



Article

Vascular Access, Complications and Survival in Incident Hemodialysis Patients

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Abstract: The arteriovenous fistula (AVF) has long been considered the optimal vascular access. However, the evolving characteristics of the ageing dialysis population limit the creation of an AVF in all patients. Thus, more patients start hemodialysis (HD) with a central venous catheter (CVC) rather than an AVF, and the supremacy of the AVF has recently been questioned. The aim of this study was to analyze the incidence and rate of access complications in 100 patients between 2010 and 2015. A total of 63 patients started HD with an AVF, while 37 began HD with a CVC. We found no differences in patient survival according to the vascular access in use at the beginning of dialysis, but patients were more likely to die while undergoing dialysis by means of a CVC than an AVF. Patients started on dialysis with a CVC had more cardiovascular disease, while patients who began dialysis with an AVF presented more hypertension. Fistulas presented a longer survival time despite more hospital admissions, but CVCs bore a higher risk of infections. Our results suggest that starting dialysis with a CVC does not confer a greater risk of death.

Keywords: end stage renal disease; dialysis; survival; arteriovenous fistula; central venous catheter; chronic patients



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1. Introduction

Extracorporeal hemodialysis (HD) represents the most widely diffused renal replacement therapy and, in Europe in 2016, there were about 301,134 patients on regular renal replacement therapy according to the European Renal Association-European Dialysis and Transplantation Association reports [1]. In Italy, instead, according to the more recent estimates from the 2011–2013 period, there were about 45–49,000 prevalent HD patients [2].

A functional vascular access is mandatory to achieve good levels of dialytic efficiency, and it is considered the lifeline of patients on maintenance HD. The ideal vascular access should have specific characteristics among which the most important are the following: ease of placement; delivery of adequate blood flow for effective dialysis; good primary patency rates; low rates of complications and side effects; long-lasting life; and low economic costs [3,4].

Currently, the three most commonly used vascular accesses for extracorporeal hemodialysis are autologous arteriovenous fistulas (AVFs), prosthetic grafts (AVGs), and central venous catheters (CVCs). The AVF is the recommended vascular access for HD by major guidelines [5–7], which is primarily because of the lower rates of morbidity and mortality compared to both grafts and CVCs. However, the use of various vascular accesses varies largely according to geographical areas [8], and despite the success of the Fistula First initiative [9], the rate of U.S. patients starting HD with a CVC is still high, with a

frequency of about 70%. In Europe, instead, 50% to 60% of incident dialysis patients begin replacement therapy by means of an AVF [10]. In general, patients on regular HD are hospitalized twice as much as non HD patients, with an average of two hospitalizations per year [11], and it has been estimated that vascular access-associated complications are responsible for about 20% of those hospitalizations [12]. Moreover, vascular access is an important predictor of death in hemodialysis patients. The relative risk of death in incident patients using CVCs is 2- to 3-fold higher than those using an arteriovenous access [13]. This is true regardless of whether the overall mortality or the cause-specific mortality are examined, especially if the cause of death is infection-related [13]. One of the topics now being addressed is whether this increased mortality is dependent on the use of a catheter itself or whether it is the result of a bias in the selection of patients for catheter placement. In fact, patients dialyzing with a catheter are, on average, older, present more comorbidities, have lower serum albumin levels, and have a poor functional status, all of which are factors that are generally associated with an increased mortality risk [13].

The aim of our study was to compare the burden of complications and admissions related to the vascular access between CVCs and AVFs.

2. Methods

We retrospectively enrolled all adult, incident, hemodialysis patients who had been undergoing dialysis for at least three months at ICS Maugeri S.p.A. SB in Pavia, between 1 January 2010 and 31 December 2015, and we followed them up until 31 December 2018. We excluded patients who started dialysis elsewhere and who were then transferred to our Center. No patient started dialysis with a prosthetic graft. We only considered AVFs and permanent central venous catheters (CVCp). All patients in the AVF group began renal replacement therapy by means of the fistula, and no cases of immature vascular access were observed in this group. For every patient, we collected demographic data and the type of vascular access at the beginning of renal replacement treatment from medical records. Biochemical data (hemoglobin, total serum proteins, serum albumin, calcium, phosphorus, parathyroid hormone (PTH)) and dialysis adequacy markers (Kt/V [14]) were collected from the hospital information system throughout the entire follow-up period; the average of all of the available measures for each patient is presented. Moreover, for every vascular access, we calculated:

- Its survival, which was considered as the time from placement or from the beginning of renal replacement therapy (“utilization time”) to its definitive failure (i.e., the need to replace it with a new vascular access), independently of the procedures performed to maintain access patency in case of malfunctioning or thrombosis;
- The number of failures (defined as the inability to use the access to dialyze the patient and the need to intervene to restore patency or to replace it);
- The number of infections (comprising CVC-related bacteremia, exit-site infection, and tunnel infection);
- The number of infection days (defined as days of antibiotic therapy);
- The number of hospital admissions related to the access or for any other cause;
- The length of stay for every admission period.

The Cumulative Illness Rating Scale (CIRS) [15] was calculated from medical charts at the beginning of dialysis, and the Severity and Comorbidity Index were evaluated. Hypertension and severe hypertension were defined as the need of at least one or three different medications, respectively, in order to control blood pressure. “Late referrals” were considered as patients without a nephrological consultation in the three months before the beginning of dialysis [16].

