The role of echocardiography in prognosis for dysfunction and abandonment of radiocephalic arteriovenous fistula in elderly Chinese patients on hemodialysis

Running head: Echocardiography predicts outcomes of RCAVF

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Acknowledgements: The data reported herein were supplied by West China Hospital of SiChuan University. The interpretation and reporting of these data are the responsibility of the authors and do not reflect the official views or opinions.

Funding resources: This work was financially supported by the 1.3.5 project for disciplines of excellence, West China Hospital, Sichuan University and the Research Program of Health Commission of SiChuan Province (18PJ362).

Author contributions: Ping Fu and Yang Yu designed this study; Chunle Zhang, Liya Wang and Yuchen Deng contributed to the acquisition of data; Yuqin Xiong analyzed and interpreted the data; Yang Yu and Yuqin Xiong drafted the manuscript; Emily Morris, Yi Li and Ping Fu revised the manuscript for important intellectual content.

Conflicts of interest: None.

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Article type : Original Article

ABSTRACT

The objective of this study was to examine the impact of cardiac structure and function at baseline on the outcomes associated with arteriovenous fistula (AVF) in patients on hemodialysis (HD). Patients who initiated HD aged ≥ 70 years and received a mature AVF creation were included retrospectively. Echocardiographic parameters measured within one week before AVF creation were acquired. The observational period for each patient was from the point of AVF creation to the last time of follow-up unless AVF abandonment or death occurred. Kaplan-Meier and Cox proportional hazard regression analyses were conducted. A total of 82 elderly Chinese HD patients with mature radiocephalic AVF (RCAVF) and EF ≥ 50% were analyzed. During the median study period of 26.8 (12-40) months, 42 (51.2%) experienced RCAVF dysfunction and 34 (41.5%) progressed to abandonment. Primary and cumulative patencies at 6, 12, 24, and 36 months were 81%, 73%, 48%, 38%, and 84%, 81%, 68%, 55%, respectively. Left ventricle end-diastolic volume (LVEDV) ≤103.5 ml (HR=2.5, p=0.019) and the right side of RCAVF (HR=3.59, p=0.003) significantly predicted RCAVF dysfunction. The main pulmonary artery internal diameter (MPAID) ≤ 21.5 mm (HR=4.3, p=0.001) as well as the right side (HR=2.95, p=0.047) were the independent predictors for RCAVF abandonment. In conclusion, LVEDV, MPAID assessed by echocardiography and the right side of RCAVF, showed significant predictive implications for the outcomes of RCAVF. Disparities among nationalities in the areas of utilization and patency of AVFs necessitate additional studies.

Key words: elderly, hemodialysis, arteriovenous fistula, echocardiography, predictors

INTRODUCTION

Aging populations have led to an increasing number of end stage renal disease (ESRD) patients on maintenance hemodialysis (HD) [1]. Current studies suggest arteriovenous fistula (AVF) as the preferred vascular access (VA) type for elderly HD patients due to longer patency and lower incidence of VA-related infection [2,3].

It has been widely acknowledged that ventricular remodeling and dysfunction, assessed by echocardiography, develop following AVF creation and dialysis initiation. Furthermore, the risk of pulmonary hypertension (PAH) due to high flow rate of AVF was increased despite improved left ventricular (LV) pressure and volume load through dialysis [4-6]. This, raised the issue that what kind of cardiac structure and function patients had at baseline, could tolerate the adverse effects derived from AVF and provide the AVF with adequate blood flow for HD treatment. To date, few studies have identified the association between pre-operative echocardiography and the outcomes of AVF.

Although preoperative retention of temporary catheter was thought to be correlated with lower patency of AVF [3.7], it remains unclear whether the previous modality and location of VA also contribute to the outcomes of AVF. In addition, different regions have varied requirements on dialysis flow, which could result in a potential discrepancy in functional life of AVFs [8,9]. Related data for elderly Chinese ESRD patients have been scarce.

Based on the above, we designed a retrospective study and aimed to: (1) explore the prognostic value of echocardiographic indexes and prior VA history for the outcomes of AVF; and (2) report the utilization and patency of AVFs for elderly HD patients in China.

