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# Comparison of outcomes between type 2 diabetic and non-diabetic incident hemodialysis patients with functioning arteriovenous fistulas

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**Abstract**

This study compared clinical outcomes of patient survival and arteriovenous fistula (AVF) patency between incident hemodialysis patients with and without type 2 diabetes mellitus (T2DM).

Between January 2011 and December 2013, 384 consecutive incident hemodialysis patients with confirmed first upper-extremity AVF placement were divided into a T2DM group (n = 180, 46.9%) and a non-DM group (n = 204, 53.1%) and analyzed retrospectively. The primary outcome was all-cause mortality, and secondary outcome was AVF patency.

Patients in the T2DM group had a higher prevalence of hypertension ($P = .02$), smoking ($P < .01$), cardiovascular disease ($P < .01$), history of cerebrovascular accident (CVA) ($P < .01$), and peripheral arterial occlusive disease ($P < .01$) than those in the non-DM group. On Kaplan–Meier survival analysis, the overall survival and AVF patency rates were significantly higher in the non-DM group relative to the T2DM group (both $P < .01$). In the adjusted model, older age (hazard ratio [HR], 1.04; 95% confidence interval [CI], 1.02–1.06; $P < .01$), T2DM (HR, 1.76; 95% CI, 1.12–2.77; $P = .014$), and history of CVA (HR, 1.76; 95% CI, 1.04–2.98; $P = .04$) were significantly associated with an increased risk of mortality. Older age and T2DM were independently associated with decreased primary (HR, 1.03; 95% CI, 1.02–1.04; $P < .01$, HR, 1.69; 95% CI, 1.22–2.33; $P < .01$, respectively) and secondary (HR, 1.03; 95% CI, 1.01–1.04; $P < .01$, HR, 2.07; 95% CI, 1.42–3.00; $P < .01$, respectively) AVF patency during follow-up.

Compared with patients in the non-DM group, patients in the T2DM group had a higher mortality rate and worse AVF patency rates.

**Abbreviations:** AVF = arteriovenous fistulas, AVG = arteriovenous graft, CI = confidence interval, CKD = chronic kidney disease, CVA = cerebrovascular accident, CVC = central venous catheter, CVD = cardiovascular disease, DM = diabetes mellitus, HbA1c = glycated haemoglobin, HR = hazard ratio, PAOD = peripheral arterial occlusive disease, T2DM = type 2 diabetes mellitus, VA = vascular access.

**Keywords:** arteriovenous fistula, chronic kidney disease, renal dialysis, type 2 diabetes mellitus

## 1. Introduction

Well-functioning vascular access (VA) is essential for efficient hemodialysis therapy in patients with chronic kidney disease (CKD).[1–3] Arteriovenous fistulas (AVFs) are widely recognized as the VA of choice for most hemodialysis-dependent patients because of fewer complications, improved access survival, and lower risk of mortality, relative to arteriovenous grafts (AVGs) or central venous catheters (CVCs).[4–7] However, many AVFs fail to become functional due to early thrombosis and maturation failure,[1] and estimates of primary AVF failure, as well as primary and secondary patency, vary considerably in the literature.[5] Viecelli et al[8] performed a systematic review of randomized controlled trials and concluded that the reporting of VA outcomes in hemodialysis trials was heterogeneous, with limited patient-reported outcomes and infrequent use of standardized outcome measures.[9,10] In a single-center prospective study of 245 patients with first-time AVF placement, Kazemzadeh et al[11] reported that the results of primary patency at 6 months, 1, 2, 3, and 4 years were 79.5%, 70%, 65%, 60.5%, and 48%, respectively. Patient characteristics have changed during the past three decades, and diabetes mellitus (DM) represents the most rapidly growing cause of CKD worldwide.[12] Because of the recent Westernization of dietary habits, the prevalence of DM has been increasing throughout Asia.[13] A recent systematic review suggested that vessel diameter remains the only predictor of a well-functioning AVF, as the impact of comorbidities, such as DM, have already taken their toll on vessels when they are assessed preoperatively.[14] It has been well established that DM, as a progressive disease, contributes to the ongoing deterioration of atherosclerotic small and medium-sized

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vessels, but controversy exists over whether DM alone can predict AVF survival.[12,15]

This study compared clinical outcomes of patient survival and AVF patency between incident hemodialysis patients with and without type 2 DM (T2DM), with functioning AVFs and to determine the risk factors associated with survival and AVF patency in these patients. We also investigated whether T2DM duration and other T2DM-related factors could affect clinical outcomes in hemodialysis patients with T2DM.