2.1. Statistics

Quantitative variables were compared using the Mann–Whitney test, while qualitative variables were compared by means of Fisher’s exact test. Survival was assessed by comparing the Kaplan–Meier curves. Data are presented as mean \pm standard devia-

tion. All statistical analyses were performed using the GraphPad Prism software ver. 7.0 (GraphPad Software, La Jolla, CA, USA). A $p < 0.05$ was considered statistically significant.

2.2. Informed Consent

At the beginning of the dialysis treatment, all patients sign an informed consent to allow the anonymous use of their clinical data for research purposes. Due to the retrospective nature of the study, no further consent was needed.

3. Results

We enrolled 100 patients who started dialysis in our center between 1 January 2010 and 31 December 2015. Follow-up ended on 31 December 2018. We divided the patients into two groups: patients who started dialysis with a functioning arteriovenous fistula (63) or patients who started dialysis with a central venous catheter (38) (Table 1). We found no differences in age (68.43 ± 13.07 vs. 69.14 ± 16.48 years, AVF vs. CVC, $p = \text{NS}$) (Figure 1) or sex (AVF 47 males, CVC 22 males, $p = \text{NS}$) (Figure 2) between the two groups. Both groups had a similar follow-up time (1111.00 ± 731.30 vs. 980.70 ± 797.70 days, $p = \text{NS}$) (Table 1). Patients who started dialysis with a fistula had greater body weight and BMI (74.06 ± 15.57 vs. 66.70 ± 11.65 kg and 27.31 ± 4.43 vs. 24.77 ± 3.02 , respectively, $p < 0.05$) (Table 1). However, both groups showed the same total serum protein and albumin concentrations (6.39 ± 0.69 vs. 6.31 ± 0.80 g/dl and 3.45 ± 0.51 vs. 3.29 ± 0.68 g/dl, respectively, $p = \text{NS}$) (Table 1). No differences were found in the hemoglobin concentration (10.19 ± 1.33 vs. 10.08 ± 2.35 g/dl, $p = \text{NS}$), serum calcium (8.92 ± 0.55 vs. 8.79 ± 0.45 mg/dl, $p = \text{NS}$), phosphorus (4.86 ± 0.93 vs. 4.66 ± 0.86 mg/dl, $p = \text{NS}$), PTH (241.80 ± 116.00 vs. 244.60 ± 144.20 pg/mL, $p = \text{NS}$), or Kt/V (1.35 ± 0.31 vs. 1.30 ± 0.25 , $p = \text{NS}$) (Table 1).

Table 1. Characteristics of our cohort.

	AVF	CVC	<i>p</i> -Value
Number of patients	63	37	
Sex (M/F)	47/16	22/15	0.1239
Age (Years)	68.43 ± 13.07	69.14 ± 16.48	0.5779
Follow-up (days)	1111.00 ± 731.30	980.70 ± 797.70	0.2722
Weight (kg)	74.06 ± 15.57	66.70 ± 11.65	0.0144
BMI (kg/m ²)	27.31 ± 4.43	24.77 ± 3.02	0.0483
Hb (g/dl)	10.19 ± 1.33	10.08 ± 2.35	0.7599
Total serum proteins (g/dl)	6.39 ± 0.69	6.31 ± 0.80	0.5972
Albumin (g/dl)	3.45 ± 0.51	3.29 ± 0.68	0.1933
Serum calcium (mg/dl)	8.92 ± 0.55	8.79 ± 0.45	0.2825
Serum phosphorus (mg/dl)	4.86 ± 0.93	4.66 ± 0.86	0.2554
PTH (pg/mL)	241.80 ± 116.00	244.60 ± 144.20	0.9095
Kt/V	1.35 ± 0.31	1.30 ± 0.25	0.3969
Diabetes (yes/no)	23/40	14/23	>0.9999
Hypertension (yes/no)	63/0	31/6	0.0020
Peripheral artery disease (yes/no)	15/48	7/30	0.6255
Coronary artery disease or chronic ischemic heart disease (yes/no)	25/38	28/9	0.0008
Late referrals (yes/no)	0/63	6/31	0.0020

BMI: body mass index; Hb: hemoglobin; PTH: parathyroid hormone.

