

## ORIGINAL ARTICLE

# Catheter Related Right Atrial Thrombus in Patients on Maintenance Hemodialysis: Results of a Single Centre Retrospective Study from a Tertiary Care Hospital

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## Abstract

**Objective:** To study the magnitude of the complication of catheter associated right atrial thrombus (CRAT) in patients with tunnelled central venous hemodialysis catheters (THC) for maintenance hemodialysis (MHD).

**Material and methods:** A retrospective study was conducted among patients with end stage kidney disease (ESKD) with THC for MHD who had undergone screening for CRAT with a 2D-echo (2DE) just before removal of the THC. The occurrence of CRAT and other clinical parameters were documented in these patients.

**Results:** A total of 28 patients (mean [SD] age 51 [15.2] years; females 17 [60.7%]) were included in the study. CRAT was observed in 5 (17.9%) patients. There was no difference in mean age in patients with or without thrombus ( $48 \pm 13.02$  vs  $51.61 \pm 15.78$  years;  $p = 0.61$ ). History of diabetes and hypertension was present in 2 and all 5 patients respectively. There was no significant difference in the period the THC was in place in patients with or without CRAT ( $13 \pm 7.8$  months vs  $10.57 \pm 5.66$  months;  $p = 0.54$ ). There was no association between catheter related blood stream infection (CRBSI) and CRAT ( $p = 0.29$ ).

**Conclusion:** The incidence of CRAT in patients with THC for MHD was 17.9%. Patients with THC for MHD should be examined for presence of CRAT before removal of THC to prevent fatal pulmonary thromboembolism.

## Introduction

Patients suffering from end stage kidney disease (ESKD) need renal replacement therapy for life sustenance. Renal replacement therapy includes three modalities namely, hemodialysis, peritoneal dialysis and kidney transplantation. Hemodialysis is the most frequently used renal replacement modality in India and elsewhere. An appropriate vascular access is necessary to carry out hemodialysis. Of the three types of vascular accesses used frequently, central venous dialysis catheters, arteriovenous grafts and arteriovenous fistula (AVF), the latter is the most appropriate option.<sup>1</sup> It is recommended to create an AVF when the estimated glomerular filtration rate (eGFR) falls below 25 ml/min, well before MHD is needed.<sup>2</sup> However, most patients are not compliant and need a

central venous hemodialysis catheter to commence hemodialysis. Many other patients present late needing immediate dialysis, in which situation a central venous hemodialysis catheter is the only available option. Hence majority of patients initiate dialysis with a central venous hemodialysis catheter.<sup>3</sup>

Hemodialysis catheters are either non-tunnelled or tunnelled, the latter being preferred both by clinicians and patients. THCs are superior to non-tunnelled catheters as the incidence of venous thrombosis and stenosis is less and the tunnelling and cuff reduce the chances of CRBSI. These properties

ensure that they can be retained in situ for a prolonged period.<sup>4</sup> However, they are more expensive and trained personnel are needed to insert them under fluoroscopy.

The frequency of insertion of THC has increased considerably in India. When compared to an AVF, THC have higher risk of infection, thrombosis and catheter related dysfunctions resulting in higher morbidity and mortality.<sup>5</sup> In view of these observations THC should only be used as a bridge till AVF matures and can be accessed for hemodialysis.<sup>7</sup>

THC may lead to asymptomatic catheter-associated right atrial thrombus (CRAT) which may contribute to increased morbidity and mortality.<sup>8</sup> The incidence of CRAT has been reported to be 18 % in patients with THC.<sup>9</sup> Removal of THC in patients with a CRAT may lead to pulmonary embolism and death.<sup>10</sup> In our centre we documented a case of CRAT diagnosed as an incidental finding on 2D echocardiography (2DE). Following this observation all patients in our unit are screened for CRAT before removal of THC. There has been only one study reported, looking at the incidence of CRAT in patients with THC. Currently there are no published data from India on the incidence of CRAT in patients with THC.

## Objectives

To study the magnitude of the complication of CRAT in patients with THC for MHD in ESKD patients and to understand the factors associated with

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**Table 1: Baseline demographic characteristics of study population**

Parameter	Result
Mean (SD) age (years)	51 (15.2)
Male n (%)	11 (39.3%)
Female n (%)	17 (60.7%)
Mean (SD) BMI (kg/m <sup>2</sup> )	24 (5.5)
Hypertension n (%)	22 (78.6%)
Diabetes n (%)	10 (35.7%)
Diabetes and hypertension both	9 (32.1%)
Mean (SD) duration of hemodialysis during screening (months)	32.4 (24.9)
Mean (SD) amount of heparin used (IU)	6196.4 (1796.8)
Mean (SD) duration of THC in place before removal (months)	11 (6)

CRAT formation.