## 2. Patients and methods

This single-center, retrospective, observational study was performed using data extracted from medical records of incident hemodialysis patients. Our hospital's institutional review board approved the study protocol (Asan Medical Center, IRB No. 2018–1289) and waived the requirement for informed patient consent because of the retrospective nature of the study.

### 2.1. Study population

Between January 1, 2011, and December 31, 2013, a total of 876 consecutive patients, aged 20 years and older, received first upper-extremity VA placement for incident hemodialysis at our hospital: 694 with AVFs (79.2%), and 182 with AVGs (20.8%). Among the 694 patients with first upper-extremity AVF placement screened for inclusion in this study, we excluded those who were lost to follow-up (n = 90, 13.0%) and those with a malignancy (n = 112, 16.1%). To ensure that we specifically analyzed the impact of T2DM on patient survival and long-term patency of functioning AVFs, we also excluded patients who received a renal transplant during follow-up (n = 59, 8.5%) and those with primary non-functioning AVFs due to early thrombosis or maturation failure (n = 49, 7.1%); finally, 384 patients (55.3%) were included in the analysis. Early thrombosis was defined as the absence of a thrill or the absence of flow on duplex ultrasound or fistulogram within 30 days of hemodialysis initiation via an AVF.[1] AVF maturation failure was defined as an AVF inadequate for successful needle cannulation after placement.[16,17] Study patients were divided into a T2DM group and a non-DM group. To evaluate the association between T2DM-related factors and long-term clinical outcomes, subgroup analyses according to DM duration, insulin use, and glycated hemoglobin (HbA1c) level were also performed in the T2DM group. In our study population, all patients had a nephrologist involved in all medication adjustments, the planning of hemodialysis, and the surveillance of AVFs.

### 2.2. Index procedures and definitions

All AVF placement procedures were performed under local anesthesia by 2 specially trained VA surgeons with more than 10 years of experience.[18–20] AVFs were categorized as forearm or upper arm according to placement location. We attempted to place upper arm AVFs in cases of inadequate forearm vessels for the placement of radio-cephalic fistulas. Postoperative surveillance was performed as previously detailed.[20]

AVF adequacy was defined as the ability to achieve at least 6 adequate hemodialysis sessions consisting of successful 2-needle cannulation without any AVF-related complications.[21] Our practice for hemodialysis initiation via a newly placed AVF is to start with lower gauge needles first, using a higher gauge with each subsequent hemodialysis session. Primary AVF patency was defined as the interval from the time of AVF placement until any intervention to maintain or restore blood flow, first AVF failure, or study end, whichever occurred first.[9] Secondary patency was defined as the time from AVF placement until AVF abandonment for any reason, regardless of the number of subsequent interventions.[5,16,20] T2DM was diagnosed based on the plasma glucose criteria outlined by the American Diabetes Association[22] or via patient self-reporting (through a self-administered questionnaire) of antidiabetic medication (insulin or oral hypoglycemic agents) use. DM duration was estimated as the difference between the age at AVF placement and the age at diabetes onset. Mean HbA1c levels were defined as the mean levels from the time of AVF placement and follow-up, and then at approximately 6-month intervals, until study end. Cardiovascular disease (CVD), a history of cerebrovascular accident (CVA) and peripheral arterial occlusive disease (PAOD) were defined as described elsewhere.[23,24]

### 2.3. Study outcomes and follow-up

The T2DM and non-DM groups were retrospectively analyzed and compared with regard to long-term clinical outcomes. All-cause mortality (from time of AVF placement to death) was the primary outcome of interest, and the secondary outcomes were primary and secondary AVF patency.