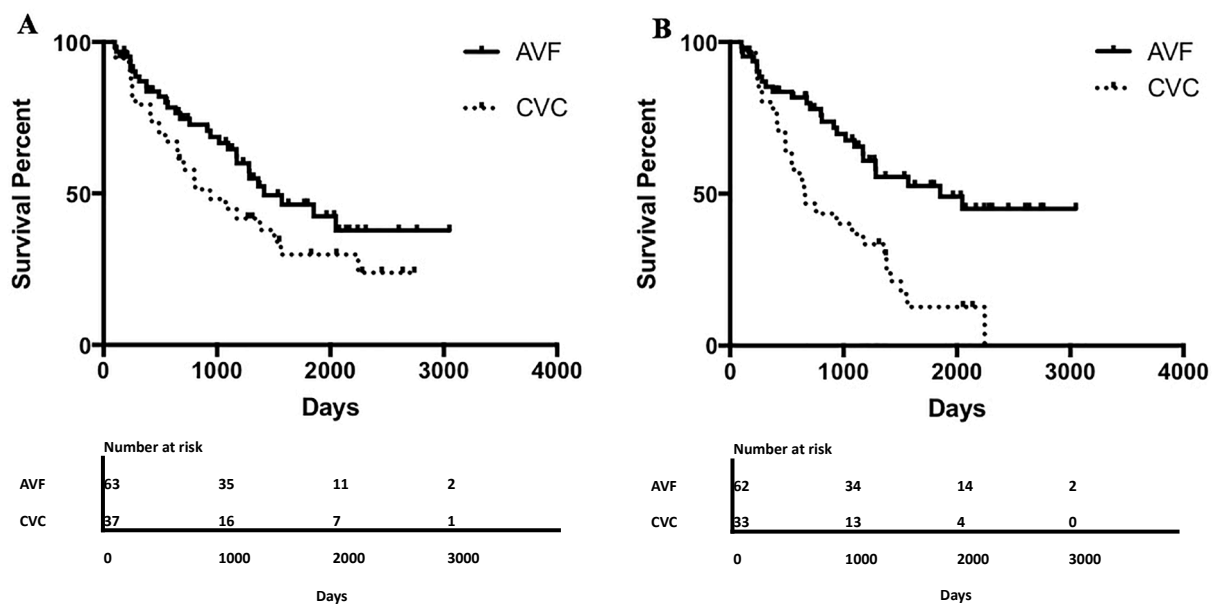


Figure 1. (A) Patient survival according to vascular access at HD initiation ($p = 0.1198$). (B) Patient survival according to the vascular access method in use at the end of follow-up ($p = 0.0004$).

The two groups did not differ in terms of diabetes or peripheral artery disease, but patients starting dialysis with a CVC had a higher prevalence of coronary artery disease or chronic heart failure and a lower prevalence of hypertension (Table 1).

We did not observe differences in patient survival according to the vascular access at the beginning of dialysis (Figure 1A).

However, patients who died during the observation period were more likely to dialyze with a CVC rather than a fistula (Figure 1B).

During the follow-up period, 11 patients were converted from a CVC to an AVF, and 2 were converted from a CVC to a graft, while 9 had a complete failure of the fistula that could not be rescued or replaced and continued to dialyze by means of a catheter. Finally, three patients were converted from an AVF to a prosthetic graft. Not considering patients who placed a graft in the course of their dialytic history, due to their small number (5), 62 patients were dialyzing with an AVF, and 33 were dialyzed with a CVC at the end of follow-up.

The Severity and Comorbidity Indexes were not different between the two groups at the beginning of dialysis (Figure 2A,B, respectively). CIRS score evaluation showed that patients starting dialysis with an AVF had less cardiovascular diseases but more severe hypertension (Figure 2C).

Fistulas showed a higher survival compared to permanent CVCs both from placement or from beginning of dialysis: 929.8 ± 792.2 vs. 437.5 ± 430.9 days ($p < 0.001$) and 854.6 ± 757.0 vs. 437.5 ± 430.9 days ($p < 0.01$), respectively (Figure 3A,B).

We found no differences in the number of access-related admissions between permanent CVCs and AVFs during follow-up (Figure 4A).

