COMPARISON OF RADIAL ARTERY DEVIATION AND REIMPLANTATION TECHNIQUE VS CLASSICAL TECHNIQUE IN CREATION OF ARTERIO-VENOUS FISTULA: A RANDOMISED CONTROL TRIAL

Thesis
Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfilment of the requirement for the degree of

Magister Chirurgiae (MCh)

In Urology

June, 2023

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DECLARATION

I hereby declare that the thesis titled "**COMPARISON OF RADIAL ARTERY DEVIATION AND REIMPLANTATION TECHNIQUE VS CLASSICAL TECHNIQUE IN CREATION OF ARTERIO-VENOUS FISTULA: A RANDOMISED CONTROL TRIAL**" embodies the original work carried out by the undersigned in All India Institute of Medical Sciences, Jodhpur.

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CERTIFICATE

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DR. ARJUN SINGH SANDHU
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All India Institute of Medical Sciences, Jodhpur

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Dedicated To My Family

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Abbreviations

AVF – Arterio-venous Fistula

BMI – Body mass index

BP – Blood pressure

CKD – Chronic Kidney Disease

DM – Diabetes Mellitus

HD – Haemodialysis

HTN – Hypertension

RADAR – Radial Artery Deviation and Reimplantation

RC AVF – Radio-cephalic Arterio-venous Fistula

RCT – Randomised control trial

USG – Ultrasonography

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Introduction

Chronic kidney disease (CKD) is a burden of enormous proportion on the global health infrastructure. Currently there are about upwards of 70 lakh patients living in CKD with CKD 3-5 stage comprising 10.6% of the total CKD burden (1). With the advent of modern healthcare system, such patients will live long enough to need renal replacement therapy in one form or another eventually. Considering the dearth of organ availability, many of such patients remain on maintenance hemodialysis (MHD) for years if not months; waiting for transplant. Not only that, the dire medical and social scenarios may preclude renal transplantation in many such patients. Such patients require a reliable repeatable vascular access for MHD. Surgically created arteriovenous fistula (AVF) is the gold standard for haemodialysis access for patients with end-stage renal disease. The AVFs are associated with better longevity of access, less morbidity for patients and decreased healthcare cost in the face of repeated vascular access. Moreover, the creation of AVF is done on a day-care basis under local anaesthesia and the patient can be discharged after few hours of observation. Although the procedure is performed relatively quickly and under local anaesthesia, the surgery is technically demanding. The AVF is notorious for failure even after a successful surgery and working AVF. Standard practice of arteriovenous fistula creation involves selecting the non-dominant upper limb and starting with the distal most site, that is radio-cephalic arterio-venous fistula (RC AVF) and selecting sites that are more proximal if the former fails. The major drawback of the procedure is the poor early patency rate. The primary patency rate of RC AVF varies from 50-65% (2). There have been many possible explanations postulated for such high rate of primary failure and failure to mature which includes abnormal hemodynamics at the anastomotic site, diameter of vessels, intimal hyperplasia and all these gradually lead to scarring or stenosis at the anastomotic site. The surgical technique also affects the future of the fistula. The influence of operative technique is likely to be most marked in cases of challenging small wrist vessels.

A multitude of various operative methods has been proposed for better outcome of the AVF including side-to-side anastomoses, vein cuffs and variation in anastomoses angle. Neointimal hyperplasia near the anastomotic site has been observed by a landmark paper by N. Sadagihanloo et al(3), in the mobilised segment (e.g., the proximal vein mobilised to form the end-to-side anastomosis). This surgically mobilised segment coincides with turbulent flow as well as with devascularisation of the vasa vasorum; these processes have been associated with endothelial cell activation and a dysfunctional local milieu leading to intimal hyperplasia and stenosis. Therefore, a surgical technique, that minimises venous dissection may improve rate of fistula maturation and access patency. This was the basis of the radial artery deviation and reimplantation (RADAR) technique. In the proposed study, we followed the RADAR

technique described by N. Sadagihanloo et al. Instead of using a traditional end vein-to side artery anastomosis, this technique uses an end artery-to-side vein anastomosis. In addition to this, we also kept the venous dissection to the minimum. In this study we compared the outcomes of RADAR technique with the classical technique for AVF creations.

Chronic kidney disease (CKD) is the end result of multitude of pathophysiologic pathways leading to reduction in renal function. Various common inciting causes like diabetes, hypertension, recurring pyelonephritis, stone diseases and congenital anomalies lead to decline in renal form and function over a period of years leading to CKD and progressing to end stage renal disease (ESRD). Likewise, the diagnosis of CKD is based on demonstrating the loss in function of kidney, that is decrease in glomerular filtration rate (GFR). The various stages of CKD are defined on the basis of GFR. The current guideline describes as decreased kidney function shown by GFR of less than 60 mL/min per 1·73 m^2, or markers of kidney damage, or both, of at least 3 months duration (4). When a patient reaches ESRD, some form of renal replacement therapy is necessary to sustain life.

Support to a weak organ is described for more than a century now. One of the well-known examples is the iron lung which saved many lives during the peak of polio era. Likewise, the first concept of dialysis, so as to remove diffusible substance from blood was developed by Abel et al in 1914 (5). In their 'Vivi diffusion' apparatus they demonstrated the use of dialyse bath separated from a rotating drum containing continuous flow of arterial blood separated by a semipermeable membrane. Since then up to today, the modern dialysis system has taken many iterations, but the basic concept remains the same that was demonstrated more than a century ago. The most crucial part in hemodialysis (HD) is to establish a reliable vascular access. A vascular access is required to remove the blood from the patient, flow it through the machine and return it back to patient. The initial such technique was described by Scribner et al in 1950s (6). Similar approach was described by Bartlett et (7)al also. They described the use of arterial access and later veno-venous access for HD. In a study conducted in 2005, it has been estimated that there were about 1.3 million people receiving renal replacement therapy and most of them (89%) received hemodialysis (8). The HD is the preferred method as it can be performed quickly or slowly as the need be, and cost effective also. In 1966, Bressica et al

described the AVF for HD (9). Till then, various puncture cannulas were being used for vascular access.

The HD machine depends on a continuous flow of blood at a rate of 250-300 ml per minute to function. The early attempts at renal replacement therapy were built on the work of Abel et al. Based on the vivi diffusion apparatus, in October 1924, Georg Haas in Germany performed the first HD in a human patient (10). Initially it was of short duration, of about 15 minutes. He used glass cannulas and later venipuncture for vascular access. He performed such treatment 11 more times and discontinued his work probably due to a lack reliable vascular access and proper anticoagulation at that time.

The modern HD as we know it today was described by Kolff in 1943 (11). He used cellophane membranes arranged in rotating drums to create the 'artificial kidney'. He had significant success in terms of removing nitrogen waste products from the blood, but he too was faced with the same persisting problem that troubled the previous scientists also, the vascular access. Because of the lack of a reliable vascular access, canulating a patient every time before HD was troublesome and lead to bleeding on multiple occasions. Several sessions of HD also rendered many vessels thrombosed and inaccessible. With the dialysis machine being more or less standardized, the medical world turned to search for a reliable repeatable vascular access with less complications.

Before the surgically created AVF was described, the vascular access was being done by an external arterio-venous fistula. Teflon made tubes were permanently implanted into vessels to create a channel between artery and vein. Such devices were being used to create external fistula between radial artery and cephalic veins. These devices were the mainstay of vascular access during the 1950s era before autologous AVFs became the standard of care vascular access mechanism. Although the concept was simple, the arrangement was faced with many complications. It had to be properly cared for, to maintain hygiene and prevent infection.

Besides, such devices were also prone to infection and clot formation making them unusable within a few months. Such patients had recurrent failure, revision surgery, infective complications and bleeding also. All these problems gave rise to the search of a solution which can overcome these issues. The autologous AVF was created with these problems in mind. The AVF is internal, so that no daily caring of any external device is needed and chances of infection is also decreased. It can have a well enough flow to support HD. Being autologous, it decreases the chances of clot formation and associated problems. Bressica et al, first described the AVF in 1966 after the success of venipuncture techniques. They described side to side AVF based on the radial artery and any of the nearby vein available. During the initial description, they did not ligate the or divide the distal end of the vein. Such patients had swelling over hand as a result of venous hypertension of which the authors were aware of. According to the reports, such edema was self-limiting and could be managed with limb elevation.

The next year following the landmark paper by Bressica et al, M. Sperling reported end to end radial artery to cephalic vein AVF using stapler (12). Such AVFs quickly rose in popularity within the next decade. This was based on the rationale to restrict the inflow of blood into the AV fistulae to the flow provided by the feeding radial artery. However, it was technically difficult to perform end to end anastomosis between the radial artery and the cephalic vein considering the vessels usually have very different caliber diameter. Various types of patch techniques were described to mitigate such issues. However, gradually this technique failed out of favor because of technical difficulties associated with the procedure and the stapler was never accepted as a primary choice for making AVF. But the idea of performing a successful end to end arterio-venous anastomosis persisted and gave rise to newer methods in the future.

Lars Röhl in 1968 published his result of a new method of performing AVF (13). He created AVFs by radial-artery-side-to-vein-end-anastomoses. In his method, he used to ligate the radial artery distal to anastomosis. This turned the anastomosis in to a functional end to end anastomosis. With the advent of this method more laterally located veins like the antebrachial cephalic vein could also be used for creating AVF which was not previously feasible. Later ligating the distal limb of the artery became optional and the classical method as we know today of creating the arterio-venous fistula came to be.

Other techniques for vascular access also continued to develop parallel to the surgically created autologous AVFs. Shaldon in 1961 demonstrated the subclavian vein access for HD (14). Such access also provided a means to assess and manage the central venous pressure and thus hydration of the patient with precision. Over the next two decades the subclavian vein remained a popular choice of temporary access. However, it later came to light that the access causes stenosis and occlusion in about 50% of cases leading to edema of the arm and it was more pronounced after creation of AVF. George Thomas described the 'Dacron applique shunt'(15). He sutured the Dacron patches to common femoral artery and vein with silastic tube connecting both the patches. This method eliminated any intravascular component as seen in previous canula placement methods and decreased the risk of thrombosis. Similarly, the patients in whom all other options have been exhausted, Gilberto Flores Izquierdo and James May proposed the saphenous vein graft method (16). In this technique, the saphenous vein is harvested, and placed in a subcutaneous planed created at the arm and anastomosed with the brachial artery and a any suitable vein with a gentle curve. Similar methods have also been described for the lower limb by creating a channel between the femoral vessels. Various other types of grafts have also been described in literature, including Dacron/ PTFE vascular grafts, bovine carotid graft, umbilical vein graft etc. Except for the Dacron/ PTFE grafts, rest all have very poor success rate and many complications and increased instances of thrombosis.

Various implantable devices have also been described since the era of glass cannulas for vascular access. One such device, called 'carbon transcutaneous hemodialysis access device' was described by Golding et al. It consisted of a vitreous carbon access port sealed with a conical polyethylene plug and a PTFE graft securely and smoothly attached to the port. For vascular access, purpose-built devices could directly be connected to the button without the need of a needle. Such devices were costly never got wide-spread acceptance.

The surgically created AVF still remains the go to reliable vascular access even today. However, there still remains relatively high chances of failure. In fact, the vascular access dysfunction is one of the leading causes of morbidity and economic burden in the ESRD population. The failure in AVFs can be divided into early and late failure. Early failure includes the cases with primary failure and the fistulas which fail to mature. Late failure cases include secondary failure due to thrombosis, infection or anastomotic stenosis. This translates to an early failure rate of about 23%-46% of all AV fistulae (17).

The most commonly observed histopathological abnormality at the site of AVF is neointimal hyperplasia. It has been shown that the anastomosis develops increased production of certain growth factors and thus in a drive of deranged healing, there occurs increased smooth muscle cells, myofibroblasts and endothelial cells within the vessel walls leading to stenosis (18). Growth factors like transforming growth factor-β and insulin like growth factors have been noted in driving the growth of such cells. It has also been proposed that the abnormal vascular remodeling because of the way the anastomosis was made so that there occurs vasoconstriction, is also a major player in the stenosis of anastomosis.