MATERIALS AND METHODS

Study population

We retrospectively reviewed ESRD patients aged ≥ 70 years who were admitted to our hospital and obtained a mature AVF creation.

Patients were excluded when: (1) they initiated HD before the age of 70; (2) their ejection fraction (EF) < 50% or echocardiographic parameters were incomplete before AVF creation; (3) they underwent HD combined with, or switched to, peritoneal dialysis; (4) they died from any cause during the hospitalization of AVF creation; (5) the dialysis remained dependent on other VAs for an unmatured AVF; (6) they had not initiated HD yet or withdrew from HD due to stable renal function based on maintenance medication until last follow-up, even if the AVFs achieved maturation; (7) they were lost to contact, or they refused to be investigated.

Clinical data collection and definitions

Clinical data were collected through electronic medical records, including demographic characteristics, etiology of ESRD, coexisting conditions, echocardiographic parameters within one week prior to AVF creation, preoperative HD status, and the location of AVF.

For each patient, the patency, dysfunction, intervention, and abandonment of the AVF were acquired by reviewing the patient's readmission records and initiating phone calls to patients' homes. The last follow-up was defined as the point of last contact at a dialysis center, outpatient clinic, inpatient ward or through phone call. The study period for each patient was from the point of AVF creation to the last time of follow-up unless AVF abandonment or death occurred. Maturation [8], primary and cumulative patency, AVF abandonment [10] were defined in accordance with published standards. In addition, serum biochemical indices were excluded from the analysis, because the concentration of serum biomarkers on entry may not represent the actual level as some patients underwent HD or blood transfusion treatment before admission to our clinic.

Statistical analysis

Patients were assigned to groups according to the dysfunction or abandonment of AVF during the study period. The continuous variables are presented as mean (standard deviation), or median (interquartile range) when the values did not show a normal distribution. Categorical variables are presented as percentages. The Kruskal–Wallis H test was used for continuous variables, while the chi-square test was applied to assess the categorical data.

Receiver operating characteristic (ROC) curves were generated to determine the optimal cut-off value. Kaplan–Meier curves were utilized to demonstrate differences in survival. Log rank tests were performed to examine the significance of the difference between the curves. Variables with $P < 0.05$ in the univariate analysis and those considered clinically important were entered into Cox proportional hazards regression models to explore predictors for outcomes of AVF. $P < 0.05$ was regarded as an acceptable threshold for significance. Data were analyzed using SPSS version 22.0.

RESULTS

Inclusion of subjects and follow-up procedure

180 HD patients aged ≥ 70 years with a total of 220 AVF surgeries at our hospital from January 2007 to October 2018 were screened through electronic medical records by two investigators. Among these surgeries, 143 AVFs achieved maturation, 66 AVFs failed to mature, and the remaining 11 failed immediately (no murmur or tremor was detected within 72 hours after AVF creation).

The final follow-up dates were observed between January 2019 and March 2019. After excluding 98 patients, 82 eligible participants with a median follow-up period of 26.8 (12-40) months were included in the final analysis. All of them received radiocephalic AVFs (RCAVFs).

Characteristics at baseline and outcomes of RCAVFs

Among the 82 elderly HD patients, 42 (51.2%) experienced RCAVF dysfunction and 34 (41.5%) progressed to abandonment. The baseline clinical, echocardiographic, and previous VA and RCAVF characteristics of the subjects were summarized in Table 1 and 2. There was no history of peripheral vascular disease (PVD) or arteriovenous graft in this cohort.

In terms of patency for the mature RCAVFs, primary and cumulative patencies at 6, 12, 24, and 36 months were 81%, 73%, 48%, 38%, and 84%, 81%, 68%, 55%, respectively. As for the cause of RCAVF dysfunction, 38 (90.5%) patients were subjected to AVF stenosis, 4 (9.5%) suffered from venous hypertension syndrome or central venous stenosis. In regard to intervention, 13 cases of balloon angioplasty, 1 case of balloon angioplasty + stent deployment, and 8 cases of surgical revision were performed for 15 patients.

