



## Outcome of Arterio-Venous Fistula Surgery With Or Without Local Use of Injection Papaverine In Patient Undergoing Hemodialysis- A Prospective Observational Study

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## ABSTRACT

**Background:** Arteriovenous fistula (AVF) is considered the optimal vascular access for haemodialysis (HD) due to its high success rate and low complication rate. Papaverine is a cost-effective and easily accessible drug with minimal side effects. This study aimed to evaluate the outcome of arteriovenous fistula surgery with and without the local use of injection papaverine at our institute.

**Aims and Objectives:** To study the outcome of arteriovenous fistula surgery with or without local use of injection papaverine in patients undergoing haemodialysis.

**Materials and Methods:** This prospective observational study was conducted in the Department of General Surgery, at tertiary health care center from September 2023 to September 2024, after approval from the Institutional Ethics Committee. A total of 60 patients with end-stage renal disease (ESRD) undergoing haemodialysis were included and divided into two groups:

- Group A (n = 30): AVF surgery with local use of injection papaverine
- Group B (n = 30): AVF surgery without papaverine

Statistical analysis was performed using SPSS version 20. A p-value < 0.05 was considered statistically significant.

**Results:** The study included 60 participants with a mean age of  $49.9 \pm 9.42$  years; 47 (78.33%) were males and 13 (21.67%) were females. Hypertension was the most common comorbidity, either alone or in combination with diabetes. AVFs were predominantly created in the left upper limb (73.33%). The most common type of AVF was radiocephalic (66.67%). Among patients receiving papaverine, 29 had mature fistulas and 1 had an immature fistula, whereas in the non-papaverine group, 28 had mature fistulas and 2 had immature fistulas ( $p = 0.553$ ). The mean maturation time was significantly shorter in the papaverine group ( $36.41 \pm 1.23$  days) compared to the non-papaverine group ( $43.64 \pm 1.74$  days) ( $p < 0.0001$ ). Complications occurred in six patients, with infection being the most common. No complications were observed in the papaverine group.

**Conclusion:** The local use of injection papaverine significantly reduced the mean maturation time of AVF. Although maturation rates were not statistically different, papaverine use was associated with earlier maturation and fewer complications. Papaverine may be a useful adjunct in improving AVF outcomes in patients undergoing haemodialysis.

**KEYWORDS:** Papaverine; Hemodialysis; Arteriovenous fistula; End-stage renal disease; Aneurysm

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## INTRODUCTION

End-stage renal disease (ESRD) is a significant health issue that has a notable impact on the population in terms of illness, death, and socioeconomic consequences [1]. Based on epidemiological research, around 10% of individuals with chronic renal failure (CRF) have a kidney transplant, while the remaining 90% who do not receive a renal transplantation are required to undergo dialysis therapy, either hemodialysis or peritoneal dialysis [2]. Currently, hemodialysis treatment offers a life-saving alternative for those with chronic kidney disease (CKD) and allows them to live for an extended period with a high standard of living [3].

Hemodialysis facilitates the passive diffusion of solutes from blood to dialysate, aiming to remove toxins and maintain the body's internal composition within normal ranges. Central venous catheters are the preferred approach for temporary access in

situations where there is an urgent requirement for hemodialysis and no other vascular access is available or has been unsuccessful [4]. Nevertheless, these devices are linked to several aggravating problems including infection, thrombosis, venous stenosis, and injury to nearby blood arteries. This has heightened the need for a dependable and secure virtual assistant [5].

Arteriovenous fistula (AVF) is considered the optimal vascular access for haemodialysis (HD) due to its high success rate and low complication rate. However, the major drawback of AVF is its non-maturation rate, which refers to the failure of the newly created fistula to develop into a functional and accessible conduit for HD sessions [6].

Papaverine is a cost-effective and easily accessible medication with minimal side effects. We wish to study the effect of Arterio-venous fistula surgery with and without local use of Injection Papaverine in our institute. Thus, the study seeks to understand the potential benefits of using Papaverine in AVF surgery and its impact on patient outcomes.