In 1983, Zarin et al demonstrated thickening and atherosclerosis in carotid bifurcation at regions with flow anomalies (19). Since then, multitude of clinical studies have resulted in the same results. The flow and wall stress results in remodeling of the intimal layer. The shear stress is directly proportional to the amount of flow and inversely proportional to the radius of

the vessel. In other words, if the flow rate increases; the shear stress will increase and if the diameter increases the stress will decrease. The body responds to this by orienting the endothelial cellular structure in the vessels in a way that results in dilatation of the vessels, reduced intimal hyperplasia and an easier flow. These remodeling tends to bring down the vascular stress to relatively normal levels. In contrast, in a anastomosis where the flow rate is low, the vessels are constricted or are stripped off their vasa vasorum; there occurs oxidative stress, proinflammatory milieu leading to neointimal hyperplasia and ultimately stenosis of the anastomosis (20).

Later Sadaghianloo et al noted that the mobilized portion of the cephalic vein develops the neointimal hyperplasia and later leads to anastomotic stenosis. This is the part that confers to maximum hemodynamic turbulence and also devascularization as a result of surgical mobilization. This process has been established to be the cause of dysfunctional healing leading to failure of anastomosis (21). Therefore, it is logical that a method, that can decrease the mobilization of the vein can theoretically lead to the decrease in such neointimal hyperplasia and more success rate compared to the classical method. This is the basis of the RADAR method of creating AVF initially proposed by Sadaghianloo et al. This method is based on various older methods of creating AVFs. During the initial days, the radial artery distal to the vein was being ligated to prevent steal phenomenon. The currently used cephalic vein mobilization allowed for creation of AVFs in cases where the vessels were widely separated and thus gained popularity. Sadaghianloo et al advocated that by handling the vein minimally, the minute vasa-vasorum over the vein can be preserved. They followed the “no touch technique” for venous dissection and only dissected the small part where anastomosis is to be performed. Following the RADAR method, he could achieve clinically significant results in his landmark study. In our study, we performed a randomized control trial comparing the classical method with that of RADAR method and found the following results.

Aims and Objectives

Primary objective:

- To assess the success rate of arterio-venous fistulas created by RADAR technique and compare that with arterio-venous fistulas created by conventional method.

Secondary objective:

- To assess the "failure to mature" rate of arterio-venous fistulas created by RADAR technique and compare that with arterio-venous fistulas created by conventional method.
- To measure the ease of doing the procedure in terms of time required to complete the procedure.
- To assess complications occurred in each group.

Outcome measures:

- The patency rate of arterio-venous fistulas at follow-up up to 3 months
- To assess the number of arterio-venous fistulas that fail to mature at follow-up up to 3 months
- To note any complications in each group.
- To note the time taken for each procedure and compare it across the groups.

Materials and Methods

PLACE OF STUDY: This study was conducted from January 2021 to December 2022 at Department of Urology, All India Institute of Medical Science, Jodhpur, Rajasthan, India.

STUDY DESIGN: Randomized Controlled trial

PATIENT SELECTION:

- **INCLUSION CRITERION**

All patients undergoing AVF creation in Department of Urology, AIIMS Jodhpur

- **EXCLUSION CRITERION**

Patients with

- Incomplete palmar arch (Allen's test negative)
- Previously Failed AVF at wrist
- Severe calcification or atherosclerosis in artery
- Un-correctable coagulopathy
- Unwilling to participate
- Radial artery diameter <2mm
- Cephalic vein diameter of <2mm and/or presence of thrombosis
- Cephalic vein length <10 cm

SAMPLE SIZE ESTIMATION:

Sample size was calculated using the following formula for randomized control trial for statistical superiority design with dichotomous variable.

$$N = \frac{1}{2} \times \left(\frac{Z\frac{\alpha}{2} + Z_{\beta}}{\arcsin\sqrt{p} - \arcsin\sqrt{P_0}} \right)^2$$

N=size per group; p=the response rate of standard treatment group (Classical AVF; 60% (22,23)); p_0= the response rate of new treatment group (RADAR AVF;85%(3)); z_x= the standard normal deviate for a one- or two-sided x.

Where $\alpha = 0.05$, $\beta = 0.20$ and keeping in mind the fact that power of study being 80%.

SAMPLE SIZE:

Minimum sample size calculated from above formula comes out to be 47 in each group which is sufficient for statistically significant result.

RANDOMISATION:

Randomisation was done by computer generated random numbers. The patients were randomized to either group using sealed envelopes method, which were opened immediately before the surgery. Block randomisation of sets of 5 was used.

Group 1. RADAR Technique (n= 47)

Group 2. Classical Technique (n=47)

METHODOLOGY:

A clearance from Ethical Committee of Institution was obtained prior to the investigation. A written informed consent was obtained from each patient before the procedure.

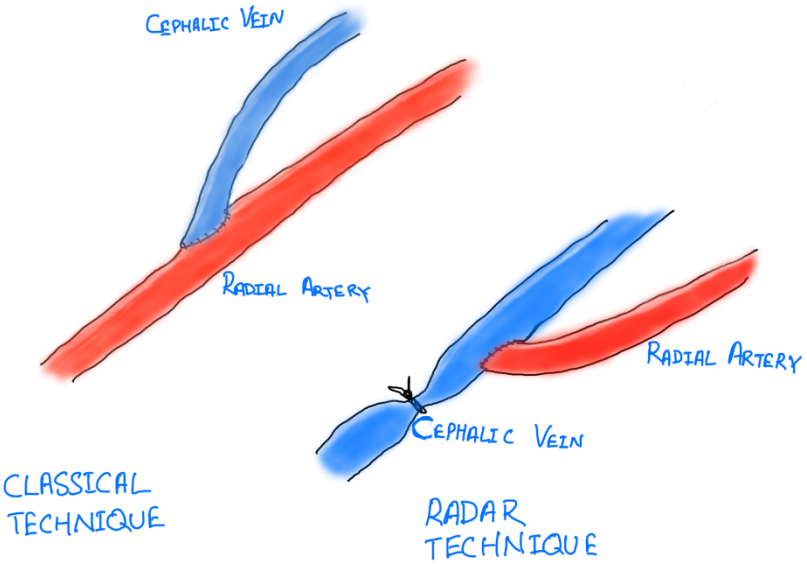
Patients baseline assessment including the demographic characteristics, medical history, physical examination, ultrasound (USG) doppler of both limbs or non-dominant limb where AVF is planned to characterise status of vessels, coagulation test and complete blood count were done and recoded in a pre-structured proforma (Annexure). The patients were assessed for fitness for surgery and any preoperative optimisation (e.g. - HD) was done if required.

The surgical technique:

All the patients undergoing AVF creation underwent preoperative clinical evaluation as well as ultrasound guided mapping of arterial and venous structures in arm for the procedure. Allen's test was done to check for palmar arch patency. After fulfillment of the inclusion and exclusion criteria, the patients were taken up for the surgery. The following is a diagrammatic representation of the procedures performed (Figure 1).

Team of Urologist who were experienced in AVF surgery performed the procedure performed all the procedures. The procedures were performed under local anesthesia or brachial block. The procedure starts with an incision of about 5 cm just above the wrist on the ulnar aspect of anterior side of arm parallel to the cephalic vein and radial artery. In the classical group, the incisions were placed ever so slightly towards the artery and in the RADAR group, the incision was made just medial to the medial border of the vein. After the incision was made,

Figure 1: Classical and RADAR technique represented graphically



skin and subcutaneous tissue was dissected carefully. In the classical group, the procedure was performed in the standard fashion. The cephalic vein was dissected. All the tributaries were dissected carefully and ligated and divided. The distal limb of the vein was also ligated and divided. The vein was then mobilised towards the radial artery. The radial artery is dissected just above the flexor retinaculum near the flexor carpi radialis tendon and the pulsation of the artery as a guide. The artery is dissected free of a length of about 2-2.5 cm. A proximal and a distal control was placed over the artery. After taking proximal and distal controls, an arteriotomy is made of a length of about 1 to 1.5 cm and the artery is flushed with heparin infused saline. The already dissected cephalic vein is spatulated for a similar length. The vein is then brought near the artery to perform end to side anastomosis using 6-0 polypropylene sutures in a watertight manner.

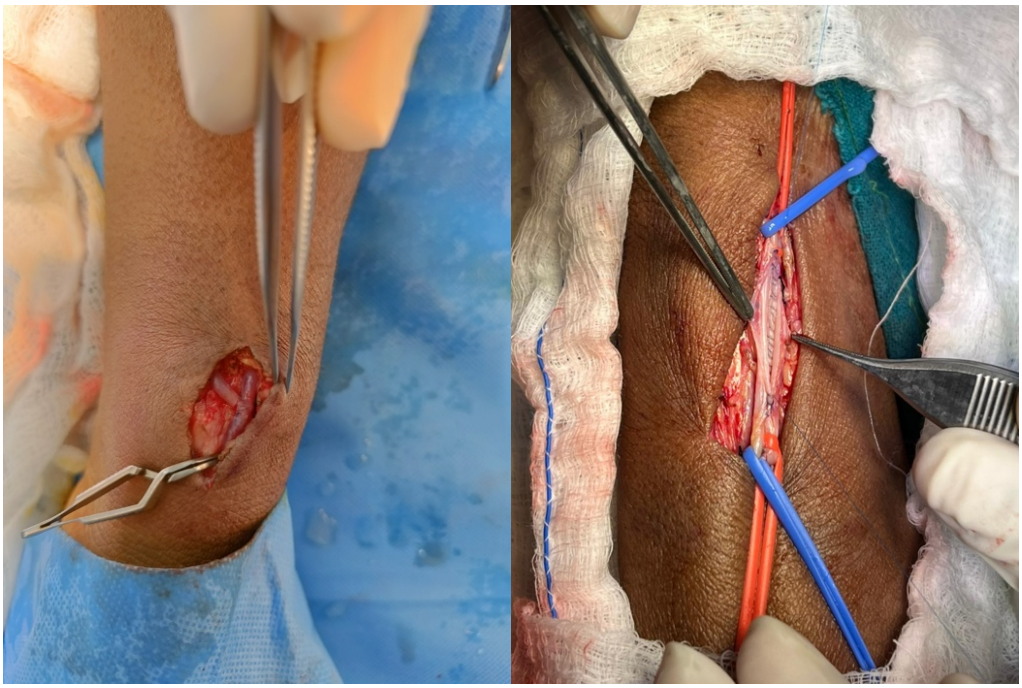
After anastomosis is done, the arterial controls removed and the anastomosis is observed for any bleeding and presence of thrill and pulsation across the anastomosis (Figure 2). After satisfactory outcome in terms of haemostasis and flow across the anastomosis, the skin is closed

Figure 2: Intraoperative images of RADAR and classical AVF

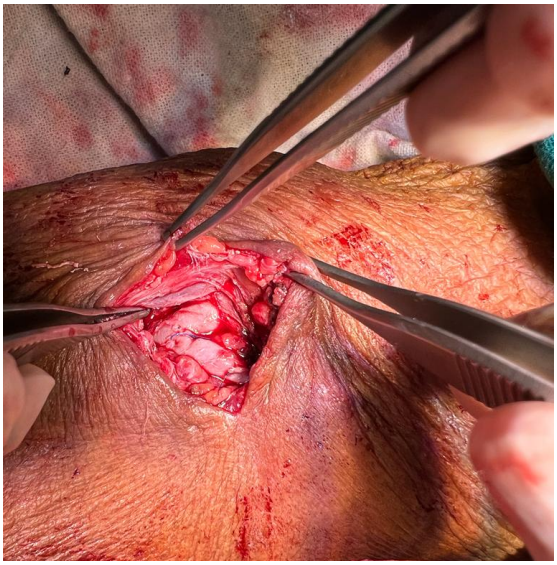
A) RADAR method of AVF creation. The radial artery is mobilized towards the cephalic vein and anastomosed. The bulldog clamp on the vein will be removed after applying a ligature.

B) Intraoperative picture of a classical AVF. The posterior layer is sutured.

C) Intraoperative image of a classical AVF showing a successful fistula



A. B.



C.

with nylon 3-0 suture in interrupted manner and a light dressing is applied so as not to compress the anastomosis.