Predictors for outcomes of RCAVF in Cox hazard regression analysis

According to the results of univariate (Table 1, 2) and ROC (data not listed) analyses, LV internal diameter (LVID), main pulmonary artery internal diameter (MPAID), LV end-systolic volume (LVESV), LV end-diastolic volume (LVEDV) and LV stroke volume (LVSV) showed significant differences between groups. Because of the correlation among the three values (LVSV=LVEDV-LVESV), only LVID, MPAID and LVEDV were selected to be included in the regression models.

As presented in Table 3, LVEDV ≤ 103.5 mmHg and the right side of operations were independent predictors for RCAVF dysfunction. Moreover, the survival curve of RCAVFs with LVEDV > 103.5 mm (Figure 1) indicated longer survival times compared to those with LVEDV ≤ 103.5 (p = 0.005).

For RCAVF abandonment, MPAID (whether presented as a continuous or categorical variable according to the optimal cut-off value of ≤ 21.5 mm), and the right side acted as significant predictors in the two Cox regression analyses (Table 4. model a and b). Furthermore, the survival of RCAVFs in the group with MPAID > 21.5 mm (Figure 2) showed better outcomes than the converse group.

DISCUSSION

Echocardiography and surgical site in predicting outcomes of RCAVF

In the present study on 82 Chinese ESRD patients who initiated HD aged ≥ 70 years, the factors involving previous VAs, reflected not only the dialysis vintage but also a potential proneness to vascular intimal hyperplasia (IH) and thrombosis. These factors were adjusted when we explored the predictors for RCAVF dysfunction and abandonment.

In the cohort with normal cardiac systolic function (EF ≥ 50%), LVEDV and the right side of RCAVF were independent predictors for dysfunction. Patients with LVEDV ≤ 103.5 ml possessed 2.5 times increased risk compared to those with LVEDV > 103.5 ml (Table 3). This might indicate an insufficient cardiac diastolic function for the gradually increased blood volume flowing back to the heart after RCAVF creation, which in turn intensified the pressure of AVF outflow tract and restricted its flow. The sustaining pressure could induce IH or stenosis of the whole HD access circuit, thereby promoting the development of AVF dysfunction.

Our clinic typically chose non-dominant upper extremity (mostly left arm in this cohort) as the surgical site in keeping with guidelines [8], the exceptional employments of right arm in 19 patients implied their poor overall vascular conditions. Besides, previous placements of right internal jugular vein catheter were prone to causing proximal traumatic stenosis of the ipsilateral AVF circuit, which might impair the function of right RCAVF. Therefore, it makes sense that the risk for RCAVF dysfunction and abandonment on the right side showed over three times greater risk than the left (Table 3, 4).

In addition to surgical site, MPAID acted as a strong predictor for RCAVF abandonment in the population without PAH at baseline. MPAID ≤ 21.5 mm before AVF creation had over fourfold the risk for AVF abandonment as those whose MPA were larger, with the risk decreasing by 32% per each 1 mm elevation (Table 4). As a structural indicator of the heart, smaller MPAID might suggested an irreversible low tolerance to the increasing blood flow that returned to the heart. Since the occlusion of AVF could reverse the deterioration of cardiac function [11], and most of abandoned AVFs in this cohort converted to other types of VA in further observation [12], prognostic analysis of echocardiographic parameters or AVF on cardiovascular outcome was not conducted in this study.

Patencies and outcomes of RCAVF in Chinese ESRD patients aged ≥ 70 years

A maturation rate of 68.4% was calculated in the 209 AVFs. RCAVF was the more common choice for the aged in our clinic compared to brachiocephalic AVF (BCAVF). This was mainly due to concerns about the greater possibility that high-flow AVF formation increased the risk for high-output cardiac failure [11.13-15]. Even though BCAVF was reported with higher patency [16], several centers published excellent results for RCAVFs in the elderly [17].

Patients in the study demonstrated superior primary patencies compared to their counterparts aged ≥70-75 years (54% at 12 months for British, 73.1% at 6 months and 57.1% at 12 months for Koreans; 39.7% at 12 months and 31.2% at 24 months for Americans), and also better cumulative patencies (66% at 12 months for British; 56% at 12 months and 51% at 24 months for Americans) [2,18,19]. Observed values were much closer to a general Chinese ESRD population [7], confirming the regional differences. Our Chinese cohort had longer maturation time and greater patency compared with the US or Europe [8,9], which was consistent with previous studies showing an inverse correlation between maturation time and AVF failure [20,21]. Also, the lower routine blood flow (200-300ml/min) during HD treatment in China, might preserve the function and lifetime of AVF. Another reason that might contribute to these differences was that our subjects had very few cardiovascular disorders (Table 1) and EF ≥ 50%, as inferior AVF blood flow was observed in patients with abnormal EF [22].