## AIMS AND OBJECTIVES

### Aim

To study the outcome of arterio-venous fistula surgery with or without local use of injection Papaverine in patient undergoing hemodialysis

### Objectives

#### Primary objective

- To record the time of arterio-venous fistula maturation
- To determine the patency of arterio-venous fistula on follow up

#### Secondary objective:

- To study the distribution and determinant variable (demographic, clinical, diagnostic) in patients undergoing hemodialysis
- To study the complication of arterio-venous fistula surgery

## MATERIALS AND METHOD

**Study Design:** A prospective observational study

**Study subjects:** End stage renal disease (ESRD) patients who were referred for hemodialysis.

**Study Centre:** tertiary health care center

**Source of data:** All Cases reporting to Department of General Surgery, for Arterio-venous Fistula surgery undergoing hemodialysis.

**Duration of the Study:** One year from approval from Institutional ethic committee.

**Sample Size:** 60 patients with 30 in each group.

**Group A:** It comprised of 30 patients who underwent Arterio-venous fistula surgery with local use of Injection Papaverine

**Group B:** It comprised 30 patients who underwent Arterio-venous fistula surgery without local use of Injection Papaverine

### Inclusion Criteria:

- Age >12 years of either sex
- Patients with ESRD who are in need of hemodialysis
- Patient suitable for Arterio-venous construction
- Patient reporting the Department of general surgery
- Patients giving written informed consent for formation of Arterio-venous fistula surgery.

### Exclusion Criteria:

- Patients with systolic blood pressure < 120 mmHg and > 200 mmHg during operation
- History of AVF construction 15 day ago.
- History of Arterio-venous construction in both upper limb and both lower limb
- Intra op Atherosclerosis of Artery

In group A, a volume of 0.1 to 0.2 cc of papaverine was injected using a 30-gauge syringe into the sub adventitia of the artery and vein and in group B, it was not given.

The end-to-side anastomosis was conducted by employing a continuous 7-0 monofilament vascular suture for distal forearm arteriovenous fistulas (AVFs), while the snuffbox AVFs were connected using a side-to-side anastomosis in a similar fashion. Follow-up evaluations were conducted at 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, and 8 weeks post-surgery. The visits continued until the fistula reached maturation. Once the fistula had reached a clinically mature stage, a second Doppler sonography was conducted to verify its maturity according to the KDOQI recommendations.

Patients who did not achieve fistula maturation within 3 months were excluded from the research. At each post-operative visit, patients were assessed for surgical site problems such as hematoma, seroma, and infection, as well as early thrombosis, venous hypertension, steal syndrome, and neuropathy.

Patient outcomes and complications were recorded and maintained in individual case records. A comprehensive analysis of the records was performed at the end of the study period.

Patient identities were kept confidential throughout the study.

To minimize additional costs and burdens on patients, only materials available within the hospital were utilized for the study.

**Statistical Analysis:**

Statistical analysis was carried out using Statistical Package for Sciences (SPSS, version 20). Appropriate statistical tests were applied to identify the association between variable, P value < 0.05 was considered as statically significant.

**Ethical consideration:**

This study was conducted after approval by scientific and institutional ethical. Before the commencement of study, informed and written consent was obtained from all the individuals selected for the study, after explaining the procedure protocol associated with the study.

**OBSERVATIONS AND RESULTS**

The total number of participants was 60, with a mean age of  $49.9 \pm 9.42$  years. The participants were predominantly male, with 47 males (78.33%) and 13 females (21.67%).

**Table 1: Comorbidity wise distribution of study subjects Comorbidity**

	Frequency	Percentage
<b>ADPKD</b>	1	1.67
<b>Chronic Nephritis</b>	6	10.00
<b>Diabetes</b>	11	18.33
<b>HTN</b>	16	26.67
<b>HTN , Diabetes</b>	17	28.33
<b>HTN, Old CVA</b>	1	1.67
<b>Multiple Myeloma</b>	1	1.67
<b>Obstructed Uropathy</b>	3	5.00
<b>None</b>	4	6.67

The table 1 shows comorbidities among participants with HTN being the most common alone and HTN and Diabetes combined constituting to major chunk. AV fistula sites were predominantly in the left upper limb (44 participants, 73.33%), compared to the right upper limb (16 participants, 26.67%). The types of AV fistula were: radiocephalic (40, 66.67%), brachiocephalic (17, 28.33%), and brachiobasilic (3, 5%). Nine participants (15%) had a history of AV fistula surgery, while 51 participants (85%) did not. Most participants underwent end-to-side anastomosis (36, 60%), while the remaining (24, 40%) had side-to-side anastomosis.