Follow-up visits with laboratory evaluations were scheduled at approximately 6-month intervals, and the latest follow-up data were obtained from medical records or follow-up physicians. For the patients who followed up at other centers (n = 53, 13.8%), direct telephone interviews with the patients or their families were conducted about each patient's general health status, function of the original AVF, and all diagnostic and radiological or surgical interventions during the interim. Risk factors of interest, clinical characteristics, and long-term clinical outcomes for all patients were recorded in an Excel database (Microsoft Corp., Redmond, WA) and analyzed retrospectively.

### 2.4. Statistical analyses

Baseline demographic and clinical characteristics, along with the clinical outcomes of the study population—including the exact time of death—were recorded according to DM status. Summary statistics are presented as frequencies or percentages for categorical data and means and standard deviations for continuous variables. Differences between the T2DM and non-DM groups were tested using the chi-squared test for categorical variables and Student *t* test for continuous variables. Univariate and multivariate analyses of the association of clinical variables with the primary (time to death) and secondary (primary and secondary AVF patency) outcomes were conducted with Cox proportional hazards modeling, using the event of interest and the period from AVF placement to the date of the event or last follow-up as the outcome. Univariate Cox proportional hazard regression models were fitted to calculate hazard ratios (HRs), with 95% confidence intervals (CIs), to estimate the associations between clinical variables and outcomes. Variables with a *P* value of less than .1 on univariate analysis were included in multivariate Cox proportional hazard regression models. Long-term event-free rates were estimated with Kaplan–Meier analysis and were compared with estimations calculated with the log-rank test between the T2DM and non-DM groups. A *P* value of less than

**Table 1**

**Baseline demographic and clinical characteristics of the study population at the time of AVF placement according to T2DM status.**

| | Total | T2DM | Non-DM | *P* value |
|---|---|---|---|---|
| No. of patients | 384 | 180 (46.9) | 204 (53.1) | |
| Age (years) | 55.9±12.8 | 58.4±10.8 | 53.7±14.0 | <.01 |
| Female sex | 129 (33.6) | 53 (29.4) | 76 (37.3) | .11 |
| BMI (kg/m$^2$) | 23.6±3.68 | 24.2±3.97 | 23.0±3.31 | <.01 |
| Location of AVF | | | | |
| Forearm | 209 (54.4) | 92 (51.1) | 117 (57.4) | .22 |
| Upper arm | 175 (45.6) | 88 (48.9) | 87 (42.6) | |
| Predialysis | 137 (35.0) | 61 (31.4) | 73 (35.8) | .73 |
| Underlying diseases | | | | |
| Hypertension | 317 (82.6) | 157 (87.2) | 160 (78.4) | .02 |
| Smoking | 91 (23.7) | 57 (31.7) | 34 (16.7) | <.01 |
| CVD | 59 (15.4) | 41 (22.8) | 18 (8.8) | <.01 |
| CVA | 39 (10.2) | 30 (16.7) | 9 (4.4) | <.01 |
| PAOD | 22 (5.7) | 17 (9.4) | 5 (2.5) | <.01 |
| Cause of CKD | | | | |
| Hypertension | 108 (28.1) | 2 (1.1) | 106 (52.0) | <.01 |
| Diabetes mellitus | 173 (45.1) | 173 (96.1) | 0 | <.01 |
| Glomerulonephritis | 40 (10.4) | 3 (1.7) | 37 (18.1) | <.01 |
| Unknown | 32 (8.3) | 0 | 32 (15.7) | <.01 |
| PCKD | 16 (4.2) | 0 | 16 (7.8) | <.01 |
| AKI | 11 (2.9) | 2 (1.1) | 9 (4.4) | .053 |
| Others* | 4 (1.0) | 0 | 4 (2.0) | <.01 |

Continuous data are expressed as mean±standard deviation, and categorical data as number (%). AKI=acute kidney injury, AVF=arteriovenous fistula, BMI=body mass index, CKD=chronic kidney disease, CVA=history of cerebrovascular accident, CVD=cardiovascular disease, DM=diabetes mellitus, PAOD=peripheral arterial occlusive disease, PCKD=polycystic kidney disease, T2DM=type 2 diabetes mellitus.