In the RADAR group, the skin incision is made just medial to the vein of a length of approximately 5cm at the wrist. The vein was exposed for a length of about 2cm with careful dissection so as not to disturb the vasa vasorum of the vein. The distal end of the vein was ligated without division. Then the radial artery is dissected like in the classical method just above the flexor retinaculum near the flexor carpi radialis tendon and the pulsation of the artery as a guide. The radial artery pedicle (i.e., the artery accompanied by its two veins) is then carefully dissected with care taken not to damage the accompanying two small venous channel on either side. Minute branches of the artery are carefully ligated and divided. After vascular control, the radial artery is then ligated and divided at the distal end. Then the radial artery is gently turned towards the minimally dissected aspect of the vein to form a smooth loop. The artery is spatulated for a length of about 1-1.5 cm. A similarly matched venotomy is made. Both the vessels are then irrigated with heparin infused saline. Then artery to vein end to side (functional end to end) anastomosis was done using 6-0 polypropylene sutures in a watertight manner. After anastomosis is done, the arterial controls removed and the anastomosis is observed for any bleeding and presence of thrill and pulsation across the anastomosis. After satisfactory outcome in terms of hemostasis and flow across the anastomosis, the skin is closed with nylon 3-0 suture in interrupted manner and a light dressing is applied so as not to compress the anastomosis.

These fistulas were constructed using a minimal dissection approach to avoid devascularization of the venous wall in the juxta-anastomotic segment. Apart from this segment of the vein being used for anastomosis, the vein was not handled, mobilized, or clamped.

Follow-up:

All patients undergoing AVF creation were reviewed on post-operative day 1, 7, 14 and then monthly until three months or fistula maturation, whichever was earlier. The patients who had a functional fistula at the end of 3 months follow-up were included as a successful AVF and included in primary patency rate for statistical analysis. Patients having clinical suspicion of stenosis, i.e. diminished perception of thrill; hematoma, seroma, ecchymosis; were subjected for doppler ultrasound scanning. Assessment of the following aspects were done between these two groups for comparison.

- Time taken for completion of procedure
- Immediate complications in terms of bleeding, hematoma, thrombosis, gangrene, pulmonary edema
- Delayed postoperative complications like – steal phenomenon, venous hypertension
- Time to maturation of fistulas (post-operative day of starting of dialysis)
- Primary failure rate
- Re-exploration

ETHICAL CONSIDERATION

The purpose of the present study was to compare efficacy and safety of RADAR technique for AVF creation with classical technique for creation of AVF in patients operated at AIIMS Jodhpur. Both procedures have been mentioned in literature and the RADAR technique being relatively new has not been evaluated as much as the classical technique. Lack of comparative literature makes this study useful in future. All investigations and procedures were performed after informing patients and their attendants that they will be part of the study only after taking full informed consent.

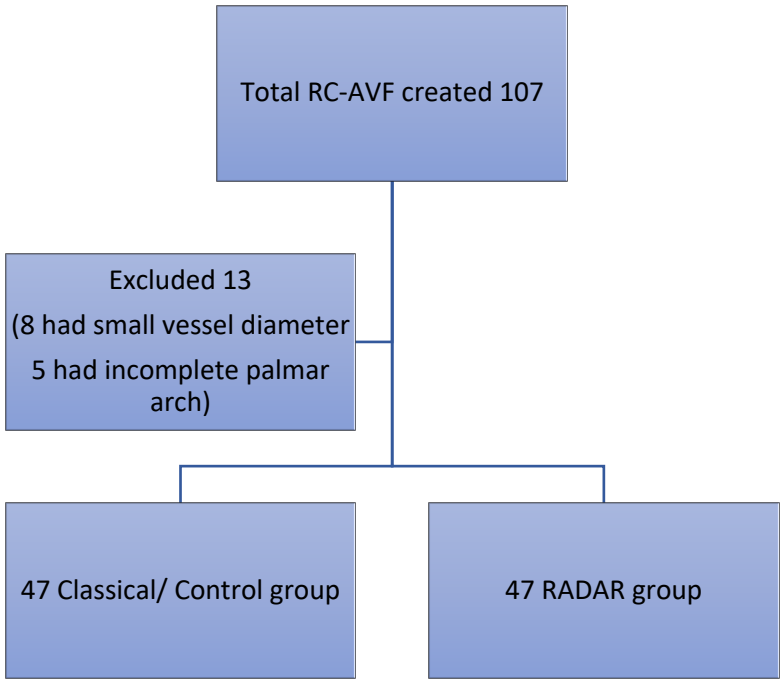
Statistical Analysis

The study was conducted as a randomised control trial, which included all the patients undergoing AVF creation in the department of urology, AIIMS, Jodhpur apart from those as mentioned in the exclusion criteria. The data so collected was entered into an excel sheet and analysis was done using SPSS 25 (SPSS Inc, Chicago, Il, USA) software. Appropriate statistical tests were applied and P value of <0.05 was regarded as significant.

Results

Between March 2021 to August 2022 a total of 107 cases were operated for RC-AVF for HD vascular access. Of these, 94 patients were enrolled in our study and 13 patients were excluded. The excluded cases had vascular characteristics pertaining to the exclusion criteria (8 patients had vessel diameter less than that mentioned in exclusion criteria and 5 patients had incomplete palmar arch). The remaining 94 cases enrolled in our study, were divided into two groups by computer generated randomization of 47 in each (Figure 3).

- Figure 3: Flow chart summary of patient recruitment and distribution into Classical/ Control and RADAR group. *RC-AVF – Radio-cephalic Arterio-venous fistula, RADAR – Radial artery deviation and re-implantation*



Demographic profile

Both the groups had similar demographic profiles and it is summarized in the following table (Table 1).

Table 1: Comparison of patient demographic profile between RADAR and Classical group

HTN - Hypertension, DM - Diabetes Mellitus, CAD – Coronary artery disease, CKD – Chronic kidney disease, HD - Hemodialysis

Variable	RADAR		Classical		P value
	No	% Or SD	No	% Or SD	
Average Age (Years)	44.36	15.85317	47.42	15.85317	0.856
Sex					
Male	37	78.7	33	70.2	0.344
Female	10	21.3	14	29.8	
Comorbidities					
HTN	44	93.6	42	89.36	
DM	4	8.51	12	25.53	
CAD	4	8.51	2	4.25	
Others	1	2.12	2	4.25	
Diameter (mm)					
Artery	2.18	0.20358	2.18	0.22824	0.159
Vein	2.29	0.24181	2.36	0.38086	0.200
CKD Diagnosis (months)	2.7553	2.16412	3.13	2.795	0.472
HD duration (months)	1.64	0.814	1.91	1.943	0.390
BMI	23.4043	1.34342	22.8745	1.77415	0.472

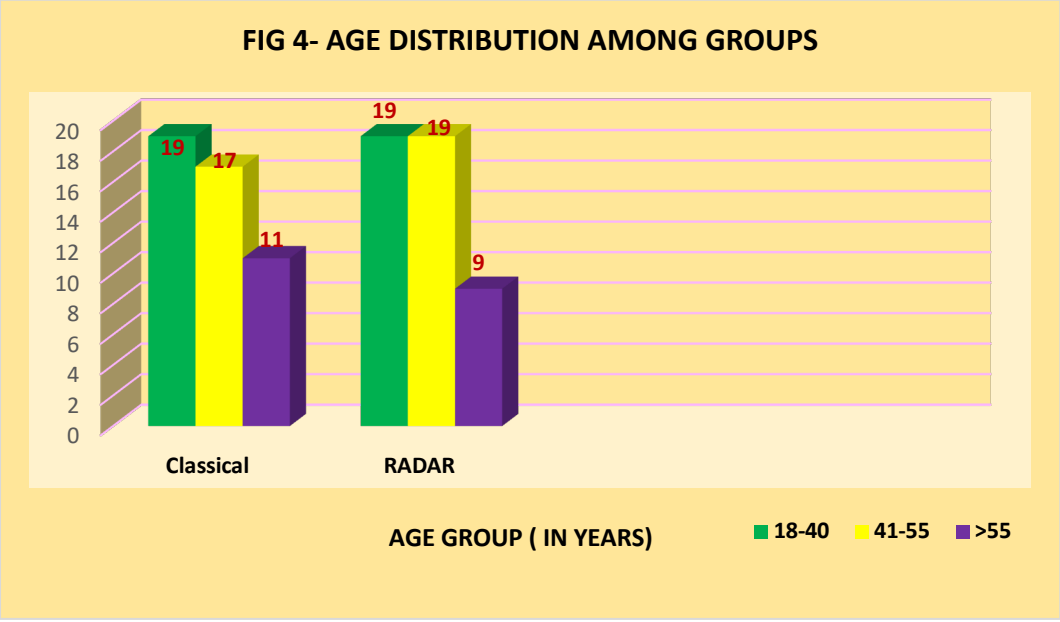
Age

The age of the study population ranged from 18 to 73 with average being 45.8 years. Comparing the individual groups, the average age in RADAR group was 44.36 and in the classical group was 47.42 years. The age distribution was classified into three categories, i.e. 18-40 years, 41-55 years and 56 years and above to assess any effect of age or uneven distribution among the groups on the outcome. The data was analyzed for any statistically significant variation (Table 2, P value – 0.856). The age category on analysis turned out to be

clinically insignificant with p value 0.856 implying a homogenous distribution of patients across both the groups (Figure 4).

Table 2: Table comparing age distribution among the two groups

		Age class			*P Value*
		18-40	41-55	56<	
Classical	No.	19	17	11	
	% within group	40.4%	36.8%	23.4%	
Radar	No.	19	19	9	
	% within group	40.4%	40.4%	19.1%	0.856
Total	No.	38	36	20	
	% within group	40.4%	38.3%	21.3%	



The average arterial diameter in both the groups was 2.18mm. The average diameter of cephalic vein in the RADAR group was 2.29mm and in the classical group was 2.36mm.

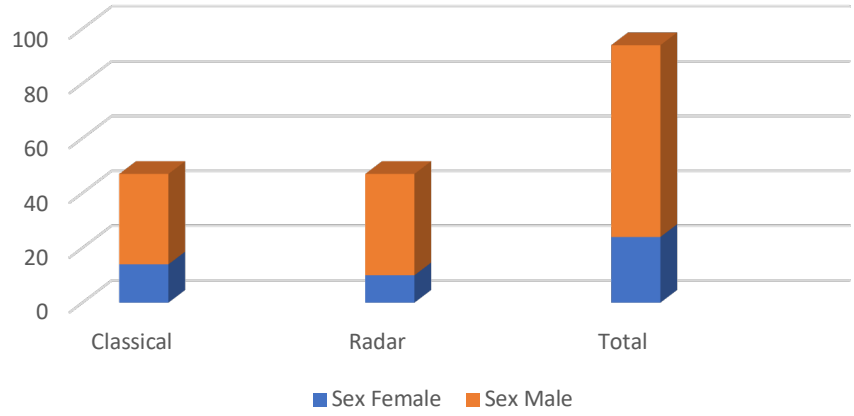
Sex

Of the 94 patients, 24 (25.5%) were female and 70 (74.4%) were male patients. There were 24 (25.5%) female patients and 70 (74.5%) male patients present in the study. When the sex distribution was analyzed in the individual group, there were 37 (78.7%) male and 10 (21.3%) female patients in the RADAR group, while the classical group had 33 (70.2%) male and 14 (29.8%) female patients (Figure 5). The sex distribution among the groups was statistically insignificant (Table 3, P value 0.344).

Table 3: Table comparing distribution of sex among the two groups

		Sex		*P Value*
		Female	Male	
Classical	No.	14	33	
	% within group	29.8%	70.2%	
Radar	No.	10	37	
	% within group	21.3%	78.7%	0.344
Total	No.	24	70	
	% within group	25.5%	74.5%	

Figure 5 - Distribution of sex



Duration of CKD

The duration of CKD diagnosis to AVF creation was noted. The diagnosis of CKD ranging from less than 1 month to 1 year with average being 2.9 months. For the RADAR group, the average duration from CKD diagnosis to AVF creation was 2.7553 (±2.16412) months and for the classical group, the average duration from CKD diagnosis to AVF creation was 3.13 (±2.795) months. Ninety-one subjects were already on maintenance HD by the time AVF was created and three cases were operated preemptively. Average time period since starting HD to AVF creation was 1.7 months which ranged from preemptive AVF creation to patients on HD for more than 6 months. For the RADAR group, the average duration from beginning of HD to AVF creation was 1.64 (±0.814) months and for the classical group, the average duration from beginning of HD to AVF creation was 1.9149 (±1.94299) months.