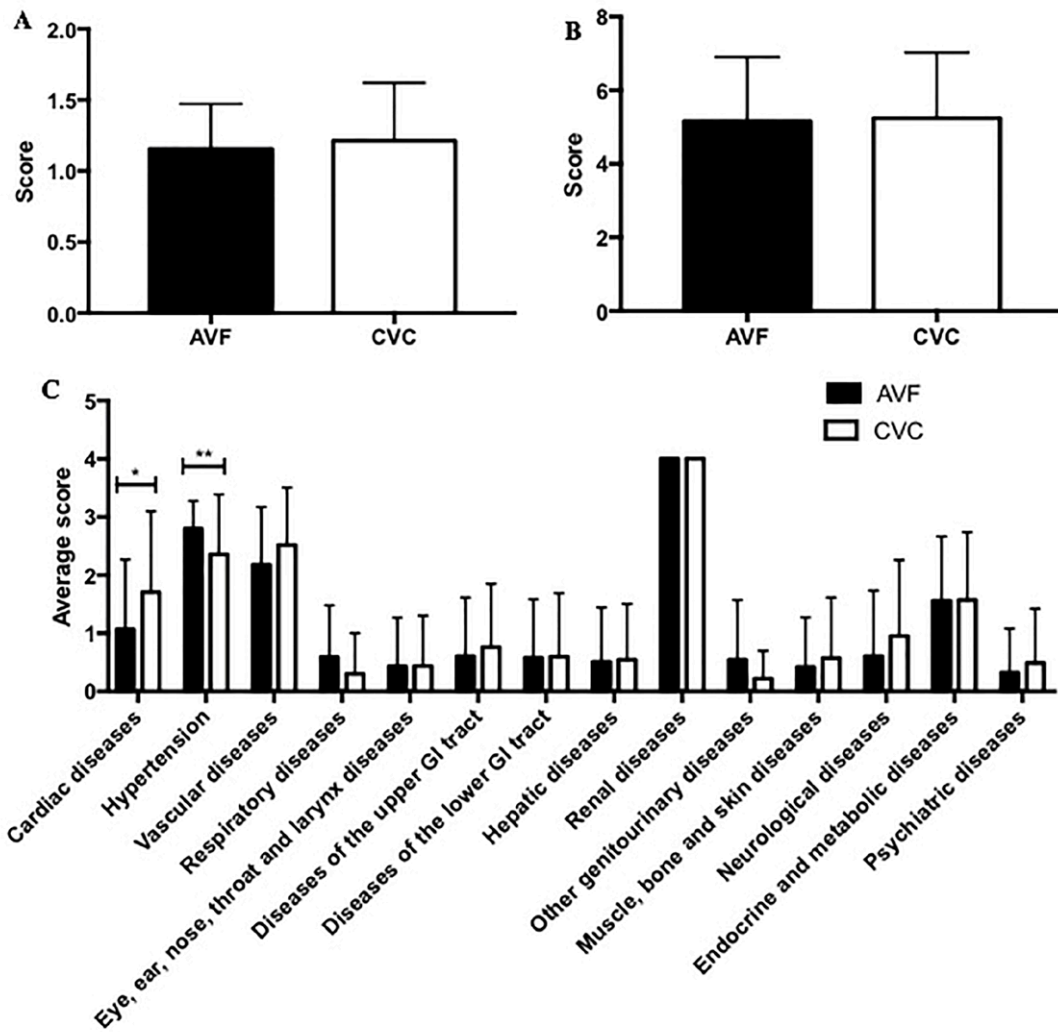


Figure 2. (A) Average Severity Index at HD initiation. (B) Average Comorbidity Index at HD initiation. (C) CIRS at dialysis initiation (* $p < 0.05$; ** $p < 0.01$).

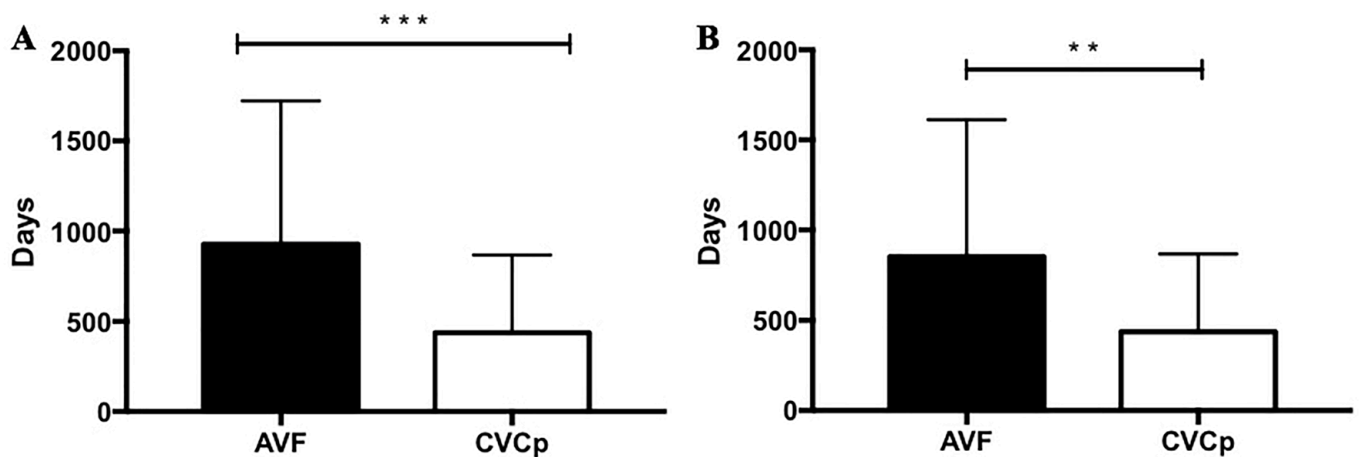


Figure 3. (A) Vascular access survival from placement ($p < 0.001$). (B) Vascular access survival from HD initiation ($p < 0.01$). *** $p < 0.001$; ** $p < 0.01$.