The main reason for RCAVF dysfunction in the study was AVF stenosis (95%). However, only 15 (35.7%) patients received endovascular or surgical interventions. Most of the others missed the opportunity for early treatment, which led to an abandonment rate of 41.5% during the study period. Generally, delayed detection and referral made it difficult to rescue the dysfunctional AVFs.

Limitations

The present study had some limitations. Firstly, there was a small sample size and some inherent bias in its retrospective nature, which means we could not rule out selective bias of patients or acquire the entirety of relevant events or precise information such as medication, dialysis prescription and nutrition status during the study period. Although patients in this study visited our clinic regularly and underwent each operation in the same surgical team, they did not receive dialysis treatments in the same HD center. Additionally, we lacked echocardiographic data for the end-point to further verify the association between changes of cardiovascular system and the function of AVF. Secondly, the deviation from the baseline data might weaken the reliability of the study. The echocardiography were performed using the same machine in our hospital by skilled specialists, not the same technician. Lastly, the study population consisting of Chinese individuals did not reflect a multiethnic cohort. Hence, the results cannot be generalized to other ethnic groups or a general population.

CONCLUSIONS

In the retrospective study of 82 elderly Chinese patients with RCAVF on HD, LVEDV and MPAID assessed by echocardiography showed significant predictive performance for the dysfunction and abandonment of RCAVF respectively, after adjustment for modality and duration of VA prior to RCAVF creation. The right side of RCAVF was also a risk factor both for dysfunction and abandonment. Significant differences existing between the Chinese population and others with respect to the patency of AVF necessitate additional studies.

STATEMENT OF ETHICS

This study adheres to the Declaration of Helsinki and was approved by the ethics committee (No. 2017204). Written informed consent was obtained from each patient.

DISCLOSURE STATEMENT

None.

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FIGURE LEGENDS

Figure 1: Curves respectively illustrating the cumulative functional survival (equal to primary patency) of RCAVF over time in groups according to the value of LVEDV. Abbreviation: LVEDV: left ventricle end-diastolic volume.

Figure 2: Curves respectively illustrating the cumulative survival of RCAVF (equal to cumulative patency) during study period in groups according to the value of MPAID. Abbreviation: MPAID: main pulmonary artery internal diameter.

Table 1. Characteristics in groups according to RCAVF abandonment

Characteristic	Total	Abandoned	No abandoned	*P*[a]
No. of patients	82	34	48	-
Age (year)	73(71-75)	74(71-76)	73(71-75)	0.29
Male no.(%)	49(59.8)	16(47.1)	33(68.8)	0.048
Etiology of ESRD no.(%)				0.61
Diabetic nephropathy	27(32.9)	13(38.2)	14(29.2)	-
Hypertensive nephropathy	37(45.1)	15(44.1)	22(45.8)	-
Others	18(22)	6(17.7)	12(25)	-
Previous medical history no.(%)				
Diabetes mellitus	40(48.8)	14(41.2)	26(54.2)	0.25
Congestive heart failure	5(6.1)	2(5.9)	3(6.3)	0.95