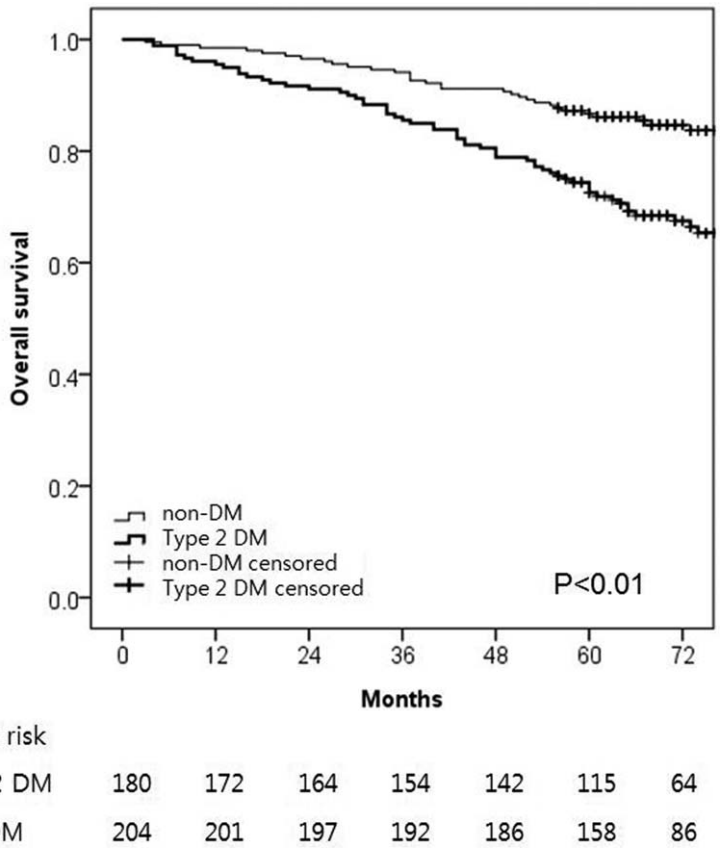
* Included 2 patients with systemic lupus erythematosis, one with hepatorenal syndrome, and one with amyloidosis.

.05 was considered statistically significant. Statistical analyses were performed with SPSS version 21.0 (IBM Corp., Armonk, NY).

## 3. Results

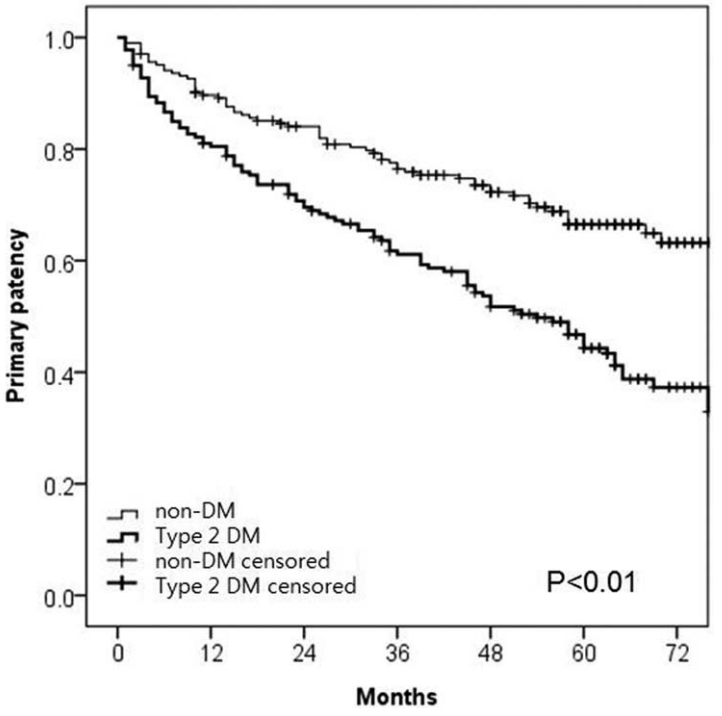
The study cohort consisted of 384 incident hemodialysis patients with identified first AVF placements who were stratified into 2 groups: a T2DM group (n=180, 46.9%) and a non-DM group (n=204, 53.1%). There was no mortality or morbidity associated with AVF placement. The baseline characteristics of the study sample according to DM status are presented in Table 1. Patients in the T2DM group were older ($P<.01$) and more often obese ($P<.01$) than those in the non-DM group. There was no significant difference in AVF placement location between the 2 groups. Patients in the T2DM group had a higher prevalence of hypertension ($P=.02$), smoking ($P<.01$), CVD ($P<.01$), history of CVA ($P<.01$), and PAOD ($P<.01$) than those in the non-DM group. DM nephropathy was identified as the cause of CKD in 96.1% of cases in the T2DM group.