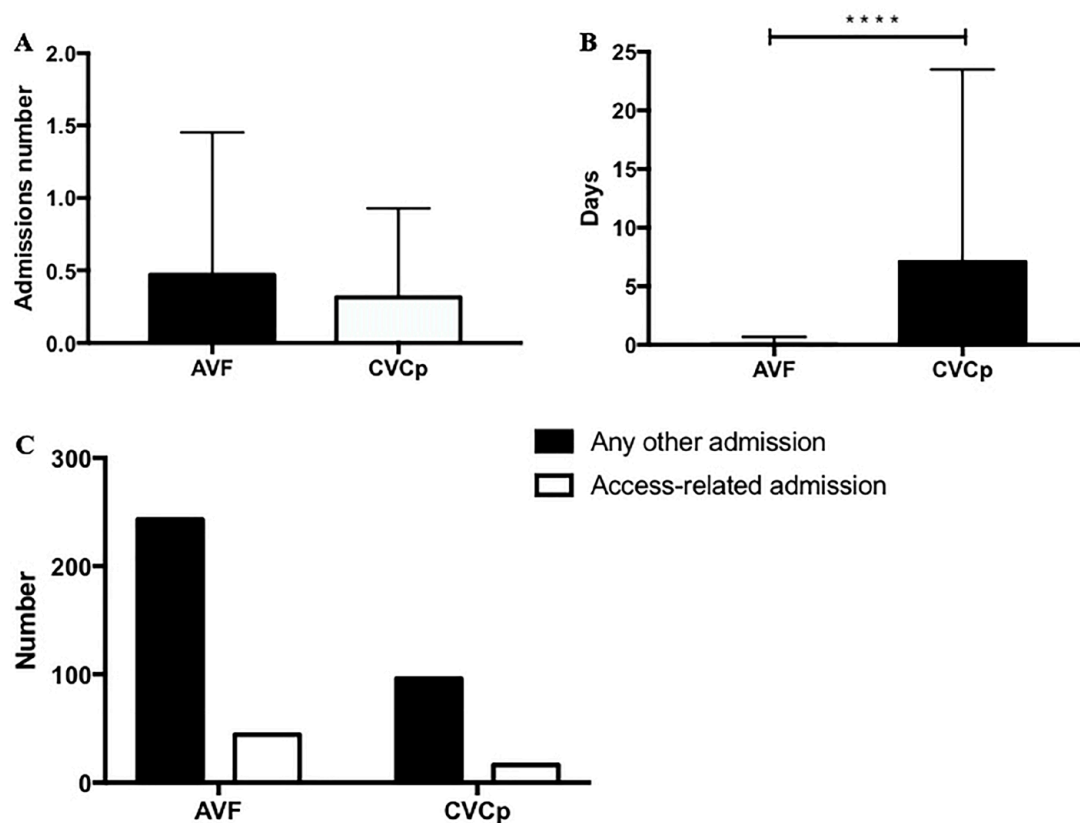


Figure 4. (A) Access-related admissions. (B) Access-related infection days ($p < 0.0001$). (C) Any other cause vs. access-related admission number. **** $p < 0.0001$.

We found that permanent CVCs had a greater number of days of access-related infections, compared to fistulas (7.08 ± 16.41 vs. 0.06 ± 0.62 days, $p < 0.0001$) (Figure 4B).

Permanent CVCs and AVFs did not show any differences in terms of the number of admissions for any other cause (2.24 ± 2.69 vs. 3.12 ± 3.42 , $p = \text{NS}$) or access-related admissions (0.32 ± 0.62 vs. 0.47 ± 0.99 , $p = \text{NS}$) (Figure 4C).

Additionally, the number of days admitted for any other cause (22.62 ± 40.60 vs. 26.05 ± 32.92 days, $p = \text{NS}$) (Figure 5A) or for access-related reasons (4.22 ± 11.01 vs. 1.39 ± 3.41 days, $p = \text{NS}$) (Figure 5B) was not different between the permanent catheter and fistula groups.

Interestingly, permanent CVCs showed a higher proportion of days admitted for access-related reasons than fistulas (211 over 1131 days vs. 129 over 2397 days, $p < 0.0001$) (Figure 5C).

Infection episodes demonstrated the greatest difference between permanent CVCs and AVFs: when normalized for the survival of the access, fistulas were associated with an overall lower number of infections ($p < 0.0001$) (Figure 6A), infection days ($p < 0.0001$) (Figure 6B), admissions for infection ($p < 0.01$) (Figure 6C), and a shorter length of stay ($p < 0.01$) (Figure 6D) compared to catheters.