Comorbidities

Except for six patients, rest all the patients had at least one comorbidity apart from CKD status. Hypertension was the leading comorbidity present in 86 (91.48%) patients followed by diabetes mellitus present in 16 (17.02%) cases. Other comorbidities like coronary artery disease (CAD) and cerebrovascular accidents (CVA) were present to a lesser extent. The various comorbidities were noted and analyzed for and heterogeneous distribution among the groups (Table 4). However, it came out to be statistically insignificant.

Table 4: Table comparing distribution of comorbidities among the two groups

	CLASSICAL		**RADAR**			
	No	%	No	%	Count	%
Asthma, BPH	1	2.10%	0	0.00%	1	1.10%

	CAD	1	2.10%	0	0.00%	1	1.10%
	DM, HTN	11	23.40%	4	8.50%	15	16.00%
	DM, HTN, CAD	1	2.10%	0	0.00%	1	1.10%
	HTN	29	61.70%	35	74.50%	64	68.10%
	HTN, CAD	0	0.00%	4	8.50%	4	4.30%
	HTN, CVA	1	2.10%	1	2.10%	2	2.10%
	No	3	6.40%	3	6.40%	6	6.40%
TOTAL		47	100.00%	47	100.00%	94	100.00%

BMI

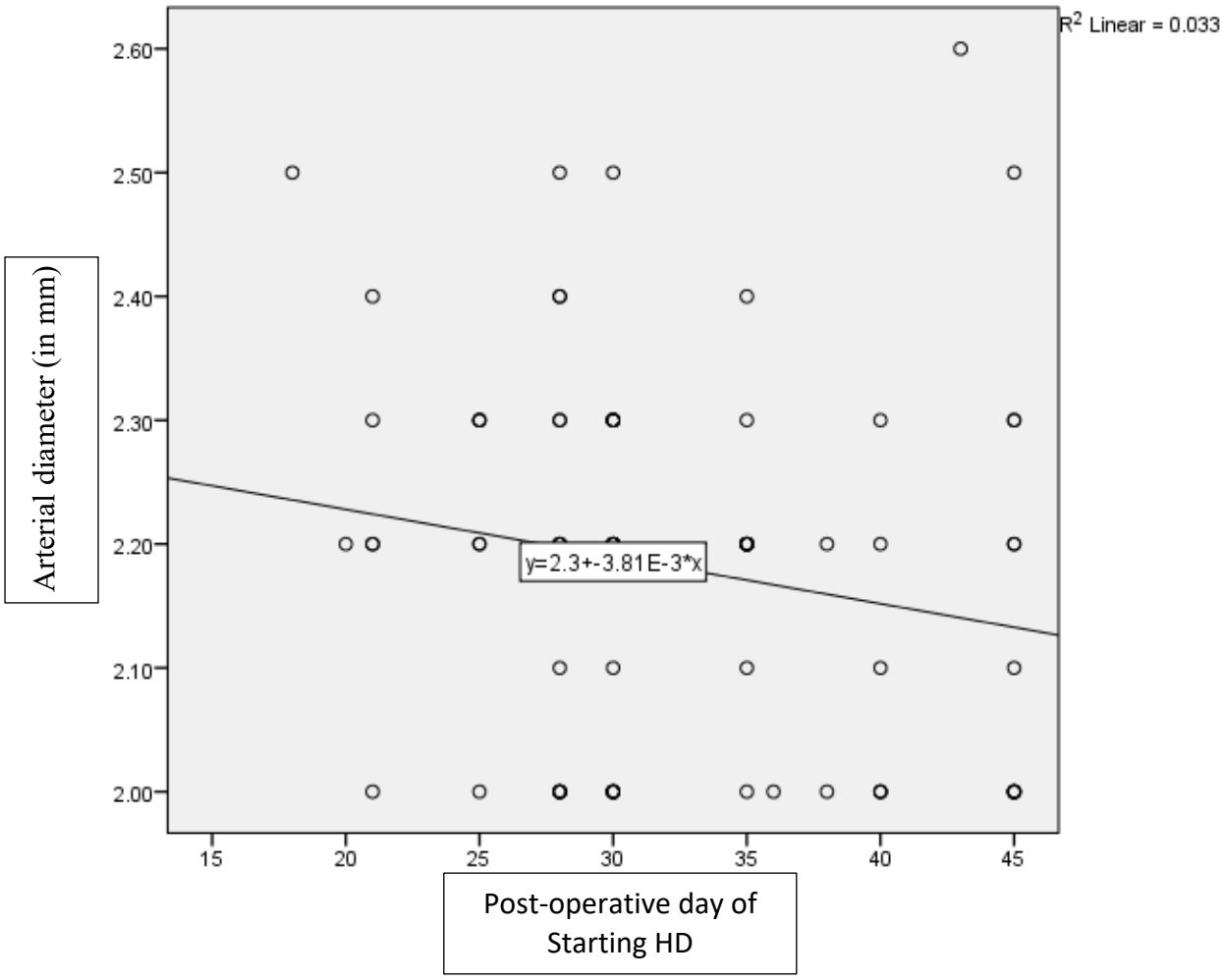
The average BMI of our study population was 23.19 kg/m². When comparing both the groups, the distribution of patients was similar with average BMI being 23.4043 (± 1.3432) kg/m² for the RADAR group and 22.8745 (± 1.77415) kg/m² for the classical group.

Vessel diameter

During the preoperative evaluation, the diameter of the radial artery and cephalic veins were noted in the preoperative USG doppler. The average diameter of artery was 2.1 (± 0.21) mm. The average diameter of artery in the RADAR group was 2.1830 (± 0.20358) mm and for the classical group the artery diameter was 2.1196 (±0.22824) mm. Both the groups had similar caliber vessels and the comparison was statistically insignificant with P value being 0.159. The average diameter of vein was 2.3 (± 0.231) mm. The average diameter of vein in the RADAR group was 2.2979 (± 0.24181) mm and for the classical group the vein diameter was 2.2128 (±0.38086) mm. However, when comparing the vessel diameters with maturation period, a linear correlation emerged. The scatter plot (Figure 6) shows the correlation of arterial diameter

with that of end result as measured by the day of starting of HD. The curve has R^2= 0.033, which indicate a greater diameter of artery in the pre-operative stage leads to better surgical outcome. Similarly, the scatter plot in Figure 7 shows the correlation between vein diameter with that of day to maturation. The R^2 for the vein scatter plot was 0.047 for the study population. Two separate scatter plots were designed for assessment of effect on time to maturation within each group. The R^2 for the vein scatter plot for the classical group was 0.004 and 0.164 for the RADAR group respectively. The clinical examination inferences of the artery and vein were independently evaluated with success rate and depicted in table 5 A and B.

Figure 6: Scatter plot showing correlation between arterial diameter and maturation time. *The curve has R^2= 0.033*



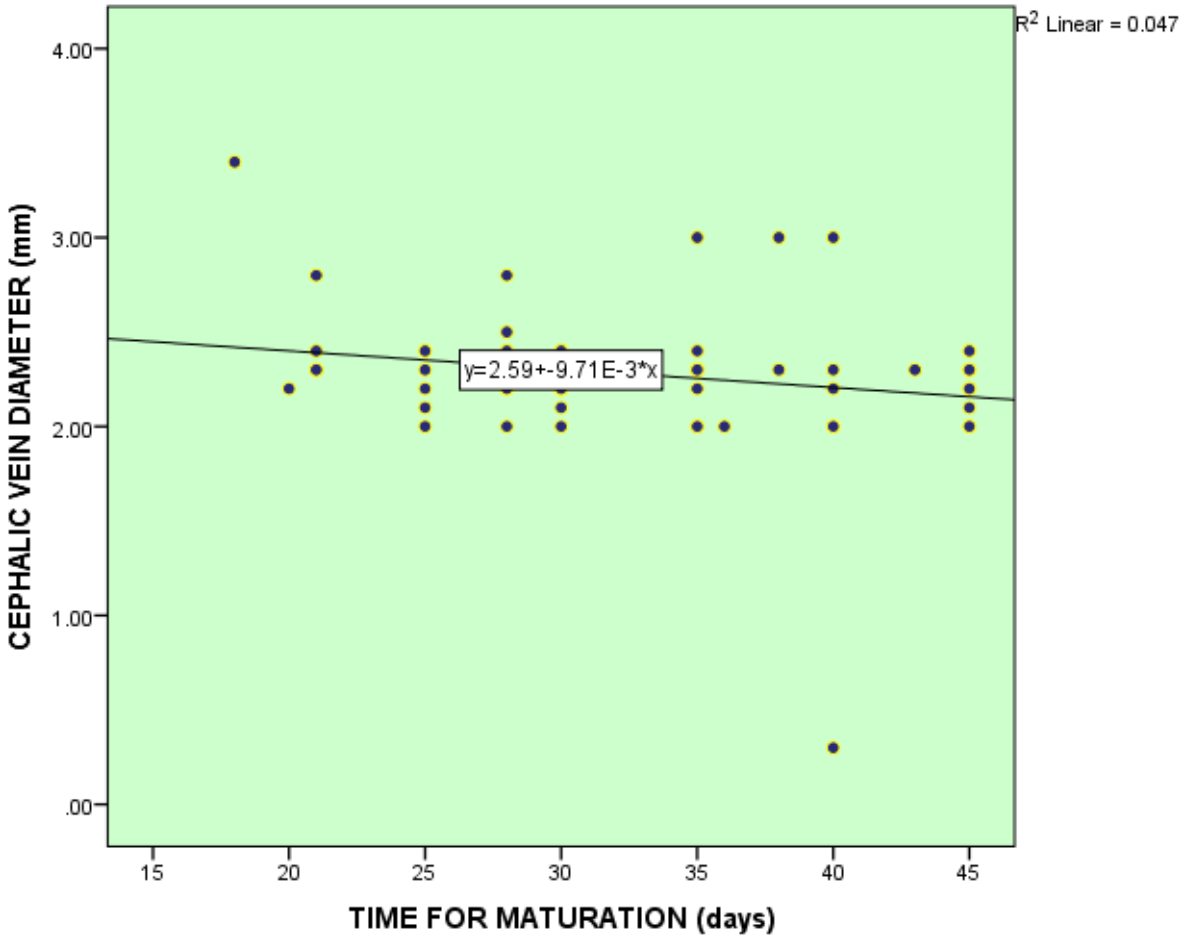


Figure 7 A : Scatter plot showing correlation between vein diameter and maturation time. *The R^2= 0.047 for the study population and 0.004 for classical and 0.164 for the RADAR group*

Table 5 A: Table comparing clinical examination of artery and success rate

Vessel examination		*Success*		*P Value*
		No	Yes	
Adequate	No.	0	1	
	%	0.0%	1.2%	
Average	No.	12	58	
	%	92.3%	71.6%	0.465
Good	No.	1	21	
	%	7.7%	25.9%	
Poor	No.	0	1	
	%	0.0%	1.2%	

Table 5 B: Table comparing clinical examination of vein and success rate

Vessel examination		*Success*		*P Value*
		No	Yes	
Adequate	No.	0	2	
	%	0.0%	2.5%	
Average	No.	1	0	
	%	7.7%	0.0%	0.038
Good	No.	11	58	
	%	84.6%	71.6%	
Poor	No.	1	21	
	%	7.7%	25.9%	