On Kaplan–Meier survival analysis, the overall survival rate and the primary and secondary AVF patency rates were significantly higher in the non-DM group compared with the T2DM group (all $P<.01$) (Fig. 1). T2DM patients had a worse survival rate as well as reduced primary and secondary patency rates at all time points compared with non-DM patients. The

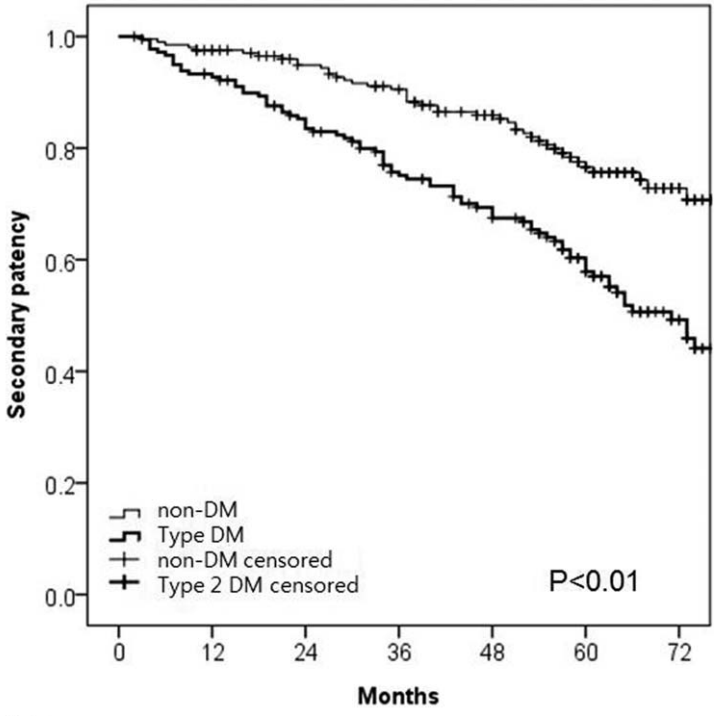



A

**Figure 1.** Kaplan–Meier survival analysis. Kaplan–Meier estimates of (A) the overall patient survival rate, and (B) primary and (C) secondary arteriovenous fistula patency rates in the type 2 DM and non-DM groups. DM=diabetes mellitus.




| B | No. at risk | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Type 2 DM | 180 | 142 | 119 | 99 | 80 | 52 | 21 |
| | non-DM | 204 | 177 | 158 | 137 | 112 | 66 | 27 |




| C | No. at risk | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Type 2 DM | 180 | 164 | 143 | 121 | 103 | 69 | 30 |
| | non-DM | 204 | 191 | 175 | 160 | 134 | 80 | 35 |

**Figure 1.** (Continued).

**Table 2**

**Factors associated with mortality.**

| | Univariate | | Multivariate | |
|---|---|---|---|---|
| | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| Age | 1.04 (1.03–1.06) | <.01 | 1.04 (1.02–1.06) | <.01 |
| Female sex | 0.77 (0.49–1.22) | .27 | NA | NA |
| BMI | 0.979 (0.92–1.04) | .47 | NA | NA |
| T2DM | 2.42 (1.57–3.74) | <.01 | 1.76 (1.12–2.77) | .014 |
| HTN | 1.00 (0.58–1.71) | .98 | NA | NA |
| Smoking | 1.50 (0.95–2.35) | .08 | 1.27 (0.80–2.00) | .32 |
| CVD | 2.22 (1.40–3.55) | <.01 | 1.39 (0.86–2.26) | .18 |
| CVA | 2.77 (1.67–4.59) | <.01 | 1.76 (1.04–2.98) | .04 |
| PAOD | 2.45 (1.27–4.74) | <.01 | 1.52 (0.76–3.02) | .24 |
| GN | 0.18 (0.04–0.72) | .02 | 0.31 (0.08–1.30) | .11 |
| PCKD | 0.25 (0.03–1.77) | .16 | NA | NA |