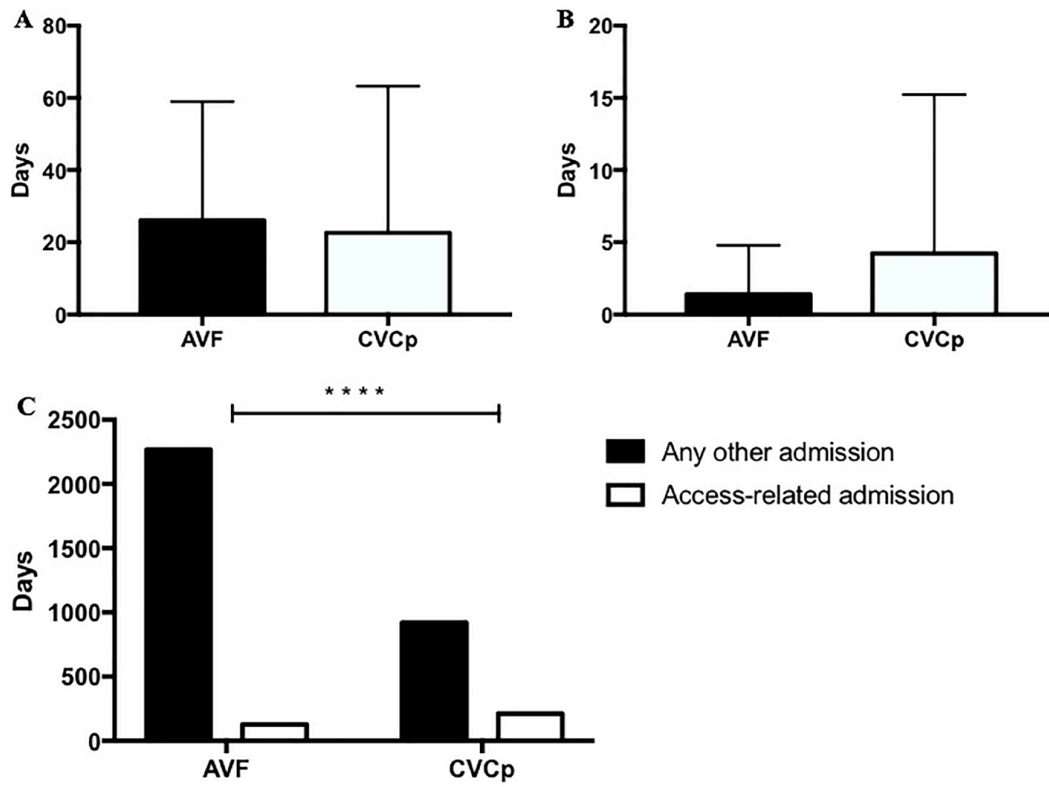


Figure 5. (A) Days of admission for any other cause. (B) Days of admission for access-related causes. (C) Any other cause vs. access-related total admission days ($p < 0.0001$). **** $p < 0.0001$.

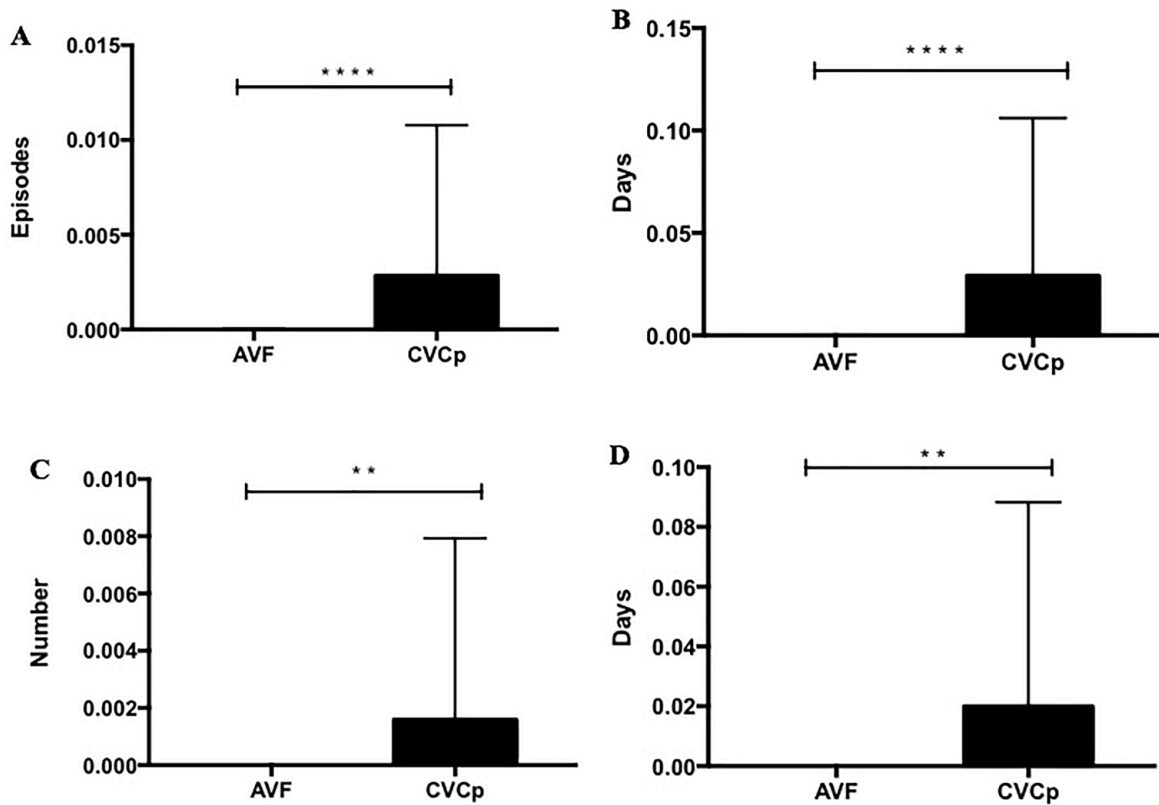


Figure 6. (A) Infection episodes normalized for access survival ($p < 0.0001$). (B) Infection days normalized for vascular access survival ($p < 0.0001$). (C) Infection-related admission normalized for access survival ($p < 0.01$). (D) Infection-related admission days normalized for access survival ($p < 0.01$). ** $p < 0.01$; **** $p < 0.0001$.

Finally, we observed an increased occurrence of failure of the access among AVFs compared to permanent catheters: A total of 74/122 AVFs failed compared to 19/50 permanent CVCs ($p < 0.01$) (Figure 7).