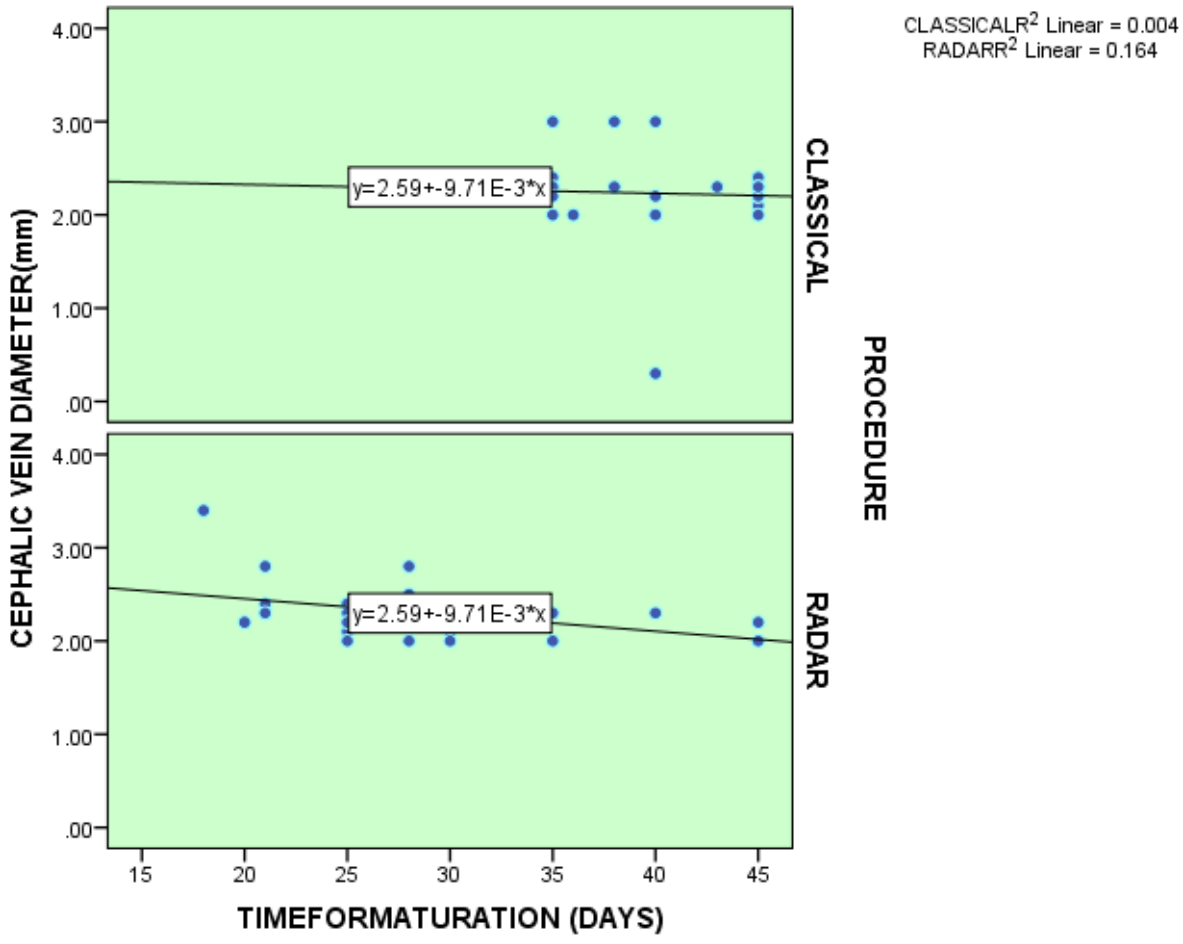


Figure 7 B : Scatter plot showing correlation between vein diameter and maturation time

From Table 5 A & B, the correlation between arterial clinical examination and success rate came out to be clinically insignificant (P value 0.465). The correlation between vein clinical examination and success rate came out to be clinically significant (P value 0.038)

All the intrinsic patient specific factors which could lead to a change in outcome and can introduce a bias like, the arterial diameter, the diameter of vein, duration of CKD and duration of HD prior to surgery were evaluated for their effect on success of the surgery individually. The individual parameters were analyzed with t-test and 95% confidence interval was calculated. The result is depicted in the table 6.

Table 6: Comparing risk factors with success of AVF surgery

INDEPENDENT SAMPLES TEST

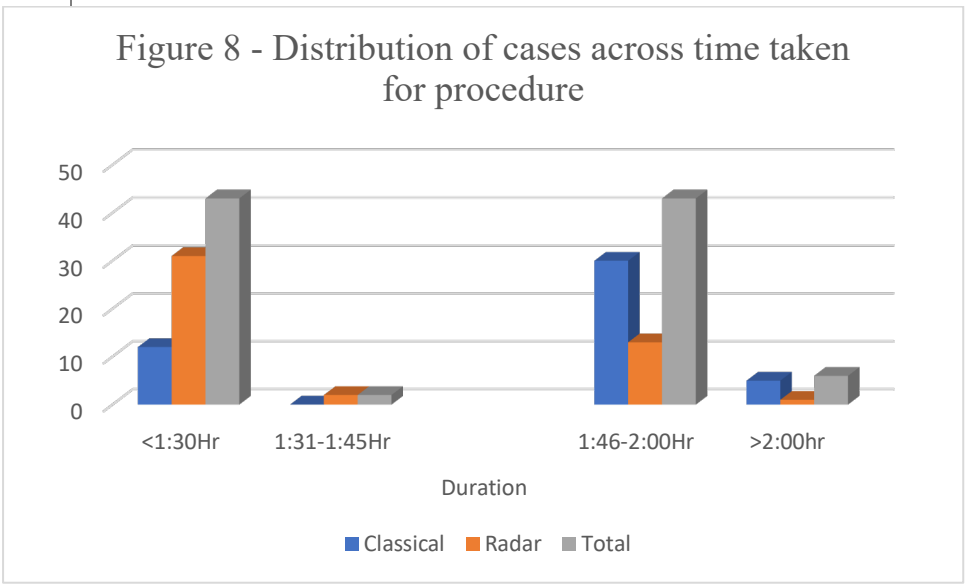
	t-test for Equality of Means			
Parameter	P VALUE	Std. Error Difference	95% Confidence Interval of the Difference	
			Lower	Upper
Artery diam.	0.553	0.03716	-0.05167	0.09592
CKD duration (month)	0.472	0.516	-1.396	0.652
HD duration(month)	0.389	0.307	-0.876	0.344
Vein diam.	0.199	0.06581	-0.04559	0.2158

The intraoperative findings were also noted and compared among both the groups. The time duration taken for completion of a procedure was measured. The average duration to complete a procedure for the RADAR group was 1 hour 40 minutes, while for the classical

group it was 1 hour 55 minutes. The time duration was split into 4 categories, i.e. 1<:30Hr, 1:31-1:45Hr, 1:46-2:00Hr, >2:00Hr and was analysed for statistically significance difference if any (Table 7, Figure 8). It was noted that, in the RADAR group; the procedure could be completed relatively quickly which was statistically significant (P value 0.001).

Table 7: Table comparing duration of surgery among the two groups

	Duration				*P Value*
	<1:30Hr	1:31-1:45Hr	1:46-2:00Hr	>2:00hr	
Classical	12	0	30	5	
Radar	31	2	13	1	0.001
Total	43	2	43	6	



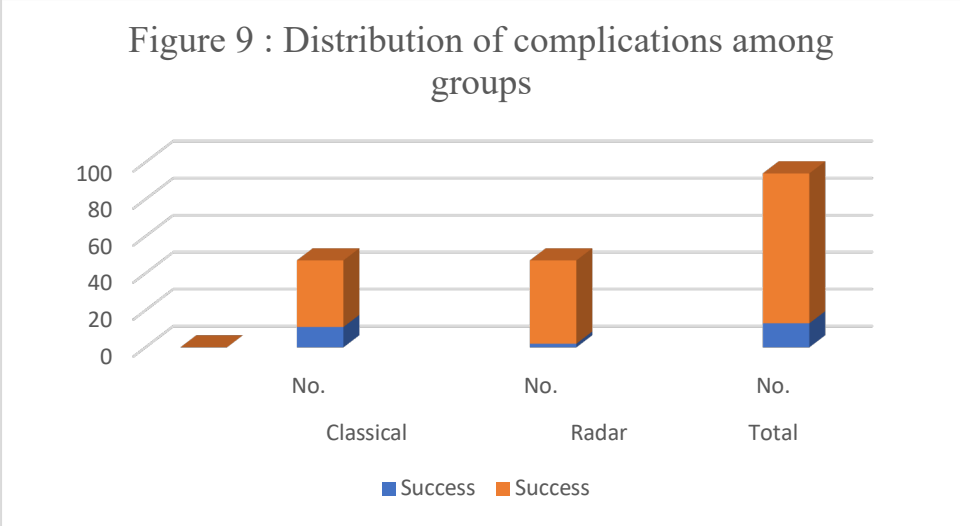
Complications

In the post-operative period, the various complications were noted into a pre-structured proforma. There were no cases of any death, ischemia or surgical site infection noted in either group (Table 7). Both the groups were followed up for 3 months or till the starting of HD whichever was earlier. Two patients, one from each group had minor complications in the form of edema over the dorsum of hand and surrounding the surgical site which resolved on

conservative management following limb elevation. Two patients in the RADAR group had acute onset breathlessness and pulmonary edema just after completion of the procedure. These two patients needed immediate HD for stabilization. None of the two patients required endotracheal intubation and could be managed with oxygen by face mask after HD. None of the patients in the classical group had such issues. One patient from each group underwent re-exploration for thrombosis on post-operative day 1. Comparing the complication rates in both the groups did produce a statistically significant result (Table 8, P value 0.044) in favor of the RADAR group (Figure 9).

Table 8: Table comparing complication rates of the two groups

		Complications		*P Value*
		No	Yes	
Classical	No.	33	14	
	% within group	70.2%	29.8%	
Radar	No.	41	6	
	% within group	87.2%	12.8%	0.044
Total	No.	74	20	
	% within group	78.7%	21.3%	

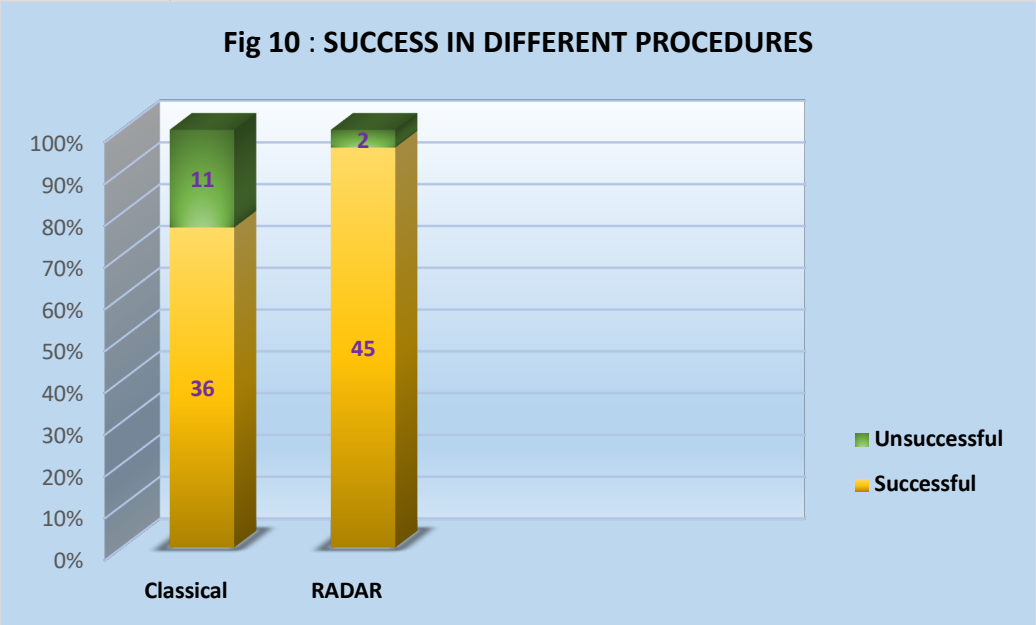


Failure

Comparing the failure rates, 11 patients in the classical group had failure while only 2 patients in the RADAR group had failure (Table 8, P value 0.007). Two patients in the classical group had low flow across the AVF. Although these patients did not technically had failure, but HD could not be started during the 3 months follow-up period and they were analyzed as failure. Out of the two patients who underwent re-exploration for thrombosis in the post-operative period, one from the classical group later went on to have functional AVF, however he was evaluated as a failure in the analysis. Similarly, one patient in the RADAR group who underwent AVF creation preemptively, was not still dialysis dependent by the end of 3-month follow-up period. This subject had functional AVF and the flow was adequate as measured by doppler USG. Hence this subject was evaluated as success and analyzed accordingly. The findings are displayed in the figure 10.

Table 9: Table comparing success rates

		Success		*P Value*
		No	Yes	
Classical	No.	11	36	
	% within group	23.4%	76.6%	
Radar	No.	2	45	
	% within group	4.3%	95.7%	0.007
Total	No.	13	81	
	% within group	13.8%	86.2%	



These cases were considered as failure and analysed as such. There were no instances of abandoned AVF or secondary failures. The primary failure cases were later operated for brachio-cephalic AVF. None of the patients underwent any endovascular procedure. When comparing the all-cause complication rates for both the groups, the result came out to be statistically insignificant (P value= 0.044).