BMI = body mass index, CI = confidence interval, CVA = history of cerebrovascular accident, CVD = cardiovascular disease, GN = glomerulonephritis, HR = hazard ratio, HTN = hypertension, NA = not applicable, PAOD = peripheral arterial occlusive disease, PCKD = polycystic kidney disease, T2DM = type 2 diabetes mellitus.

primary and secondary patency rates in the T2DM group were 80.5% and 92.7% at 1 year, respectively, and 69.5% and 83.5% at 2 years, respectively. The primary and secondary patency rates in the non-DM group were 89.7% and 97.5% at 1 year, respectively, and 84.0% and 94.9% at 2 years, respectively. The mean duration of overall survival (from time of AVF placement to death) was 73.4 months (95% CI, 69.4–77.3 months) in the T2DM group and 83.0 months (95% CI, 80.2–85.7 months) in the non-DM group. The mean primary and secondary AVF patency durations for the T2DM and non-DM groups were 50.6 months (95% CI, 45.7–55.5 months) and 68.7 months (95% CI, 64.1–73.3 months), and 61.0 months (95% CI, 56.7–65.3 months) and 77.3 months (95% CI, 73.6–80.9 months), respectively.

Table 2 shows the regression analysis results according to mortality risk. In the adjusted model, older age (HR, 1.04; 95% CI, 1.02–1.06; $P < .01$), T2DM (HR, 1.76; 95% CI, 1.12–2.77; $P = .014$) and history of CVA (HR, 1.76; 95% CI, 1.04–2.98; $P = .04$) were significantly associated with an increased risk of mortality. Older age and T2DM were independently associated with decreased primary (HR, 1.03; 95% CI, 1.02–1.04; $P < .01$, HR, 1.69; 95% CI, 1.22–2.33; $P < .01$, respectively) and secondary (HR, 1.03; 95% CI, 1.01–1.04; $P < .01$, HR, 2.07; 95% CI, 1.42–3.00; $P < .01$, respectively) AVF patency during the follow-up period (Tables 3 and 4).

Among the 180 patients in the T2DM group, we excluded two patients who were followed-up at other centers and had no follow-up HbA1c data, and we performed subgroup analysis according to DM duration (<10 years vs ≥10 years), use of insulin (vs oral hypoglycemic agent), and poor glycemic control, as reflected by the HbA1c level (<6.5% vs 6.5–7.5% vs ≥7.5%). In this subgroup analysis, there were no differences in overall survival or primary and secondary AVF patency rates according to DM duration, use of insulin, or HbA1c level (Supplemental Table S1, http://links.lww.com/MD/D429). In the adjusted model for the T2DM group, CVD (HR, 1.78; 95% CI, 1.02–3.10; $P = .04$) was significantly associated with an increased risk of mortality (Supplemental Table S2, http://links.lww.com/MD/D430). For primary AVF patency, there was no identified independent risk factor (**data not shown**), whereas CVD (HR, 1.85; 95% CI, 1.15–2.96; $P = .011$) was significantly associated with decreased secondary AVF patency, and PAOD showed trends associated with decreased secondary patency (HR, 1.89; 95% CI, 1.00–3.58; $P = .052$) (Supplemental Table S3, http://links.lww.com/MD/D431).