## Materials and Methods

This is a retrospective, observational study conducted at Bombay Hospital Institute of Medical Sciences, a tertiary care hospital in Mumbai. ESKD patients on MHD having a THC in situ between August 2017 to July 2018 who underwent 2DE before removal of the THC as a part of the unit protocol, were included in the study. Patients who died or were lost to follow-up were excluded from the study. Patients with acute kidney injury were excluded from the study.

The THCs were inserted by the same experienced critical care consultant under ultrasound guidance. The procedure was done in the interventional radiology laboratory. All THCs were Palindrome® manufactured by Covidien (now Medtronic). The tip was placed in the mid right atrium in 26 patients and at the junction of superior venacava and right atrium in 2 patients.

The 2DE studies were carried out by the same experienced cardiologist using Philips EPIQ 7C machine. Assessments were performed in apical, parasternal and subcostal views in accordance with the current recommendations. When CRAT was identified, its size, mobility, echogenicity and attachment to the

**Table 2: Laboratory parameters in study population**

Parameter	Mean (SD)
Hemoglobin g/dL (n=28)	9.90 (1.24)
Albumin g/dL (n=28)	3.34 (0.73)
Calcium mg/dL (n=27)	6.31 (3.41)
Phosphorous mg/dL (n=27)	4.95 (1.69)
Uric acid mg/dl (n=26)	5.67 (2.69)

THC were assessed.

The frequency of occurrence of CRAT was documented along with the duration of THC in situ, use of antiplatelets or anticoagulants, use of erythropoietin, history of thrombosis of previous non-tunnelled dialysis catheter or AVF, heparin usage, any variation in heparin locks, demographic characteristics, comorbid conditions, cause of ESKD, type and frequency of dialysis, blood pump speeds and blood tests (haemoglobin, complete blood count and complete biochemistry) were recorded. Any complications related to THC insertion were recorded.

This study protocol was approved by the hospital's ethics committee.

### Statistical Methods

A t-test was performed for comparing the means of 2 set of continuous data. Fisher's exact test and Pearson Chi-Square tests for comparing two categorical datasets were used. Variables were expressed as "mean ± standard deviation", while categorical variables were expressed as number and percentage. R programming language was used for doing these statistical tests. To check if CRAT was linked to some parameters and if there were any nonlinear relationship between the various variables and CRAT, classification and regression trees method was used. A *p* level less than 0.05 was considered significant in the statistical analysis.

## Results

A total of 28 patients were included

in the study. The baseline demographic characteristics and the laboratory parameters of overall study population are shown in Tables 1 and 2 respectively.

The mean (SD) age of overall patient population was 51 (15.2) years. The study population was dominated by females (17[60.7%]). History of hypertension was more common than history of diabetes in study population (78.6% vs 35.7%). Three patients (10.71%) had ischemic heart disease.

Viral serology was negative in all patients except one who had presence of HCV antibodies. Another patient showed presence of antinuclear antibodies.

CRAT was observed in 5 (17.9%) of the 28 studied patients. The demographic characteristics, cause of CKD, history of diabetes and hypertension and duration of THC are shown in Table 3. The characteristics of CRAT on 2DE study are shown in Table 4.

Out of the 5 patients, 3 were males and 2 were females. The mean age in patients with or without thrombus was 48±13.02 and 51.61 ± 15.78 years, respectively, with no significant difference (*p* = 0.61).

The range of duration of hemodialysis during screening ranged from 10 months to 72 months. The duration of THC in these patients ranged from 8 months to 24 months. The mean duration of THC in patients with or without CRAT was 13±7.8 months and 10.57±5.66 months. There was no significant difference in duration of THC between the two groups (*p* = 0.54).