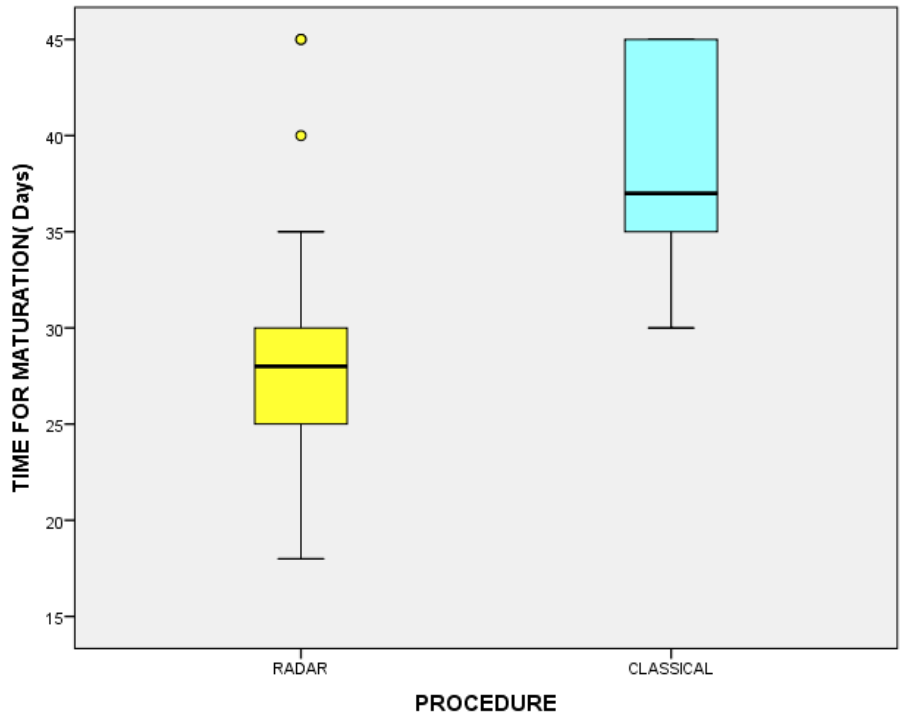
Time to maturation

The average time to maturation of fistula was measured as when the fistula was ready to support HD. This was noted down as a secondary outcome to measure efficiency of one particular procedure over another. The post-operative day on which HD was started was noted in previously mentioned proforma. The duration of maturation period was divided into two categories for analysis, that is less than 4 weeks and more than 4 weeks. Analyzing the data (Table 10), the RADAR group had statistically significant result (P value 0.001). The

Table 10: Table comparing maturation rates of the two groups

		Maturation		*P Value*
		< 4 week	>4 week	
Classical	No.	0	47	
	% within group	0.0%	100%	
Radar	No.	28	19	
	% within group	59.6%	40.4%	0.001
Total	No.	28	66	
	% within group	29.8%	70.2%	

Figure 11 : Chart depicting the difference in maturation time between the two procedures.



Patency rate

Once HD was started for a patient, the patient was evaluated at the end of 3 months follow-up period to assess whether HD was being continued or not (Table 11). This was the patency rates of each group. All the patients after initiation of HD had continued HD at the end of 3 months. On evaluation, ten patients from the classical group and 3 patients from the RADAR group were not undergoing HD. One patient in the classical group who had thrombosis of AVF was later re-explored and had a functional AVF leading to discrepancy in the number when compared with success rate. Similarly, one patient who underwent preemptive AVF creation was not on HD at the end of 3 months but he had a functional AVF in situ. The P value was calculated and turned out to be 0.036 (statistically significant).

Table 11: Table comparing patency rates of the two groups

		Continuation of dialysis		*P Value*
		No	Yes	
Classical	No.	10	37	
	% within group	21.3%	78.7%	
Radar	No.	3	44	
	% within group	6.4%	93.6%	0.036
Total	No.	13	81	
	% within group	13.8%	86.2%	

All the patient specific factors, that can affect the surgical outcome, were analysed with t- test to analyze the individual factor's influence and the results were noted (Table 12). The duration of CKD diagnosis to AVF creation was noted for each patient. In the classical group it was 3.13 (±2.795) months and in the RADAR group it was 2.76 (±2.164) months. The

Table 12: Independent T Test Between Procedure and Continuous Variables

	Classical (mean)	*SD*	*RADAR (Mean)*	*SD*	*p Value*
Duration of CKD (months)	3.13	2.795	2.76	2.164	.472
Duration of Hemodialysis (months)	*1.91*	*1.943*	*1.65*	*.814*	*.389*
Radial artery diameter (mm)	2.1630	.20616	2.1872	.14237	.509
Cephalic vein diameter (mm)	2.2277	.36576	2.3021	.23636	.244
Time for maturation (in days)	*37.78*	*5.683*	*28.33*	*5.437*	*.001*

p value was calculated to be 0.472. The duration of HD before the procedure was evaluated. The average duration of HD before the procedure in the classical group was 1.91 (±1.943) months and for the RADAR group, it was 1.65 (±0.814) months. The p value was calculated

to be 0.389. The average diameter of the radial artery in the classical group was 2.163 (± 0.20616) mm and in the RADAR group it was 2.1872 (± 0.14237) mm. The p value was calculated to be 0.509. Similarly, when comparing the cephalic vein diameter, for the classical group; the average diameter was 2.2277 (±0.36576) mm and for the RADAR group it was 2.3021 (±0.23636) mm. The p value was 0.244. The average duration to maturation in the classical group was 37.78 (±5.683) days and in the RADAR group it was 28.33 (±5.437) days. The p value in the duration of maturation category came to be 0.001 which was suggestive of clinically significant outcome.

All the outcome factors, i.e.; success rate, complication rate, time to maturation and continuation of dialysis, were evaluated with univariate analysis to calculate the odds ratio with respect to procedure (Table 13). The RADAR group was taken as reference for calculation. The unadjusted odds ratio for the success rate was 0.145 with 95% confidence interval being 0.030 the upper and 0.699 the lower limit. The P value was calculated to be 0.016.

Table 13 UNIVARIATE REGRESSION ANALYSIS OF OUTCOMES W.R.T. PROCEDURE

	NO.	**% OF PROCEDURE**	**UNADJUSTED OR**	**95% CI**		**P VALUE**
				Upper	Lower	
SUCCESS						
RADAR (REF)	45	95.74				
CLASSICAL	36	76.59	0.145	0.030	0.699	0.016
COMPLICATION						
RADAR (REF)	6	12.8				
CLASSICAL	14	29.8	2.899	1.004	8.372	0.049
MATURATION TIME						

RADAR (REF)	28.33					
CLASSICAL	37.78		18.874	15.136	22.613	0.001
CONTINUATION DIALYSIS						
RADAR (REF)	44	93.61				
CLASSICAL	37	78.72	.252	.065	.985	.048

The unadjusted odds ratio for the complication rate was 2.899 with 95% confidence interval being 1.004 the upper and 8.372 the lower limit. The P value was calculated to be 0.049. The unadjusted odds ratio for the maturation time was 18.874 with 95% confidence interval being 15.136 the upper and 22.613 the lower limit. The P value was calculated to be 0.001. The unadjusted odds ratio for the continuation of dialysis was 0.252 with 95% confidence interval being 0.065 the upper and 0.985 the lower limit. The P value was calculated to be 0.048.

The various factors which are supposed to affect the success rate were evaluated with univariate regression analysis and the unadjusted odds ratio and 95% confidence interval was

Table 14 Univariate Regression Analysis Of Variables W.R.T. Success

	Unadjusted OR	**95% CI**		**p Value**
		Lower	Upper	
Age (years)				
18-40(ref)				.360
40-55	.628	.180	2.194	.466
>55	2.879	.313	26.506	.351
SEX				
Male	.333	.099	1.118	.075
Female (ref)				
CKD DURATION	.909	.742	1.114	.358
HEMODIALYSIS DURATION	1.376	.657	2.880	.397
BMI	1.144	.793	1.651	.472
Radial artery diam.	3.961	.088	178.903	.479
Cephalic vein diam.	15.969	14.160	25.856	**.003**
EXAMINATION OF VEINS				
Adequate(ref)				.300
Average	2.636	.220	31.655	.445
Good	10.500	.460	23.781	.141
PROCEDURE				
RADAR (Ref)	.145	.030	.699	.016
Classical				
MATURATION TIME	.744	.540	1.025	.070

Cont.Dialysis	.005	.001	.036	.001
Complication	.000	.000		.996

calculated (Table 14). Out of which, the cephalic vein diameter came out to be statistically significant with P value being 0.003. The RADAR procedure was associated with higher success rate with P value being 0.016. Rest of the parameters came out to be statistically insignificant.

The statistically significant factors were then analyzed for significance with multivariate analysis (Table 15). The P value for the RADAR procedure came out to be 0.018. The P value for cephalic vein diameter came out to be 0.002.

Table 15 MULTIVARIATE REGRESSION ANALYSIS W.R.T. SUCCESS OF PROCEDURE

	Adjusted OR (AOR)	**95% CI**		**p Value**
		Lower	Upper	
RADAR (Ref)	.091	.013	.663	.018
Classical				
Cephalic vein diam.	3.907	2.397	3.175	.002

In our study, we found that the RADAR technique is better than the classical technique in terms of patency rate, ease of doing the procedure and complication rate. The RADAR group also had superior outcome in terms of time to maturation as the AVFs made in the RADAR group were ready for HD earlier than in the classical group. Longer duration to maturation was more pronounced in the classical group as two patients despite having a functional fistula, did not have enough flow rate across the fistula to support HD at the end of 3 months follow up period. The study was completed within the stipulated time period and the predetermined sample size of 47 in each group could be achieved. There were no cases of loss of follow up and all the cases could be evaluated and analyzed properly in the pre-operative and post-operative period. All the patient specific factors, like – age, sex, comorbidities, vessel diameter etc. were homogenously distributed among the groups.

To our knowledge, this is the first instance of comparing the RADAR method with the classical method in a randomized control trial. When evaluate the various aspects of the study, many new findings came up.

The initial pre-operative work-up included the USG doppler study of vessels. Our study showed that the initial diameter the veins can significantly affect the outcomes of the procedure (Figure 4,5). Irrespective of the procedure, the vein diameters were independent predictors of a successful AVF creation. Our findings of better outcome with larger diameter of vein corresponds to previous studies done in this field. This was similar to a study conducted by Harold et al (24). A study conducted by Zadeh et al also found a similar relation between the preoperative vein diameter and time to maturation with a larger vein diameter resulting in a favorable outcome in terms of time to maturation. This finding was also corroborated with our pre-operative clinical examination findings. When the clinically observed vessel status was compared with success rate, it turned out to be statistically significant. This finding further solidifies the role of clinical examination before a patient is undertaken for AVF creation.

The sex distribution ratio in our study was M: F :: 70:24 overall. Similar ratio was also reflected in each of the groups also. For the classical group, the ratio of F: M was 14:33 and in the RADAR group the F:M ratio was 10:37. There was no statistically significant difference in sex distribution in either of the groups (0.344). Some of the previous studies have demonstrated a higher failure rate and longer duration of maturation in female sex. A study by Miller et al showed a clinically significant failure rates among female patients (25). They observed a female to male success ratio of 31:51 in terms of percentage. However, a similar study by Feldman et al did not show any significant difference among male and female patients in terms of success of the surgery. In our study too, the difference among male and female patients was not significant in terms of success of the procedure.

The various comorbidities result in poorer outcome following any kind of procedure and the AVF is no exception. However, it has been known historically that, HTN favors AVF patency. The higher blood pressure maintains adequate flow across the newly created AVF and helps preventing thrombus formation. This observation was initially made by Lazaries et al (26). They noted that higher blood pressure (BP) was associated with significantly better outcome and patients with BP on the lower side were prone for thrombus formation at the anastomosis site. We had 86 (91.48%) patients with HTN which might be a leading cause of higher success rate in our study when compared with other similar studies. Similarly, DM has been associated with poorer success rates among patients undergoing AVF creation. Thomsen et al in their study found that DM was associated diabetes vasculopathy and lead to more failure rates in the population with DM (27). In our study 16 (17.02%) patients had DM. We did not find any correlation between DM and failure rates among our study population. The duration since diagnosis of CKD to AVF creation and the period of maintenance HD have also been implicated as significant predictors of outcome. It has been observed since long that advanced uremic condition (longer duration since diagnosis of CKD to AVF creation) can lead to higher

failure rates. George et al in their study noted that patients undergoing AVF creation preemptively had a higher success rate (28). Similarly, patient who were on HD for a longer period of time had poorer outcome after AVF creation (24). In our study, the duration from diagnosis of CKD to AVF creation was on an average 2.7 months for RADAR and 3.1 months for the classical group. The average duration of HD to AVF creation was 1.6 months in the RADAR group and 1.9 months in the classical group. When compared for success rates of AVF creation, both the CKD duration and HD duration the outcome was statistically insignificant. The p value for CKD duration and HD duration when analyzed with t-test for equality of means, came out to be 0.47 and 0.36 respectively. This is contrary to some of the previously done studies (28). This discrepancy can be due to the fact that the time period from diagnosing CKD to performing AVF was relatively short. Similarly, the time duration from starting of maintenance HD to AVF creation was also short. Three patients underwent AVF creation preemptively also. Therefore, we cannot comment on the effect of preoperative HD status and duration of advanced CKD status on AVF outcome.