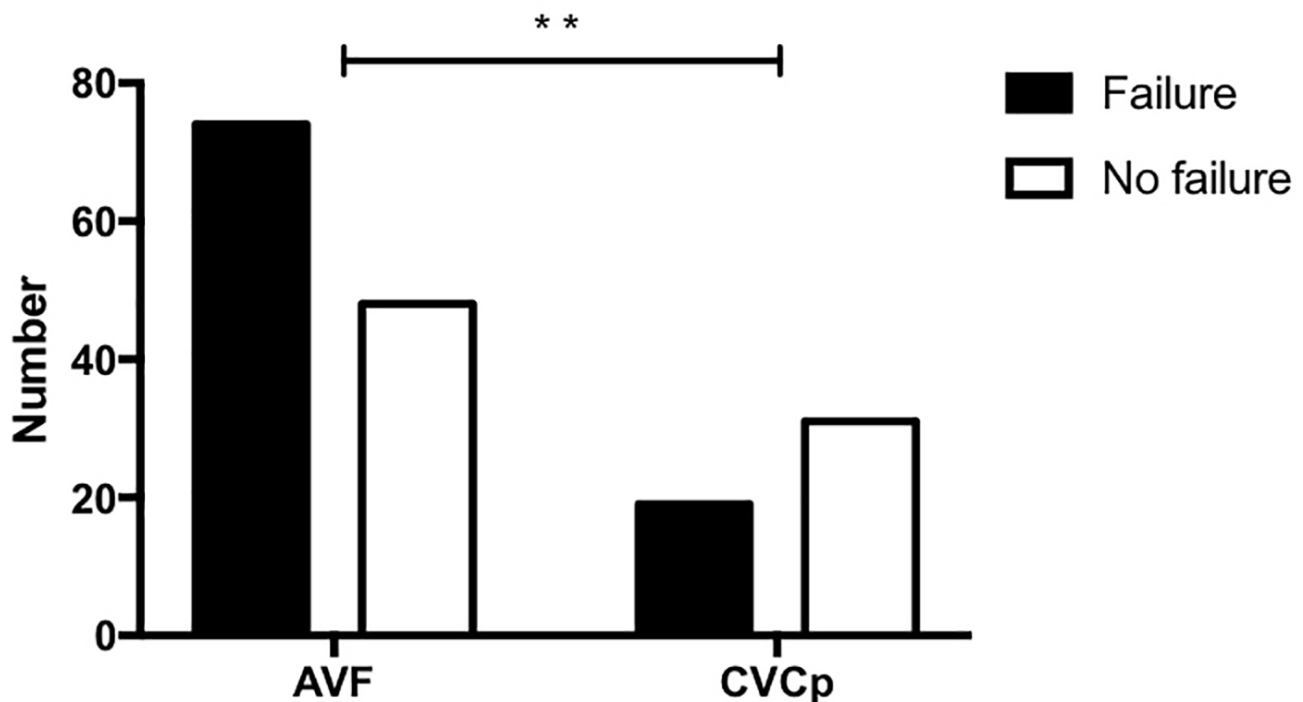


Figure 7. Number of failures ($p < 0.01$). ** $p < 0.001$.

4. Discussion

The hemodialysis vascular access is the “life line” and “Achilles’ heel” of uremic patients, and its efficiency is mandatory to perform an adequate renal replacement therapy. [17] Among different types of vascular accesses, central venous catheters bear the highest rate of complications and are usually associated with a short patient survival, while native vessel fistulas are considered as the optimal access [18]. However, it is not always possible to place a fistula in advance, as several patients start dialysis in urgency because of a late referral or due to the lack of suitable vessels to create an arteriovenous anastomosis [4]. Of note, the extended lifespan and the medical progress achieved in the last few decades allow patients to start renal replacement therapy at an older age; thus, the burden of comorbidities increases along with the likelihood of presenting cardiovascular disease risk factors. As a consequence, some authors have started wondering whether central venous catheters should be the first choice in a subset of dialysis patients [19].

Moving from these premises, our study shows that beginning hemodialysis with a CVC does not increase mortality compared to AVFs.

We did not take temporary catheters into consideration, as they should only be used for a few days and as a bridge to a different type of access that has proven superior in terms of reduced complications and patency rates, as suggested by the guidelines [7].

The two groups were similar in terms of gender and age. Even if patients in the fistula group had a greater BMI, the serum total protein and albumin concentration did not differ between the two groups, suggesting that there were no differences in the nutritional status. Our cohort is an elderly population, as the mean age in our sample was 68 years of age [20]. Our results demonstrate that placing a fistula seems to be feasible, even in elderly patients. This finding is particularly interesting if we consider the global ageing process of the world population [21]. Longevity, fortunately, is a characteristic of the Italian population; thus, this issue is particularly relevant in our country. Nowadays, Nephrologists must cope with

an overwhelming demand of dialysis care due to the extended lifespan that allows patients to start renal replacement treatment at extreme ages [22].

We did not find any difference in patient survival according to the vascular access method used at the beginning of dialysis. It must be acknowledged that among patients who started dialysis with a CVC, few were later converted to a fistula and continued dialyzing with an autologous access. Unfortunately, the small sample of our study did not allow a sub-analysis of this group of patients. Nevertheless, according to our results, the early conversion of a CVC into a fistula offers a survival advantage to dialysis patients, as they started treatment with an AVF from the beginning. Unadjusted survival on dialysis in our cohort was a little shorter than the European average: 74% and 64% (vs. 74.3%) at two years and 42.5% and 30% (vs. 51.1%) at five years for AVF and CVCp, respectively (Figure 1A) [23]. However, it should be noted that our patients were older at the start of renal replacement therapy compared to the European median (72 years for both AVF and CVCp vs. 69 years) [23].

We found that patients who died during the follow-up period were more likely to die using a CVC as vascular access. Since the relative proportions of AVFs and CVCs did not change from the beginning of the study and since only a small proportion of patients who switched from an AVF to a CVC died during the observational period, we would need a longer follow-up to demonstrate that CVCs confer a greater risk of mortality in our population.