Coronary heart disease	3(3.7)	2(5.9)	1(2.1)	0.37
Preoperative assessment				
Systolic blood pressure (mmHg)	146(130-155)	149(122-155)	146(133-156)	0.70
Diastolic blood pressure (mmHg)	75.9(11.2)	74.7(7.7)	76.8(13.2)	0.01
Ejection fraction (%)	66.1(5.5)	66.7(5.9)	65.7(5.3)	0.37
LAID (mm)	38.7(5.2)	38.5(5.9)	38.8(4.6)	0.18
RAID (mm)	36(33-39)	35(33-38)	37(34-39)	0.28
LVID (mm)	48(46-52)	47(45-49)	49(46-54)	0.012
RVID (mm)	21(20-23)	20(20-22)	22(20-23)	0.05
AAOID (mm)	34.3(3.4)	34(3.7)	34.4(3.2)	0.47
MPAID (mm)	22(21-24)	21(20-23)	23(21-26)	0.001
LVESV (ml)	34.5(29-44)	30(27-40)	36.5(32-48)	0.004
LVEDV (ml)	107(94-127)	100(91-112)	111(98-139)	0.009
LVSV (ml)	70(62-86)	67(61-80)	75(64-93.5)	0.022
Previous vascular access history				
No. of PVA[b]	0(0-3)	0(0-2)	0(0-3)	0.91
Functional length of tcCVCs[b] (month)	0(0-72)	0(0-17)	0(0-72)	0.56
Functional length of AVFs[b] (month)	0(0-1)	0(0-1)	0(0-1)	0.94
Immediate AVFs failure no.(%)	4(4.9)	3(8.8)	1(2.1)	0.16
AVF maturation failure no.(%)	6(7.3)	4(11.8)	2(4.2)	0.19
Duration of FV-ntCVCs (month)	0(0-2)	0.75(0-2.5)	0(0-0.7)	0.036
Duration of IJV-ntCVCs (month)	0(0-2)	0(0-0)	0(0-2.2)	0.025
Length of previous dialysis (month)	0.2(0-0.7)	0.1(0-0.5)	0.2(0-0.7)	0.45
Outcomes of current RCAVF				
Right RCAVF no.(%)	19(23.2)	11(32.4)	8(16.7)	0.1
Maturation period (month)	2.5(2-3)	2.5(2-3)	2.5(2-3)	0.79
Primary patency (month)	23.8(11-31)	14.5(8-27)	26.5(14.5-38.5)	0.002
No. of interventions[b]	0(0-4)	0(0-4)	0(0-3)	0.27
Length of follow-up (month)	26.8(12-40)	19.5(9-39)	27.5(21.8-41.8)	0.045

Abbreviation: RCAVF: radiocephalic arteriovenous fistula; LAID: left atrium internal diameter; RAID: right atrium internal diameter; LVID: left ventricle internal diameter; RVID: right ventricle internal diameter; AAOID: ascending aorta internal diameter; MPAID: main pulmonary artery internal diameter; LVESV: left ventricle end-systolic volume; LVEDV: left ventricle end-diastolic volume; LVSV; left ventricle stroke volume; PVA: permanent vascular access; tcCVC: tunnelled cuffed central venous catheter; FV: femoral vein; ntCVC: non-tunnelled central venous catheter; IJV: internal jugular vein.

[a]: *P* value for comparison among two groups excluding the total group.

[b]: Variables are presented as median(full range) since their median(interquartile range) are both 0(0-0).

Table 2. Characteristics in groups according to RCAVF dysfunction

Characteristic[a]	Total	Unusable	Usable	P^b
No. of patients	82	42	40	-
Age (year)	73(71-75)	74(71-76)	72.5(71-75)	0.44
Male no.(%)	49(59.8)	22(52.4)	27(67.5)	0.16
Preoperative assessment				
Systolic blood pressure (mmHg)	146(130-155)	146.5(124-155)	146(134-157)	0.45
Diastolic blood pressure (mmHg)	75.9(11.2)	74.8(9.4)	77.1(12.9)	0.024
LVID (mm)	48(46-52)	47(45-49)	50(47-54)	0.006
LVESV (ml)	34.5(29-44)	30(28-41)	36(32-51)	0.01
LVEDV (ml)	107(94-127)	100(91-112)	112(99-141)	0.009
LVSV (ml)	70(62-86)	67(61-81)	76(67-94)	0.011
Previous vascular access history				
No. of PVA[c]	0(0-3)	0(0-2)	0(0-3)	0.38
Functional length of tcCVCs[c] (month)	0(0-72)	0(0-17)	0(0-72)	0.17
Functional length of AVFs[c] (month)	0(0-84)	0(0-84)	0(0-51)	0.76
Duration of FV-ntCVCs (month)	0(0-2)	0.28(0-2.3)	0(0-0.6)	0.06
Duration of IJV-ntCVCs (month)	0(0-2)	0(0-1)	0(0-2.2)	0.16
Right RCAVF (%)	19(23.2)	14(33.3)	5(12.5)	0.025
Length of follow-up (month)	23.8(11-31)	16.5(8-28)	26(14.5-39.5)	0.007