**Table 2: Local use of Injection papaverine wise distribution of study subjects.**

Local use of inj. papaverine	Frequency	Percentage
<b>Yes</b>	<b>30</b>	50.00
<b>No</b>	<b>30</b>	50.00

Table 2 shows Local use of injection papaverine distribution equal numbers of participants had local use of injection papaverine (30, 50%) and no use (30, 50%).

Outcome distribution among those with local use of injection papaverine, 29 had mature fistulas and 1 was immature. Among those without its use, 28 had mature fistulas and 2 were immature. The P-value for this distribution was 0.553, which is not statistically significant.

**Table 3: Mean Maturation time based on Local use of Injection papaverine**

Local use of Injection papaverine	Mean (days)	P value
<b>Yes (n=30)</b>	36.41	< 0.0001
<b>No (n=30)</b>	43.64	

Table 3 shows mean maturation time based on local use of injection papaverine, Participants with local use of injection papaverine had a mean maturation time of  $36.41 \pm 1.23$  days, while those without its use had a mean maturation time of  $43.64 \pm 1.74$  days. The P-value (< 0.0001) indicates statistical significance.

**Table 4: Complications among study subjects Complications**

	Frequency	Percentage
<b>Infection</b>	3	50.00
<b>Hyperfunctioning, Stenosis</b>	1	16.67
<b>Hematoma</b>	1	16.67
<b>Aneurysm</b>	1	16.67
<b>Total</b>	6	100.00

Table 4 shows complications among study subjects it was observed complications included infection (3, 50%), hyperfunctioning with stenosis (1, 16.67%), hematoma (1, 16.67%), and aneurysm (1, 16.67%). A total of 6 participants experienced complications. No complications were reported among participants who received local use of injection papaverine (0, 0%).

## DISCUSSION

The study population undergoing arterio-venous fistula surgery consisted of 60 individuals, with a mean age of  $49.9 \pm 9.42$  years with majority of participants (50%) were within the 46-55 years age range, followed by 23.33% in the 36-45 years age range. The remaining participants were distributed across various age groups, with the youngest being less than 25 years (1.67%) and the oldest being more than 65 years (6.67%). In terms of gender distribution, the study population was predominantly male, comprising 78.33% (47 males) of the total participants, while females accounted for 21.67% (13 females).

In a similar study by **Iyem H et al.**, fistulae were created among 384 patients, 58.5% were male and 41.5% were female with mean age was 46 (range 12–72) years [7]. **Mohapatra SK et al.**, created 120 fistulae among 89 men (74.16%) and 31 (25.83%) females with mean age of patients being 44.6 years (range from 16 to 65 years) [8]. **Prabha V et al.**, reported the mean age of  $52.22 \pm 14.04$  years (range, 20 to 70 years) [9]. In another study by **Patel P et al.**, among 104 participants with ESRD in the study, 87 (83.7%) were male and 17 (16.3%) were female and the age range of participants was from 20 to 70 years with a mean ( $\pm$ SD) age was 51 ( $\pm$ 13.5) years [10].

A significant proportion of participants had hypertension (HTN), either alone (26.67%) or in combination with other conditions, such as diabetes (28.33%) or a previous cerebrovascular accident (CVA) (1.67%). Diabetes was also a common comorbidity, affecting 18.33% of the participants. Other notable comorbidities included chronic nephritis (10%), obstructed uropathy (5%), and multiple myeloma (1.67%). Additionally, one participant had Autosomal Dominant Polycystic Kidney Disease (ADPKD) (1.67%) and 6.67% of the participants reported no comorbidities.

Another Indian study that reported comorbidities among chronic kidney disease patients conducted by **Jacob SR et al.**, found hypertension (61.4%), diabetes (47.3%), cardiovascular disease (30.6%), Chronic obstructive pulmonary disease (10%) malignancies (2.6%), and retinopathy (28%) [11]. **Cha J et al.**, reported around 70.8% of patients with end stage renal disease had 1 or more comorbidities, and the most common comorbidities were hypertension, diabetes, and cardiovascular disease [12]. In the present study, the majority of arteriovenous (AV) fistula sites were located in the left upper limb, with 44 participants (73.33%) compared to 16 participants (26.67%) in the right upper limb which is in concordance with the study conducted by **Iyem H et al.**, in which surgical intervention was performed on the left upper extremity in 284 patients (64.5%) and on the right upper extremity in 126 patients (35.5%) [7]. The majority of arteriovenous (AV) fistulas are created in the left upper limb, primarily because healthcare providers typically prefer to use the non-dominant arm for fistula creation. As most people are right-handed, the left arm is often chosen, allowing for better functionality and minimizing disruption to daily activities.