Two patients had history of diabetes whereas history of hypertension was present in all 5 patients. Of the 10 diabetic patients, 2 (20%) had CRAT, while 3 of the 18 non-diabetic individuals (16.7%) had CRAT, with no significant difference between the groups (*p* = 1.0). CRAT formation was detected in 22.7% (5/22) of the hypertensive patients and in none of the

**Table 3: Characteristics of patients with CRAT**

Age (yrs)	Gender	BMI (kg/m <sup>2</sup> )	Cause of CKD	History of DM	History of HTN	Duration of HD during screening (mths)	Duration of THC (mths)
32	F	26.15	LN	No	Yes	10	8
47	F	23.28	HTN	No	Yes	72	24
39	M	25.46	DN	Yes	Yes	15	5
62	M	27.88	Unknown	Yes	Yes	13	10
60	M	34.28	CGN	No	Yes	60	18

\*CGN: Chronic glomerulonephritis; LN: Lupus nephritis; DN: Diabetic nephropathy; DM: Diabetes mellitus; HTN: Hypertension; HD: Hemodialysis

**Table 4: Characteristics of CRAT**

Age (years)	CRAT size (cms)	Fixed to CVC	Mobility	Echo findings
32	1.8 × 2	Yes	immobile	Global hypokinesia
47	1.5 × 1.2	Yes	immobile	LVH
39	3.5 × 2.5	Yes	immobile	LVH
62	3 × 3	Yes	immobile	RWMA, LVH
60	4 × 2	Yes	immobile	LVH

LVH: Left ventricular hypertrophy; RWMA: Regional wall motion abnormality

non-hypertensive patients ( $p = 0.55$ ).

A total of 10 (35.7%) patients in the study were on antiplatelets. All patients were receiving erythropoietin. None of the patients were on any form of anticoagulation therapy. All patients received fractionated heparin during hemodialysis. All patients received thrice a week hemodialysis. Both ports of the THC were locked with unfractionated heparin solution in all patients.

## Discussion

A large proportion of patients with ESKD needs THC for initiating MHD as they present late with ESKD needing immediate dialysis or they may have refused an AVF earlier. Some patients need THC because of secondary AVF failure.<sup>11</sup> In this study 12(42.8%) patients had THC as their first vascular access, 8(28.5%) had it after an initial non-tunnelled dialysis catheter and 8 (28.5%) had THC placed because of secondary AVF failure.

THC placement procedure may be complicated by arterial punctures, pseudoaneurysm, hematoma, air embolism, pneumothorax and malposition.<sup>12</sup> None of these complications were encountered in the current study, as the procedure was performed by an experienced operator, under ultrasound and fluoroscopic guidance in the interventional radiology laboratory.<sup>13</sup>

Other complications seen with THC include CRBSI, catheter malfunctioning, venous thrombosis and stenosis.<sup>14</sup> In the current study, 3 THCs were removed because of malfunctioning, 4 because of CRBSI, 1 following successful live related kidney transplantation and 19 following AVF maturation and 1 patient died with THC in situ. None of the patients in the study had venous thrombosis. Six patients (21.4%) out of the 28 studied had CRBSI. Four of these had their THCs removed, 2 of whom had CRAT. Two patients were treated appropriately with antibiotics and did not require removal of THC for CRBSI. These two were removed later after AVF maturation. 33.3% (2/6) patients with CRBSI had CRAT. This association was not statistically significant ( $p = 0.2855$ ). Dilek et al too in their study did not find any correlation between CRBSI and CRAT.<sup>9</sup>

CRAT is a less frequently observed

complication but has serious life-threatening implications.<sup>10,15</sup> In the current study, CRAT was observed in 17.8% (5/28). There is limited data regarding the frequency of occurrence of CRAT. In the only study looking at the incidence of CRAT, the incidence was found to be 18% (9/50).<sup>9</sup> Since CRAT is largely asymptomatic, it generally goes undetected in clinical practice and hence the incidence of this serious complication is underestimated or may go undetected. CRAT was detected by 2DE in most published data.<sup>9</sup> Magnetic resonance imaging and computerised tomography scan have been used to detect intracardiac thrombi.<sup>8</sup> But 2DE is freely available, is non-invasive with no risk of radiation and is a cheaper screening tool prior to THC removal. The sensitivity and specificity of 82.2% and 95.3% respectively of 2DE in detecting intracardiac masses ensures its efficacy.<sup>16</sup>

What predisposes patients to develop CRAT is unclear. The duration of the THC in situ does not seem to be a risk factor for CRAT. In the current study the duration of THC in patients with or without CRAT was  $13.0 \pm 7.81$  and  $10.56 \pm 5.66$  months respectively, and this was not significant ( $p = 0.5384$ ). This is comparable to outcomes in previously published data.<sup>9</sup> The age, BMI, cause of kidney disease, use of antiplatelets, haemoglobin values, history of secondary AVF failure due to thrombosis, low ejection fraction or diastolic dysfunction had no relation to CRAT formation. All patients were on similar protocol of unfractionated heparin during dialysis. All patients received erythropoietin for the management of anaemia. All patients were on thrice weekly hemodialysis. In the current study, CRAT was found in 2 females (2/5). In two other studies there were more females in the patient population presenting with CRAT.<sup>8,9</sup> All patients with CRAT were hypertensives, two patients had diabetes mellitus and none had ischemic heart disease.

