13.26)	
eGFR(ml/min/1.73 m2 BSA) after 4 months of AV Fistula construction	9.69±3.83	(5.09,18.27)	
P value at the time vs after 4 months of **AV**			0.077[n]

Fistula construction			s

s= significant, ns= not significant, P value reached from paired t-test.

The difference before 4 months vs at the time of AV Fistula construction was statistically significant ($p<0.05$) and at the time vs after 4 months of AV Fistula construction was not significant ($p>0.05$).

DISCUSSION

This prospective observational study was carried out to compare the changes in Blood Urea and Serum Creatinine level before and after Arterio Venous fistula construction and compare the changes in estimated glomerular filtration rate that can be associated with Arterio-Venous fistula formation.

Ghonemy et al[13] found the ages ranged from 25 to 76 years with mean of 46.47.78± 09.85 years, which is closely resembled with the present study. On the other hand Golper et al[12] found subjects with median age were 68 years. In another study O'Hare et al.[14] and Iwashima et al[4] found the mean age of the patient were 70 years and 68±11 years respectively, which all are higher with the current study. The higher mean age and age range maybe due to geographical variations, racial, ethnic differences, genetic causes and different lifestyle may have significant influence on CKD patients.

The prevalence of CKD Stages 2–5 has continued to increase since 1988 as have the prevalence of diabetes and hypertension, which are respectively etiologic in approximately 40.0% and 25% of CKD cases.[15] Ghonemy et al.[13] found 17.0% DM and 14.0% Hypertension in their study. Similar findings also observed by Monroy-Cuadros et al[16].

It was observed in this study that almost two third (62.5%) patients had radio cephalic and 37.5% Brachio Cephalic fistula. National Vascular Access Improvement Initiative[17] showed similar findings. It was observed that mean right and left kidney size was 7.46±0.56 cm and 7.98±0.62 cm with the range of 6.5 to 8.5 cm and 7 to 9 cm respectively. Steddon et al[18] showed that kidney size of CKD stage 5 patients were <9 cm (exception: DN, Multiple Myaloma etc).

In the present study it was observed that the mean Serum Creatinine level was significantly ($p<0.05$) increased at the time from before 4 months but at the time with after 4 months was almost similar ($p>0.05$). Similarly, it was observed that the mean blood urea level was significantly increased at the time from before 4 months but at the time with after 4 months was almost similar ($p>0.05$). Golper et al[12] had anecdotally observed after AVF creation that there appears to be a slowing of the decline in kidney function as measured by the estimated glomerular filtration rate (eGFR). A functioning AVF may be associated with a slowing of the eGFR decline. Prior to AVF formation, the rate of change was-5.90 mL/min per year (95% CI: -5.28,-6.51), while after AVF formation the rate of change was-0.46 mL/min per year (95% CI:-1.05, 0.14). The slopes of the eGFR decline (i.e. negative rate of change) before and after AVF creation are statistically different, indicating a slower decline after AVF creation (interaction $P<0.05$).

In this study it was observed that the mean eGFR was significantly decreased at the time of AV fistula construction when comparing with 4 months before AV fistula construction but when comparing eGFR at the time of AV fistula construction with after 4 months

of AV fistula construction the result was almost similar (p>0.05).

CONCLUSION

This study concluded that rate of progression of CKD is decreased after construction of AV fistula.

LIMITATIONS

This study has some limitations include small sample size, only one centre study, short duration of study period as well as sample was taken by purposive sampling.

RECOMMENDATIONS

Further studies can be undertaken by including large number of patient over a long period of time.

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