In the present study, the radiocephalic fistulas were the most common, accounting for 66.67% (40 participants) of the total, followed by brachiocephalic fistulas (28.33%, 17 participants), and brachio basilic fistulas (5%, 3 participants). Correspondingly, in the comparable study by **Mohapatra SK et al.**, radiocephalic (Cimino-Brescia fistula) was created in 78.3% (n=94) and at cubital fossa (brachial fistula) in 21.6% (n=26) [8].

**Weale AR et al.**, reported that among a total of 658 patients, 361 had a radiocephalic arteriovenous fistulas (RCAVFs), and 297 had brachiocephalic arteriovenous fistulas (BCAVFs) [13]. The radiocephalic fistula is the most commonly used type of arteriovenous fistula (AVF) for hemodialysis access. This is due to its favorable location in the forearm, which provides good blood flow and a lower risk of "steal syndrome" compared to upper arm fistulas. Additionally, a radiocephalic fistula preserves the option to create a more proximal fistula if needed, in the event that the initial fistula fails to mature properly. This approach is often recommended by current guidelines from reputable organizations, such as the National Kidney Foundation [14,15].

The 50% participants (n=30) received local use of injection papaverine whereas remaining 50% did not received. In terms of outcomes, 29 participants who received injection papaverine had mature fistulas, while 1 had an immature fistula. In contrast, 28 participants without injection papaverine had mature fistulas, and 2 had immature fistulas. However, the difference in outcomes was not statistically significant (P-value = 0.553). Notably, the present study found mean maturation time was significantly shorter in participants who received local use of injection papaverine ( $36.41 \pm 1.23$  days) compared to those who did not ( $43.64 \pm 1.74$  days), with a P-value of less than 0.0001, indicating statistical significance.

The results of the present study and the study conducted by **Manani R et al.**, show similarities in terms of the impact of papaverine on arteriovenous fistula (AVF) maturation time [2]. Both studies found that the use of papaverine significantly reduced the maturation time of AVF. In the present study, the mean maturation time was  $36.41 \pm 1.23$  days in the papaverine group, compared to  $43.64 \pm 1.74$  days in the control group (P < 0.0001). Similarly, in the study by Manani R et al, the mean maturation time was 37.94 days in the papaverine group, compared to 44.23 days in the control group (P = 0.004) [2].

However, both studies found no statistically significant difference in maturation rate and post-operative complications between the papaverine group and the control group. In the present study, the difference in outcomes was not statistically significant (P-value = 0.553), while in the study by **Manani R et al.**, there was no statistically significant difference in maturation rate and

post-operative complications between the two groups [2].

The study reported a total of 6 complications among the study subjects, which accounted for 100% of the complications. The most common complication was infection, which occurred in 3 participants (50% of the total complications). The remaining complications were evenly distributed, with 1 participant each experiencing hyperfunctioning/stenosis (16.67%), hematoma (16.67%), and aneurysm (16.67%). Further, no complications were reported among participants who received local use of injection papaverine (0, 0%).

Thrombosis of the fistula is the most common complication, occurring in 3.0% to 14.5% of cases, both early and late after surgery [16,17,18,19]. In the present study, however, infection was the common complication. Whereas similar to our study, in the study by **Mohapatra SK et al.**, the most common early complication encountered with the primary AVF was infection which was seen in 9 out of the 33 cases [8].

## CONCLUSION

To conclude, the present study found that the local use of injection Papaverine significantly reduced the mean maturation time of AVF, from  $43.64 \pm 1.74$  days to  $36.41 \pm 1.23$  days. Although the difference in outcomes between the two groups was not statistically significant, the study suggests that the use of injection Papaverine may improve the maturation rate of AVF. The study also reported a low complication rate, with infection being the most common complication whereas no complications were reported among patients who underwent injection Papaverine. Overall, the findings of this study highlight the importance of optimizing AVF surgery outcomes in patients undergoing hemodialysis, and suggest that the local use of injection Papaverine may be a useful adjunct in improving AVF maturation rates.

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