It has been shown that patients with chronic kidney disease are at an increased risk of venous thromboembolism due to a host of factors.<sup>17</sup> Mechanical irritation of the right atrial free wall by THC tip or high blood flows may lead to endothelial damage which may activate coagulation cascade, platelet aggregation and thrombi formation.<sup>1</sup> There was less central

venous thrombosis when THC tips were placed in the right atrium as compared to tips placed in the superior vena cava in one study.<sup>18</sup> Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines recommend that the THC tip should be positioned, with the aid of fluoroscopy, in the right atrium or at the junction of superior vena cava and right atrium, to ensure adequate blood flow and lesser incidence of THC dysfunction.<sup>19</sup> In the current study 26 patients had their THC tips positioned in the mid right atrium and 2 at the junction of superior vena cava and right atrium. Right jugular vein was the preferred site of cannulation and was used in 22 patients while in the remaining 6, left jugular was used. All the five patients with CRAT had right jugular THC. Since the study population was small, a correlation could not be made.

Studies looking at prevention of CRAT in haemodialysis patients using anticoagulation and antiplatelets have not shown any benefit of these strategies.<sup>20</sup> KDOQI guidelines recommend not using antiplatelets and anticoagulation for prevention of CRAT and venous thrombosis, as this increases the risk of bleeding.

The treatment options include anticoagulation, endovascular techniques and surgery. Anticoagulants have been proposed as the first-line treatment of CRAT provided there are no contraindications.<sup>8</sup> If anticoagulation is used, 2DE at regular intervals should monitor progress.<sup>21</sup> Endovascular techniques may be considered if facilities are available in the institute. Surgical thrombectomy can be considered in cases where the thrombus is more than 6 cms.<sup>8</sup> Both endovascular and surgical techniques carry a certain element of risk leading to serious complications.<sup>8</sup>

In this study, of the five patients with CRAT three were treated with anticoagulation. These three patients had large CRAT measuring  $4 \times 2$  cms,  $3 \times 3$  cms and  $3.5 \times 2.5$  cms. One of the patients died of an unrelated cause. Complete resolution of the CRAT in the other two patients occurred after 4 months. This ensured that the risk of pulmonary thromboembolism was mitigated while removing the THC. The remaining two of the five patients with CRAT, needed removal of the THC because of infections. One had fungal

sepsis requiring immediate removal of THC, other had methicillin sensitive staphylococcus aureus infection which did not respond to appropriate antibiotics. Before removal, an informed consent was obtained from the patients and their families, explaining the risk of pulmonary thromboembolism and its consequences. Subsequently none of these two patients developed pulmonary thromboembolism and both recovered from the sepsis. The CRAT was smaller in these two patients measuring  $1.5 \times 1.2$  cms and  $1.8 \times 2$  cms. It is possible that infected CRAT is probably more adherent to the THC, which needs to be proved.

In a retrospective analysis of reported cases the overall mortality was 18.3% (13/71), significant predictors being advanced age, presence of complications and non-removal of the THC.<sup>8</sup> In another retrospective study looking at the incidence of CRAT, a mortality of 44.4% (4/9) over a 2 years follow-up was reported.<sup>9</sup> The current study data did not show any significant relationship between the presence of CRAT and mortality. Out of the five patients with CRAT, one died due to an unrelated cause.

Although all efforts are made to counsel patients with chronic kidney disease to have an early AVF placed when the eGFR is 25ml/min, most patients do not comply resulting in the need for THC to initiate hemodialysis. CRAT was found in 17.8% (5/28) of patients in the current study. With the more widespread usage of THC in recent years, an increased number of CRAT may be encountered. Since the risk of fatal pulmonary thromboembolism is high during the removal of the THC, mandatory screening with a 2DE before removal may reduce fatal outcomes. The frequency of occurrence of this

complication and being primarily asymptomatic but potentially life threatening, screening for CRAT once in two months could be beneficial in early diagnosis and possible therapy with anticoagulation with finally removal of THC. A larger prospective observational study is needed to validate this.

### Conclusion

The frequency of CRAT in patients with THC was 17.9% in the current study. There is limited data about incidence of CRAT in Indian patients on MHD. The present study provides insights into the possibility of asymptomatic CRAT in patients with THC used for MHD. The results may provide guidance in ensuring screening for asymptomatic CRAT with a 2DE before removal of THC thus reducing the risk of serious pulmonary thromboembolism.

### Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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