Abbreviation: RCAVF: radiocephalic arteriovenous fistula; LVID: left ventricle internal diameter; LVESV: left ventricle end-systolic volume; LVEDV: left ventricle end-diastolic volume; LVSV; left ventricle stroke volume; PVA: permanent vascular access; tcCVC: tunnelled cuffed central venous catheter; FV: femoral vein; ntCVC: non-tunnelled central venous catheter; IJV: internal jugular vein.

[a]: Variables with $p<0.05$ in the comparison or those considered clinically important are listed

[b]: *P* value for comparison among two groups excluding the total group.

[c]: Variables are presented as median (full range) since their median (interquartile range) are both 0(0-0).

Table 3. Cox proportional hazard regression models for RCAVF dysfunction

Variable (per 1 unit increased) or (yes vs. no)	HR	95%CI	*P*
Male	1.2	0.58-2.47	0.63
Age (year)	1.06	0.96-1.17	0.23
Diabetes mellitus	0.81	0.41-1.58	0.53
DBP (mmHg)	0.97	0.94-1	0.08
LVID (mm)≤48.5	1.8	0.76-4.24	0.18
LVEDV (ml)≤103.5	2.5	1.17-5.37	0.019
Previous No. of PVA	0.63	0.22-1.76	0.38
Previous functional length of AVFs (month)	1.01	0.98-1.05	0.5
Previous functional length of tcCVCs (month)	1	0.89-1.12	0.99
Previous duration of FV-ntCVC (month)	1.14	0.92-1.41	0.25
Previous duration of IVJ-ntCVC (month)	0.92	0.75-1.13	0.42
Right RCAVF	3.59	1.54-8.39	0.003

Abbreviation: RCAVF: radiocephalic arteriovenous fistula; HR: Hazard rate; CI: confidence interval; DBP: diastolic blood pressure; LVID: left ventricle internal diameter; LVEDV: left ventricle end-diastolic volume; PVA: permanent vascular access; tcCVC: tunnelled cuffed central venous catheter; FV: femoral vein; ntCVC: non-tunnelled central venous catheter; IJV: internal jugular vein.

Overall (score) χ^2=26.65, p=0.009.