The average BMI was 23.139 kg/m^2 in our study population. We did not observe any correlation between BMI and success or failure rates of AVF. However, it has been proposed that, obesity is a poor predictor of AVF success. Kats et al in his study observed that obese patients had on an average poor patency rates (29). This finding doesn't correspond to our findings. The discrepancy may be attributed to the smaller number of obese patients in our study population and most patients belonging to the normal BMI range with average being 23.139 kg/m^2.

Similar results were noted by Sadagihanloo et al (3). In this land mark paper, they noted that the RADAR group had excellent primary patency rates, secondary patency rates and maturation rates also. There were also significantly less intervention rates. In our study, the RADAR group had similar or low complication rates when compared with the classical method

and the complications in both the groups when compared were statistically significantly different from each other in favor of the RADAR group (P value = 0.44). Two patients in the RADAR group had pulmonary edema in the immediate post-operative period needing HD. While these can be an isolated event, due to pre-existing undiagnosed cardiac condition or it might be due to the immediate high flow rates across the AVF following the RADAR procedure. In a recent meta-analysis conducted by Al-Jaishi et al (2) showed a cumulative primary failure rate of 23%. In our study, the classical group had primary failure rate of (23.4%), which is similar to previously reported studies. However, the RADAR group had significantly lower rates of primary failure rates at only 4.2%. The reason for this result may be dependent on the physics of the procedure itself. When a fistula is made, there occurs non-laminar flow of blood. Such turbulent flow is prone for thrombus formation. A higher flow rate, as that occurs in the RADAR group could have been a cause to prevent the establishment of minute scaffolding on which larger thromboses get established. The gentle curvature created in the radial artery during RADAR procedure helps in smooth transfer of the arterial pressure and blood towards the venous channel. In addition to this, minimal handling of the vein preserves its microvascular integrity and later proper healing without narrowing. This prevents anastomotic stenosis and neo-intimal hyperplasia seen in the venous side of anastomosis (3). All these factors result in a higher success rate of AVF. This also reflects in the long term follow up as lesser degree of secondary failure rates and the AVFs mature in short duration of time also.

In our study, we measured the time duration for each procedure as an indicator for ease of doing the procedure. As per our knowledge, ours is the only RCT comparing the RADAR method with the classical method. Nevertheless, we could not find any other study comparing the time duration taken for various methods to create AVF. In our study, the time required to perform the procedures were divided into four categories for evaluation, i.e., up to1:30 Hr,

1:31-1:45 Hr, 1:46- 2:00 Hr and 2:00Hr <. All the procedures were compared and the time duration to perform a procedure came out to be significant (P value 0.001) in favor of the RADAR group. Such finding can be attributed to relative simplification of steps of doing the procedure in the RADAR group. In the RADAR group, the vein is handled as little as possible so that time is saved which would otherwise have been spent dissecting a large segment of the vein out of its natural position. Similarly, the artery is ligated and mobilized towards the vein which was rather easy after proper vascular control. All these factors lead to a better primary success rate and shorter duration to maturation.

Since the advent of AVF, it has been troubled by failures. Unlike other procedures, the AVF after its creation is subjected to adverse conditions continuously in the form of turbulent blood flow, pricks for HD and also the CKD status of the patient itself. Moreover, the surgical procedure itself has some inherent factors for failure. One of such factors is the angle between the two vessels being anastomosed. If the angle is too acute, then the blood flows with excessive turbulence and may lead to stenosis later. Likewise, overzealous dissection of the vein can lead to damage to the vasavasorum of the vein. These factors lead to a cascade of abnormal wound healing and result in neointimal hyperplasia in the venous channel of the AVF. The RADAR technique addresses both these issues and this might be the cause behind the higher success rate in the RADAR group. In the RADAR technique the artery is mobilized in a gentle curve so as to make a favorable angle for anastomosis. Not disturbing the venous channel helps in preserving the vasavasorum and possibly contributes the higher success rate in this group.

The AVF for HD has been through many iterations over the period of years. All the forms are associated with failure rates which are quite high and the search for an ideal method is still on going. One study by L. Wolowczyk et al published in January 2000 retrospectively analyzed the patency rate of RC-AVF done in the snuff box (30). The authors analysed the AVFs done in the snuff box between 1985 to 1997 and followed up the patients for patency

rates. There were 11% occurrence of thrombosis within the first 24 hours. The maturation rate was 80% at six weeks. The patency rate was 65% at 1 year. This approach could provide with a long segment arterialization of vein with preservation of more proximal veins for further intervention if required. However, this method had higher failure rates when compared with the classical method which had failure rates around 20-25% (Our study 23.4%). Hence this method could not gain popularity and was abandoned in favor of the classical method.

Allon et al evaluated the effect of preoperative mapping of vessels with ultrasound (USG) for planning of surgery (31). They noted that with USG mapping and better planning, the fistulas could be made with higher success rate. The rate of adequacy increased from 46 to 54%. Marked improvement was noted among diabetic (21 to 50%) and female patients (7 to 36%). Such cases are supposedly have compromised vascular status in terms of atherosclerosis and small diameter of vessels. By carefully selecting the appropriate vessels, the success rate could be improved. In our study, we examined every patient and assessed the vascular status clinically. We also did USG doppler of all patients in the preoperative phase and included patients for the procedure when the doppler was suggestive of adequate vessel diameter (i.e., 2mm) and no evidence venous thrombosis. We also examined the patients for completeness of the palmar arch and patients with incomplete palmar arch were excluded from the study. The patients with smaller diameter of vessels, although excluded from the study, underwent AVF creation nonetheless with variable success or at different site (brachio-cephalic AVF). This ensured that optimal patient selection is being done. The better vascular status also reflected in results (Table 5 A&B, Figure 7 A&B). The findings are suggestive of larger diameter of vessels is associated with better outcomes in terms of time to maturation. This phenomenon is more associated with the vein. The clinical examination also confers this finding signifying the importance of a complete and proper clinical examination.

In a study published in 2001, Gibson et al compared prosthetic grafts, simple autogenous fistulas and venous transposition fistulas for primary failure, patency rate re-intervention rate (32). They found that prosthetic grafts had a higher risk of primary failure when compared with autologous AVF (Relative risk 1.41). On long-term follow up, the autologous AVF had a primary patency rate of 39.8%. The autologous AVF had greatest success rate when compared with prosthetic graft or venous transposition. Our results also confer to these findings with our classical group having similar success rates and the RADAR group having even better results in terms of patency rates.

While analyzing the various patient factors in success or failure of AVF, one of the crucial factors that sometimes is overlooked, i.e., the surgeon. The surgeon plays crucial role in performing any surgery and the role of the surgeon is indispensable in high stake surgeries like AVF creation. One study by Prischl addresses this issue (33). They analyzed the outcome of AVF from various parameters including the operating surgeons. They concluded that, when the groups are matched demographically; the surgeon is the most important factor determining the outcome of the procedure. Similarly in our study, only the same group of experienced surgeons performed all the cases. The performing surgeons had more than 50 cases experience in doing the classical AVF and also performed 10 RADAR procedures each before the study was initiated. This led to standardization of surgical steps and overcame the learning curve and associated failure rates.

The timing of creating AVF is also of paramount importance. In a study published in 1998 by Hakim et al, discusses this point in detail (34). They noted that, early placement of a vascular access improves the survival of the access and also improves the patient outcomes as well. The longer a patient lives with CKD, the chances of a successful AVF surgery decreases. The CKD status is usually associated with higher BP and persistently high BP leads to remodeling of the peripheral vessels and leads to atherosclerosis and thickening of the arteries.

Advanced CKD status with high urea content also leads to damage to the peripheral vessels and more prone to thrombosis. In our study, the average duration from starting of HD to AVF creation was within 2 months, while 3 cases underwent pre-emptive AVF creation. This might be a reason behind the better outcome in our study population. This study further acknowledges the many nuances of AVF and recommends to perform vascular access surgery as early as possible for better patient outcome and AVF survival too.

Age is a significant factor in any patient undergoing some kind of surgery. Elderly age subjects are associated with poorer wound healing, unfavorable changes in the vascular structure which leads to higher failure rates in AVF surgery. A study by Smith et al found that increasing age was associated with poorer outcome in patients undergoing AVF (28). In our study population, the age ranged from 18- 73 years with the average being 45.8 years. To bring out effect of age on success rate, the age was further classified into three categories. However, no statistically significant result could be found. This can be attributed to the age group in our study population, as majority of our subjects were less than 50 years of age.

We found that clinical examination of veins closely corelates with outcome and also predicts a shorter duration of maturation. Marko et al, also found similar findings in his study (35). He found that proper clinical examination is as good as or even better than doppler USG in predicting the outcome.

There has been only one more study comparing the classical group and RADAR group by Nirvana et al (3). Along with this, we compiled few more similar studies for comparison (Table 16). This comparison shows that, our study is comparable to previous studies as far as the classical group is considered. The RADAR group performed better than many previous study cohorts.

Table 16 : Comparison among various studies

Study	Type	Age	Sex (M)	No.	Failure	Primary Patency
Field et al (36)	Retrospective	61.7	59%	210		49%
Korten et al(37)	Retrospective	65	55%	148	11%	
Jennings (38)	Retrospective	61	39%	134		80%
Gibson et al (32)	Retrospective	66	53%	492		56.1%
Marko (35)	Prospective	51.4	47%	116	20%	
Nirvana et al (3)	Ambispective					
RADAR		66	70%	53	9.43%	73.58%
CLASSICAL		70	74%	73	27.3%	68.49%
Our study	RCT					
RADAR		44.3	37	47	4.2%	95.8%
CLASSICAL		47.4	33	47	23.4%	76..6%

This distribution clearly demonstrates the superiority of the RADAR technique over the standard classical technique. Our study had one of the best outcomes of all the studies compared here.

Limitations of the study

The study had a short follow-up period. As it was time bound, longer follow up could not be done.

Conclusions

The AVF creation is a technically demanding surgery with high failure rates. Proper patient selection and preoperative optimization is of paramount importance in success of the procedure. The RADAR procedure is a safe and more efficient alternative to the current classical method of AVF creation. Longer duration of follow-up is required to assess the long-term outcomes in the future.

Summary

Surgically created arteriovenous fistulas (AVFs) are the gold standard for hemodialysis access for patients with end-stage renal disease. Standard practice of arteriovenous fistula creation involves selecting the non-dominant upper limb and starting with most distally with radio-cephalic arterio-venous fistula (RC AVF). The primary patency rate of RC AVF varies from 20-25%. It has been suggested the neointimal hyperplasia at the mobilized venous segment causes stenosis of the anastomosis. Therefore, the RADAR technique, in which the vein is minimally moblised, should result in a higher success rate. In our study we recruited 94 patients in two randomised groups and performed the AVF by the classical method or the RADAR method. The RADAR group had higher primary success rate (P=0.007), less rate of complications (P=0.04), shorter duration of surgery (P= 0.00) and early time to maturation (0.001) when compared with the classical group. The RADAR procedure is a safe and a more efficient alternative to the current classical method of AVF creation. Longer duration of follow-up is required to assess the long-term outcomes in the future.

Recommendations

- All patients should undergo preoperative detailed clinical evaluation and USG doppler to assess the vascular status.
- The patients should undergo AVF creation following diagnosis of CKD as soon as possible preferably before the need of maintenance HD.
- RADAR procedure should be adopted whenever feasible. (After ensuring patency of palmar arch)
- During dissection, the vein should be mobilized as little as possible.
- Preoperative cardiac evaluation maybe considered in high-risk patients.