Surprisingly, we did not find any differences in terms of the Comorbidity or Severity Index at the beginning of dialysis between the two groups. This suggests that catheters are placed regardless of the clinical status of the patient. As expected, we had more late referrals among patients who started dialysis with a CVC than in the fistula group.

CIRS evaluation showed that patients who started the renal replacement treatment with a fistula had less cardiovascular diseases but more severe hypertension. These findings suggest that although not more comorbid, patients starting dialysis with a CVC, might have a worse cardiac performance that is associated with less severe hypertension, impairing the maturation of the fistula. We decided not to include fistulas that had a primary failure in our analysis because a fistula that failed within hours after placement could not be responsible for the long-term complications evaluated in this study. The severity of cardiac disease, however, should not be considered as an absolute contraindication to place a fistula as demonstrated by the fact that 11 (13 if we include the 2 patients who placed a graft) patients were converted from CVC to AVF in the course of the study. Sometimes, the placement of a graft or a more proximal native vessel fistula overwhelms the expertise of most nephrologists; thus, a vascular surgeon is needed to perform the intervention with a non-negligible delay that imposes the use of a CVC to begin dialysis. In Italy, most nephrologists are able to perform small surgeries to place distal fistulas, but they must refer to vascular surgeons for more complicated interventions. The picture is completely different in the U.S., where nephrologists do not traditionally have the necessary surgical expertise [24].

Recent data presented by Kim et al. showed a higher mortality rate in patients starting dialysis with a CVC. However, the population included in their study was much younger than ours, and almost half of the patients who started dialysis with a CVC were late referrals. Moreover, their analysis included temporary as well as permanent CVCs, and the average follow up was much shorter. Finally, 721 and 155 out of 1071 patients who started dialysis with a CVC were converted into an AVF or a AVG, respectively, within the first year: this could have jeopardized the mortality results, as the remaining patients dialyzing with a CVC could have also been the ones with the worst prognosis, independently of the vascular access type [25].

Our results demonstrated that fistulas present a longer survival than CVCs. Since fistulas should be placed far in advance of the beginning of the dialytic treatment in order to give them enough time to mature, we compared AVF survival from either the placement or from the first dialysis session, and fistulas proved to be twice as long-lived compared to CVCs.

CVCs did not differ from AVFs in terms of the total number of admissions or access-related number of admissions. Nevertheless, CVCs showed a higher proportion of admission days due to access-related complications compared to AVFs. These results suggest that both types of vascular access bear the same risk of hospitalization, and we can assume that this risk is increased compared to the non-dialytic chronic kidney disease population. However, we cannot exclude that this increased risk was due to the dialysis status and not to the vascular access itself. CVCs seemed to be associated with longer stays when the patient was admitted for an access problem. In addition, even if we did not observe any difference in the number of admissions for any cause, the longer survival time of the fistulas must be emphasized: the increased lifespan of the fistulas was associated with the same amount of total hospitalizations and length of stay as the CVCs that, instead, occurred in half the same time.

Moreover, our study demonstrated that infection episodes were reduced in patients with a fistula compared to CVCs. This result could explain why the length of stay for the CVC group for access-related complications was longer than for AVFs. Fistula complications that led to hospitalization were mainly thrombosis or stenosis of the access method, causing it to malfunction while admissions for catheter complications were mostly due to infections. A thrombosed catheter is usually replaced with a new one, while every effort is made to save and restore the patency of a fistula. Thus, admissions for CVC complications are usually longer than those of AVFs. Even if this difference was not associated with a different mortality rate between groups, it has a profound impact on patients' quality of life, as they are forced to spend more time in the hospital in addition to coming to the dialysis unit three times a week for their regular sessions.

Finally, we observed a statistically higher number of AVF failures compared to CVC failures: the shorter CVC lifespan does not allow repeated failures; moreover, a failing catheter is replaced with a new one in a timely manner.

Our study has several limitations. First of all, it is a monocentric, retrospective study. The small sample size did not permit a subgroup analysis of the oldest patients or the patients shifting from one access type to another. Furthermore, we did not consider the temporary catheters placed during the follow-up in the analysis of complications, even if they could have modified the prognosis of our patients, jeopardizing the results. Finally, we did not consider anticoagulant therapy, which could have a role in maintaining vascular access patency.

Nonetheless, it is worth mentioning that no study focusing on the comparison of hemodialysis vascular access has confronted temporary catheters with fistulas because they are not supposed to stay in place for longer than a few days, and their use should be limited to emergency situations. Our study, however, had the merit of including elderly patients, reflecting the actual dialysis population, and it is a reflection of everyday practice.

5. Conclusions

Our study showed that starting dialysis with a CVC does not confer a greater risk of death, but patients are more likely to die dialyzing by means of a catheter than an AVF.

Moreover, fistulas carry a much lower risk of infection than CVCs.

Finally, even if more admissions are needed to cope with fistula malfunctioning and to maintain its patency, AVFs last longer than catheters and are associated with a shorter length of stay when the patient is admitted for a vascular access-related complication. Due to the small sample size and the single center experience, our results should be interpreted with caution, and larger studies are warranted to confirm our findings.

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Informed Consent Statement: At the beginning of the dialysis treatment, all patients sign an informed consent to allow the anonymous use of their clinical data for research purposes. Due to the retrospective nature of the study, no further consent was needed.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: All the authors declare no conflicts of interest.

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