Table 4. Cox proportional hazard regression models for RCAVF abandonment

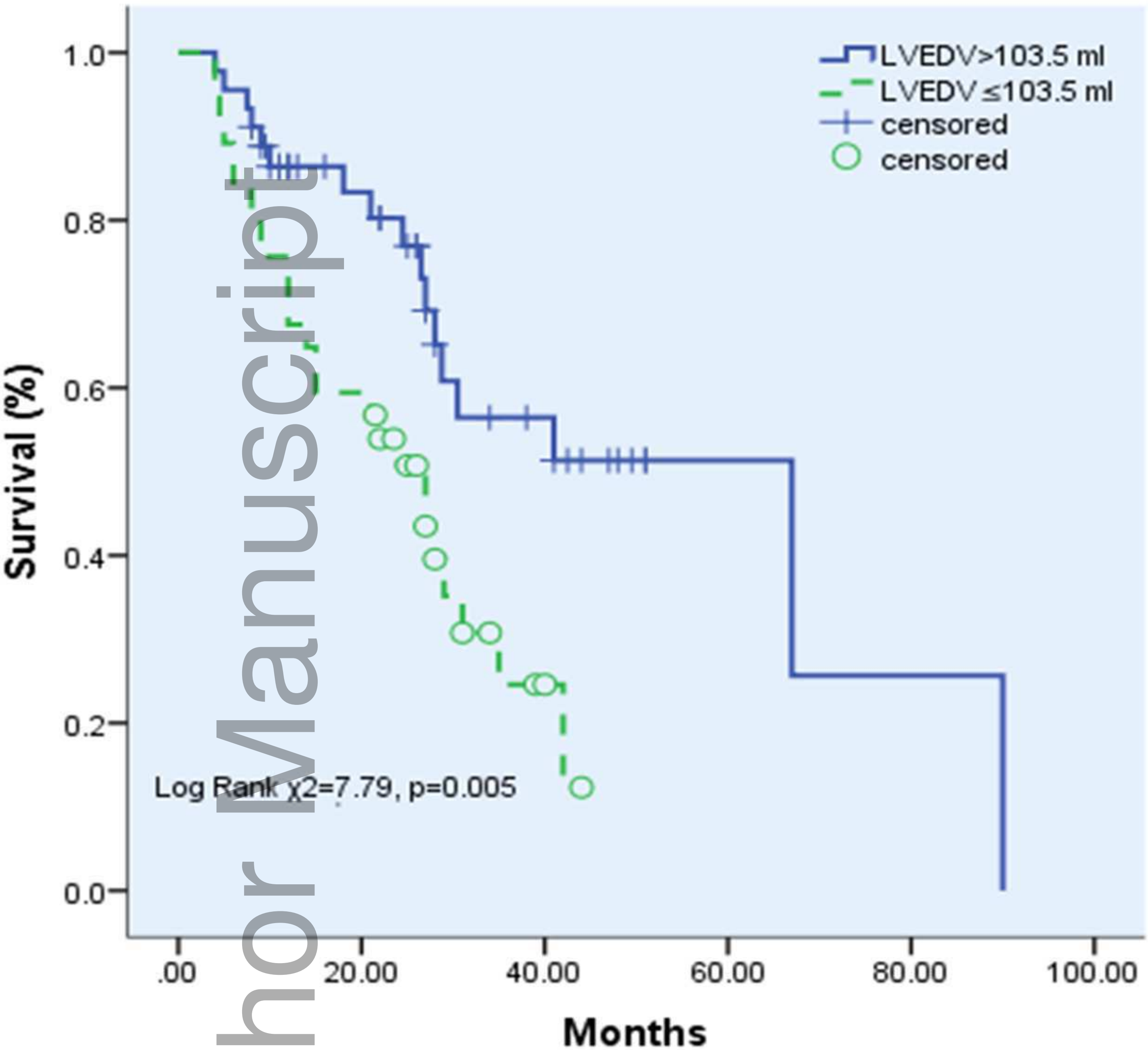
Variable (per 1 unit increased) or (yes vs. no)	HR(a)	95%CI	*P*	HR(b)	95%CI	*P*
Male	0.48	0.19-1.21	0.12	0.61	0.26-1.42	0.25
Age (year)	1.04	0.94-1.16	0.48	1.06	0.95-1.17	0.29
Diabetes mellitus	0.99	0.44-2.21	0.98	1.2	0.55-2.63	0.65
DBP (mmHg)	0.98	0.93-1.03	0.37	0.98	0.94-1.03	0.48

LVID (mm)	1.05	0.89-1.23	0.57	1.07	0.92-1.26	0.39
MPAID (per 1 mm increased or ≤21.5 mm)	0.68	0.55-0.83	< 0.001	4.3	1.89-9.8	0.001
LVEDV (ml)	0.99	0.97-1.02	0.55	0.98	0.96-1.01	0.14
Previous No. of PVA	3.52	0.48-25.82	0.22	5.61	0.64-49.26	0.12
Previous functional length of AVFs (month)	0.91	0.80-1.02	0.12	0.89	0.78-1.01	0.07
Previous functional length of tcCVCs (month)	0.81	0.62-1.07	0.14	0.82	0.63-1.09	0.17
Previous duration of FV-ntCVC (month)	1.27	0.96-1.66	0.09	1.19	0.91-1.56	0.2
Previous duration of IVJ-ntCVC (month)	1.02	0.78-1.34	0.89	0.96	0.72-1.27	0.75
Right RCAVF	3.23	1.09-9.55	0.034	2.95	1.02-8.54	0.047

Abbreviation: RCAVF: radiocephalic arteriovenous fistula; HR: Hazard rate; CI: confidence interval; DBP: diastolic blood pressure; LVID: left ventricle internal diameter; MPAID: main pulmonary artery internal diameter; LVEDV: left ventricle end-diastolic volume; PVA: permanent vascular access; tcCVC: tunnelled cuffed central venous catheter; FV: femoral vein; ntCVC: non-tunnelled central venous catheter; IJV: internal jugular vein.

model a (MPA as continuous variable): Overall (score) χ^2=35.16, p=0.001.

model b (added MPA ≤21.5mm): Overall (score) χ^2=37.13, p < 0.001.