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Annexure

ANNEXURE-1 A

GOVERNMENT OF INDIA

ALL INDIA INSTITUTE OF MEDICAL SCIENCES,

JODHPUR-342005, INDIA

INFORMED CONSENT FORM (in English)

I _____ s/d/w of _____ , a resident of

_____ ,

hereby declare that I give informed consent to participate in the Thesis study labelled **"COMPARISON OF RADIAL ARTERY DEVIATION AND REIMPLANTATION TECHNIQUE VS CLASSICAL TECHNIQUE IN CREATION OF ARTERIO-VENOUS FISTULA: A RANDOMISED CONTROL TRIAL".** Dr Shakti Swarup Sarangi has informed me to my full satisfaction, in the language I understand, about the purpose, nature of study and various investigations to be carried out for the study. I have been informed about the duration of the study and possible complications caused by study.

I give full consent for being enrolled in the above study and I reserve my rights to withdraw from the study whenever I wish without prejudice of my right to undergo further treatment at this hospital and its associated hospitals.

_____ _____

Name of Subject Date Signature of subject

We have witnessed that the patient signed the above form in the presence of his/her free will after fully having understood its contents.

_____ _____

Name of Witness Date Signature of witness

_____ _____

Name of Investigator Date Signature of Investigator

ANNEXURE-1 B

GOVERNMENT OF INDIA

ALL INDIA INSTITUTE OF MEDICAL SCIENCES, Jodhpur

सूचित स्वीकृति पत्र (in Hindi)

अध्यन का विषय: "आर्टेरियोवेनस फिस्टुला के निर्माण में रेडियल धमनी की स्थानांतरित बनाम शास्त्रीय तकनीक की तुलना - एक यादृच्छिक नियंत्रित परीक्षण"

जांचकर्ता का नाम: डॉ. शक्ती स्वरुप षडंगी

मुझे जो सूचना पत्र दिया गया है, मैंने उसे ध्यानपूर्वक पढ़ लिया है और मुझे अच्छे से समझा दिया है। मुझे प्रशन पूछने का पूरा अवसर दिया गया है। मुझे इस अध्ययन के लक्ष्य, इसके लाभ अथवा हानि, इसकी अपेक्षित अवधि और अन्य बातें विस्तार में बताई गयी हैं। इस अध्यन में भाग लेना पूरी तरह मेरी मर्ज़ी पर निर्भर करता है और मैं स्वतंत्र रूप से जब चाहूं इस अध्यन से अलग हो सकता हूँ और ऐसा करने पर मेरे इलाज पर कोई असर नहीं पड़ेगा।

मेरे बारे में जो जानकारी एकत्रित की जा रही है वह अध्यन के लिए है, और में जानकारी के इस्तेमाल के लिए अनुमति देता हूँ। मैं इस अध्यन में भाग लेने के लिए पूरी तरह से सहमत हूँ।

(हस्ताक्षर / बाए अंगूठे का निशान)

मरीज़ का नाम:

घर का पता:

हम यह प्रमाणित करते हैं कि मरीज़ ने परचा पढ़ कर अपनी सहमति से हस्ताक्षर किये हैं।

गवाह के हस्ताक्षर
नाम:

अन्वेषक के हस्ताक्षर
नाम:

ANNEXURE-2A
PATIENT INFORMATION SHEET (in English)

Study Title: COMPARISON OF RADIAL ARTERY DEVIATION AND REIMPLANTATION TECHNIQUE VS CLASSICAL TECHNIQUE IN CREATION OF ARTERIO-VENOUS FISTULA : A RANDOMISED CONTROL TRIAL

Student : Dr. Shakti Swarup Sarangi
Supervisor : Dr. Arjun Singh Sandhu
Professor and Head
Department of Urology, AIIMS Jodhpur

INTRODUCTION: This statement describes the purpose, procedure, benefits and risks of the study and your right to withdraw from the study.

PURPOSE OF THE RESEARCH STUDY: Arterio-venous fistula creation is the preferred method for creation of vascular access in chronic kidney disease patients. Radio-cephalic AVF is created most commonly. However, primary failure rate due to stricture near the anastomotic site is very high. It is theorised that by moving the vein less, the AVF can have better outcome. Thus, this study is conducted to assess the benefits of RADAR technique to create AVF.
STUDY PROCEDURES: After detailed history and physical examination, patients will undergo a set of investigations that is routine blood investigations and radiological imaging. After that patient will undergo AVF creation. One group will undergo the classical method and the other group will undergo RADAR method, where the radial artery is mobilised for anastomosis. Randomization will be done by computer generated random numbers and patients would be randomized to either group using sealed envelopes which will be opened immediately before the surgery. This randomization will not affect treatment of either group of patients in any way.

WITHDRAWAL FROM STUDY: You are free to decide whether to participate or not in the study or withdraw from the study anytime. If you choose not to participate in the study or withdraw from the study, you will continue to receive the same amount of care and treatment at AIIMS, Jodhpur.

POTENTIAL BENEFITS AND RISKS: In group 1 (Classical technique) patients are at low risk for gangrene of hand and it is more commonly performed technique while in group 2 (RADAR technique) patients will have better primary success rate of AVF.

FOLLOW UP: Patient will be followed up postoperatively until 3 months or fistula maturation.

CONFIDENTIALITY OF STUDY AND MEDICAL RECORDS: If you agree to participate, all information disclosed during the study will be recorded in a proforma and will be kept fully confidential. You will continue to receive routine hospital care, as needed.

SUBJECT'S RIGHTS: If you have any questions, please feel free to ask.

CONTACTS: At any time in the course of study, if you wish to get any kind of information, kindly contact the following:

Dr. Shakti Swarup Sarangi
Department of Urology,
AIIMS Jodhpur, 342005
Tel: 8860504007

Dr. Arjun Singh Sandhu
Professor and Head
Department of Urology,
AIIMS Jodhpur, 342005

ANNEXURE-2B

PATIENT INFORMATION SHEET (in Hindi)

रोगी सूचना पत्र

अध्यन का विषय: "आर्टेरियोवेनस फिस्टुला के निर्माण में रेडियल धमनी की स्थानांतरित बनाम शास्त्रीय तकनीक की तुलना - एक यादृच्छिक नियंत्रित परीक्षण"

जांचकर्ता का नाम: डॉ. शक्ती स्वरुप षडंगी

निरीक्षक : डॉ. ए एस संधु

आचार्य एवं विभागाध्यक्ष

यूरॉलॉजी विभाग

एम्स, जोधपुर

परिचय: इसमें इस अध्यन का उद्देश्य, तरीके, फायदे अवं खतरे और आपके अध्यन को छोड़ने सम्बंधित जानकारी है|

उद्देश्य: आर्टेरियोवेनस फिस्टुला (AVF) क्रोनिक किडनी रोग के रोगियों में डायलिसिस एक्सेस का निर्माणकी पसंदीदा इलाज है। रेडिओसेफालिक फिस्टुला सबसे अधिक बनाया जाता है । हालांकि एनास्टोमोटिक साइट के पास संकुचन होने के कारण प्राथमिक विफलता दर बहुत अधिक है। यह सिद्ध किया गया है कि शिरा को कम स्थानांतरित करने से, एवीएफ के बेहतर परिणाम हो सकते हैं। इस प्रकार यह अध्ययन AVF बनाने के लिए RADAR तकनीक के लाभों का आकलन करने के लिए आयोजित किया जाता है।

प्रक्रिया: विस्तृत इतिहास और शारीरिक परीक्षा के बाद, रोगियों की नियमित रक्त जांच और इमेजिंग का एक सेट से गुजरना होगा। उसके बाद AVF निर्माण प्रक्रिया से गुजरना होगा। एक समूह शास्त्रीय विधि से गुज़रेगा और दूसरा समूह राडार विधि से गुज़रेगा, जहाँ रेडियल धमनी को एनास्टोमोसिस के लिए जुटाया जाता है। यादृच्छिकीकरण कंप्यूटर द्वारा किया जाएगा। यादृच्छिक संख्या और रोगियों उत्पन्न मुहरबंद लिफाफों जो सर्जरी से ठीक पहले खोला जाएगा। यह यादृच्छिकीकरण किसी भी तरह से रोगियों में से किसी समूह के उपचार को प्रभावित नहीं करेगा।

अध्ययन से निकलना: आप यह तय करने के लिए स्वतंत्र हैं कि अध्ययन में भाग लेना है या नहीं, अध्ययन से वापस लेना है या नहीं। यदि आप अध्ययन में भाग नहीं लेना चुनते हैं, तो आपको एम्स, जोधपुर में समान देखभाल और उपचार प्राप्त करना जारी रहेगा।

संभावित लाभ और हानी: समूह 1 रोगियों (शास्त्रीय विधि) रोगियों को हाथ के गैंग्रीन के लिए कम जोखिम होता है, और यह आमतौर पर किया जाता है जबकि समूह 2 (RADAR तकनीक) में रोगियों को एवीएफ की बेहतर प्राथमिक सफलता दर होगी।

फॉलो अप : रोगी को 3 महीने या फिस्टुला परिपक्वता तक फॉलो किया जाएगा।

गोपनीयता: अगर आप इस अध्यन में भाग लेने के लिए तैयार हैं, तो आपकी सारी जानकारी एक प्रोफोर्मा में ली जायेगी, जिसे पूरी तरह से गुप्त रखा जाएगा| आप इस अध्यन में भाग लेने के लिए अवं बीच में छोड़ देने के लिए स्वतंत्र हैं| इससे आपके इलाज पर कोई फरक नहीं पड़ेगा| आपको अस्पताल की सुविधाएं पहले की ही तरह नियमित रूप से मिलती रहेंगी |

इससे सम्बंधित किसी भी जानकारी के लिए आप निम्नलिखित से संपर्क करें|

डॉ. शक्ती स्वरुप षडंगी

सीनियर रेसीडेंट

यूरॉलॉजी विभाग

एम्स जोधपुर

8860504007

डॉ. ए एस संधु

आचार्य एवं विभागाध्यक्ष

यूरॉलॉजी विभाग

एम्स जोधपुर

Annexure – 3

Proforma for AVF

Name: Hospital ID:

Age: Sex: Address:

BMI:

CKD since:

HD since:

Cause of CKD:

DM: HTN: Cardiac Conditions: Any other comorbidities:

Previous surgery:

Previous Fistula creation history:

If failure, reason and duration of dialysis

Long-term medications

Doppler

Examination:

General Condition:

Dominant hand:

Clinical examination Right

Left

Radial artery

Ulnar Artery

Cephalic Vein (compressibility, length)

Veins in fore arm and arm

Allen's test

Preoperative optimisation:

Intraoperative:

Surgical method: Randomisation

Surgeons:

Time to completion:

Comments

Post-operative

	Thrill	Bruit	Pulsation
Post op			
POD1			
POD10			
POD 14			
POD 28			

Dialysis started on POD:

Any difficulty in dialysis

Remarks if any:

Annexure 4

IEC Certificate

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2021/3483 **Date: 12/03/2021**

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2021/3324**

Project title: **"Comparison of radial artery deviation and reimplantation technique vs classical technique in creation of arterio-venous fistula: A randomised control trial"**

Nature of Project:	**Research Project Submitted for Expedited Review**
Submitted as:	**M.Ch. Dissertation**
Student Name:	**Dr. Shakti Swarup Sarangi**
Guide:	**Dr. Himanshu Pandey**
Co-Guide:	**Dr. Gautam Ram Choudhary, Dr. Arvind Sinha, Dr. Mahendra Singh, Dr. Vijay Kumar Sarama Madduri, Dr. Manish Chaturvedy, Dr. Nitin Kumar Bajpai & Dr. Alok Sharma**

Institutional Ethics Committee after thorough consideration accorded its approval on above project.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.
- In case of any issue related to compensation, the responsibility lies with the Investigator and Co-Investigators.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation. If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member Secretary

Member secretary
Institutional Ethics Committee
AIIMS, Jodhpur

Basni Phase-2, Jodhpur, Rajasthan-342005; **Website:** www.aiimsjodhpur.edu.in; **Phone:** 0291-2740741 Extn. 3109
E-mail : ethicscommittee@aiimsjodhpur.edu.in; ethicscommitteeaiimsjdh@gmail.com