## 4. Discussion

In our study of Korean hemodialysis patients, subjects with primary non-functioning AVFs due to early thrombosis or maturation failure were excluded to ensure that we specifically analyzed the impact of T2DM on patient survival and AVF patency. Of all functioning first upper-extremity AVF placements for incident hemodialysis during the 3-year study period, T2DM patients accounted for 46.9% of cases. Compared with patients in the non-DM group, patients in the T2DM group had a higher mortality rate as well as worse primary and secondary AVF patency rates. Although patients in the T2DM group were older and more often obese—meaning that they had a higher prevalence of atherosclerotic risk factors and comorbidities than those in the non-DM group— T2DM was an independent risk factor for death and lower AVF patency in the adjusted model. DM duration, use of insulin, and HbA1c level were not significantly associated with overall survival or primary and secondary AVF patency rates.

**Table 3**

**Factors associated with primary AVF patency.**

| | Univariate | | Multivariate | |
|---|---|---|---|---|
| | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| Age | 1.03 (1.02–1.05) | <.01 | 1.03 (1.02–1.04) | <.01 |
| Female sex | 0.82 (0.58–1.14) | .24 | NA | NA |
| BMI | 1.02 (0.98–1.06) | .40 | NA | NA |
| T2DM | 2.07 (1.51–2.83) | <.01 | 1.69 (1.22–2.33) | <.01 |
| HTN | 0.87 (0.58–2.88) | .48 | NA | NA |
| Smoking | 1.09 (0.76–1.55) | .64 | NA | NA |
| CVD | 1.60 (1.10–2.34) | .02 | 1.12 (0.76–1.66) | .57 |
| CVA | 1.55 (1.00–2.41) | .052 | 1.02 (0.65–1.62) | .92 |
| PAOD | 1.52 (0.86–2.67) | .15 | NA | NA |
| GN | 0.31 (0.14–0.69) | <.01 | 0.50 (0.22–1.15) | .10 |
| PCKD | 0.84 (0.37–1.90) | .69 | NA | NA |

AVF = arteriovenous fistula, BMI = body mass index, CI = confidence interval, CVA = history of cerebrovascular accident, CVD = cardiovascular disease, GN = glomerulonephritis, HR = hazard ratio, HTN = hypertension, NA = not applicable, PAOD = peripheral arterial occlusive disease, PCKD = polycystic kidney disease, T2DM = type 2 diabetes mellitus.

**Table 4**

**Factors associated with secondary AVF patency.**

| | Univariate | | Multivariate | |
|---|---|---|---|---|
| | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| Age | 1.03 (1.02–1.05) | <.01 | 1.03 (1.01–1.04) | <.01 |
| Female sex | 0.76 (0.51–1.13) | .18 | NA | NA |
| BMI | 1.02 (0.97–1.07) | .52 | NA | NA |
| T2DM | 2.31 (1.59–3.34) | <.01 | 2.07 (1.42–3.00) | <.01 |
| HTN | 0.87 (0.56–1.38) | .56 | NA | NA |
| Smoking | 1.21 (0.81–1.81) | .34 | NA | NA |
| CVD | 1.95 (1.29–2.94) | <.01 | 1.38 (0.90–2.12) | .14 |
| CVA | 1.90 (1.19–3.05) | <.01 | 1.26 (0.77–2.06) | .35 |
| PAOD | 2.34 (1.32–4.17) | <.01 | 1.57 (0.86–2.87) | .15 |
| GN | 0.30 (0.11–0.81) | .02 | 0.53 (0.19–1.47) | .22 |
| PCKD | 0.34 (0.08–1.38) | .13 | NA | NA |

AVF = arteriovenous fistula, BMI = body mass index, CI = confidence interval, CVA = history of cerebrovascular accident, CVD = cardiovascular disease, GN = glomerulonephritis, HR = hazard ratio, HTN = hypertension, NA = not applicable, PAOD = peripheral arterial occlusive disease, PCKD = polycystic kidney disease, T2DM = type 2 diabetes mellitus.