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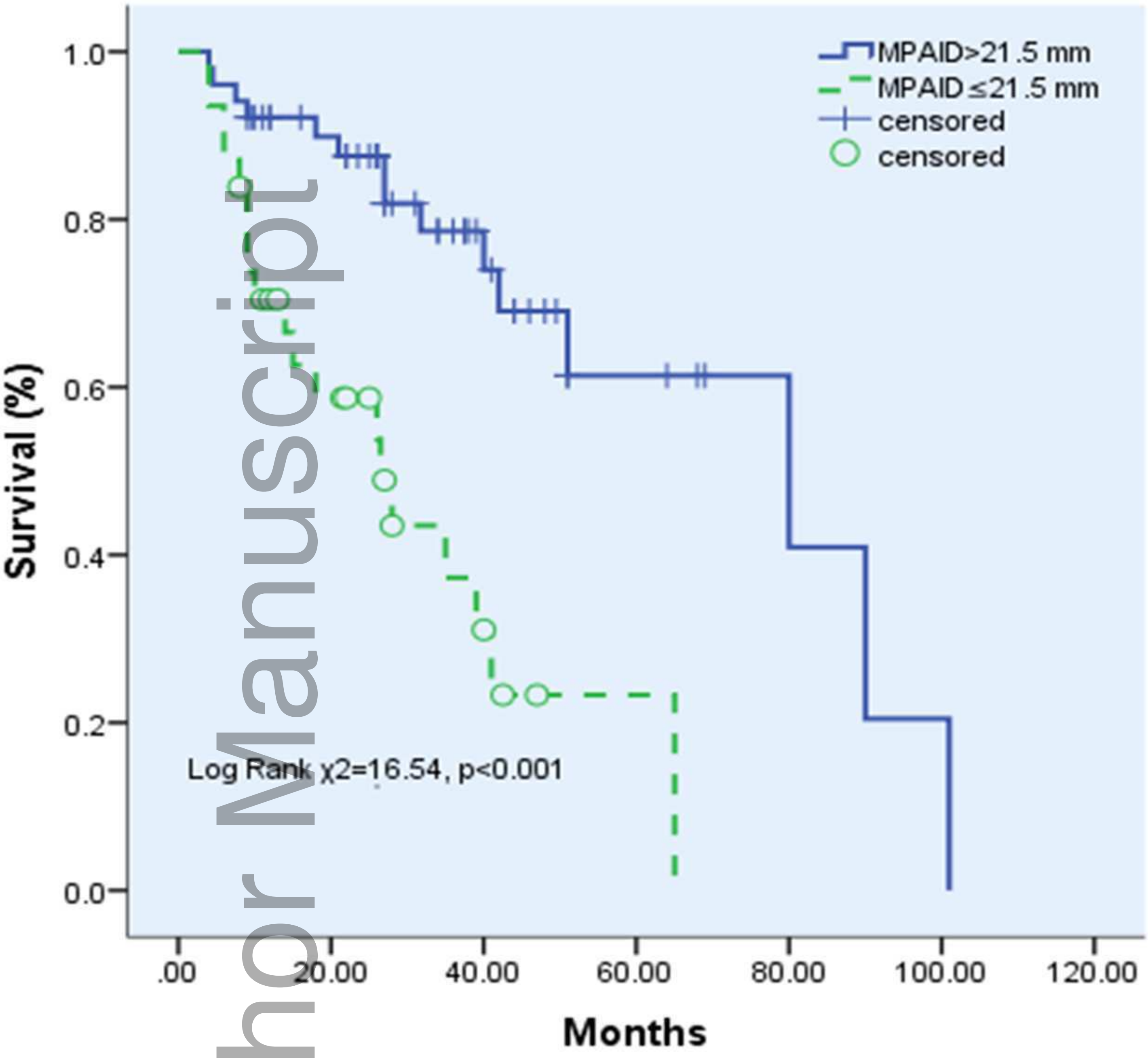

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