Compared with previously published meta-analyses of patency data,[17,25] our study reported excellent results. In this single-center analysis, all AVF placement procedures were performed by 2 specially trained VA surgeons with more than 10 years of experience. Furthermore, in our study population, all patients had a nephrologist involved in the planning of AVF placement and patient care, and we had a policy of aggressive endovascular and surgical intervention to maintain and restore the patency of failing or failed AVFs.[26] We speculate that the planning of AVF placement in collaboration with a nephrologist and our aggressive management strategy for dysfunctional AVFs reduced maturation failure and achieved higher secondary patency rates compared with previous studies.[17,25]

Hemodialysis-dependent patients with CKD often have complicated medical and anatomic issues that must be addressed for AVF placement on an individual basis.[27] Many factors have been suggested as potential predictors of successful maturation and patency of an AVF.[28,29] However, conflicting evidence exists regarding the determinants of AVF maturation and patency across numerous studies.[30–32] Some studies have suggested a significant negative association between age, female sex, and DM and AVF patency rates[33,34] whereas a study of cumulative access survival in AVF found that age, female sex, DM, and PAOD did not show significant associations with access survival.[35] DM and ongoing CKD are well established to be significant risk factors for progressive atherosclerotic changes in small to medium sized vessels, resulting in increased arterial calcification and stenosis, which can also limit blood flow through a newly created AVF and decrease patency during follow-up.[32] Although DM and CKD have a significant effect on vessels, the evidence that DM alone can predict AVF survival is controversial, as the rate of AVF patency in DM patients has been similar to that of non-DM patients in some published series.[12,15] In addition to the heterogeneity of study populations and outcome definitions across studies, these conflicting data reflect the poor predictive value of accepted prognostic factors for AVF outcomes that we found in this study.

Preoperative assessment, including additional duplex ultrasound, of vessel suitability performed before AVF placement took into account any impact of DM and DM-related atherosclerotic changes already present in the vessels, which could lead to the conclusion that vessel diameter is the most important predictive factor in determining functional maturation of AVFs irrespective of the presence of DM.[15] However, in our analysis with the exclusion of primary non-functioning AVFs, we evaluated the sustained impact of T2DM alone on the durability of functioning AVF performance; vessels naturally deteriorate with age and are also damaged by concurrent comorbidities.[3] Considering that DM is an ongoing disease with progressive atherosclerotic changes in small to medium-sized vessels (in addition to the aging process), this potentially explains our observation of a significant decrease in AVF performance over time in T2DM patients.

In addition to DM itself, controversy exists regarding DM-related factors—for example, a longer duration of DM (≥10 years), use of insulin, and poor glycemic control reflected by the HbA1c level—and their impact on patient and AVF outcomes among hemodialysis-dependent DM patients. Recently, Hoshino et al[36] reported that HbA1c levels in diabetic hemodialysis patients in Japan differed considerably from those in the United States and confirmed the U-shaped association of HbA1c level and mortality, with both low and high HbA1c levels linked to higher mortality rates. Our subgroup analysis findings indicate that these DM-related factors were not associated with outcomes in these patients, although CVD was independently associated with overall survival and secondary AVF patency. We believe that the small sample size may have influenced these findings. Considering the importance of domestic guidelines (according to ethnicity and country) for glycemic control,[36] additional large cohort studies are required to evaluate the association between DM-related factors and outcomes in Korean patients with T2DM and CKD.

Our study has important limitations. Potential selection and information biases on the part of the physicians or patients are an inherent feature of retrospective studies. There were several key variables not available in our data sources, such as vessel diameter and vessel quality, which may have accounted for some of the differences in outcomes relative to other studies. Moreover, other important factors are also unavailable because a substantial proportion of patients who received AVF placement at our tertiary medical center received hemodialysis via AVF within a certain period. Subsequently, once stability had been established, they received hemodialysis and were followed up at other hospitals. Therefore, infection-related and other outcomes were not included in the data analysis plan for this study. Our study cohort consisted of only Korean patients; thus, our findings may have limited generalizability to other ethnic groups and placement of any other

types of VA. Finally, as with all observational studies, we cannot draw conclusions about causality.

In conclusion, among incident hemodialysis patients with identified first AVF placements, compared with patients in the non-DM group, patients in the T2DM group had a higher mortality rate as well as worse primary and secondary AVF patency rates. We also observed that CVD was independently associated with overall survival and secondary AVF patency in the T2DM group. Future studies are needed to better clarify the sustained impact of T2DM on patient and AVF outcomes.

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