Survival of Primary Arteriovenous Fistula in 463 Patients on Chronic Hemodialysis

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Aim. To assess the survival of the primary arteriovenous fistula created for dialysis in 463 chronic hemodialysis patients, because the main causes of morbidity among such patients are associated with vascular access-related complications.

Methods. We analyzed 269 (58%) men and 194 (42%) women with median age of 58 years (range 12-83), who underwent 0-14,784 (median 1,584) hours of hemodialysis. Data analyzed were age, gender, body weight loss during hemodialysis session, smoking habits, cause of renal failure, diabetes, myocardial infarction, stroke, malignant neoplasm, arterial hypertension or hypotension, drugs (salicylates, dipyridamole, coumarin anticoagulants, heparin, oral antidiabetics, insulin), number of hemodialysis sessions and hours of hemodialysis per week, fistula location, platelet count, hematocrit, institution in which the fistula had been created, and dialysis center where the fistula had been used. Kaplan-Meier and univariate analysis (Mantel-Cox and generalized Wilcoxon test) with 0.05 statistical significance were used for data analysis, and the outcome of the fistula survival was determined with logistic regression.

Results. Out of 597 patients with primary arteriovenous fistula, 134 patients were lost to follow-up. In the remaining 463 patients the fistula survival was 73%, 63%, 44%, 10%, 3%, and <1% after 1, 2, 3, 4, 5, 10, 15, and 20 years, respectively. Factors affecting the survival of arteriovenous fistula were administration of heparin (p=0.004) and dipyridamole (p=0.001), hemodialysis-dependent hypotension (p=0.005), diabetes (p=0.009), presence of malignant neoplasm (p=0.003), institution in which the fistula had been created (p<0.001) or used (p=0.037), hours of hemodialysis per week (p=0.023), and number of hemodialysis sessions per week (p=0.007).

Conclusion. Primary arteriovenous fistula survival was shorter in end-stage renal disease patients with diabetes, hypotension, who underwent less than 3 hemodialysis sessions (<12 h) per week without heparin administration. Insufficient surgical experience, dipyridamole administration, and concomitant neoplasm contributed to arteriovenous fistula failure.

Key words: arteriovenous fistula, surgical; kidney failure; renal dialysis; risk factors

A large proportion of patients (around 60%) with the end-stage renal disease are not suitable candidates for kidney transplantation therapy. However, a vast majority of potential transplant recipients need dialysis before transplantation and for most of them the program of chronic dialysis remains the method of choice. The achievement of a relatively comfortable, productive, and socially acceptable way of life in these patients depends on the creation and regular function of a simple and reliable vascular access. Hemodialysis patients are hospitalized for 13.8 days per year on average (1), and vascular access-related complications are the main cause of their morbidity (2), resulting in 15% of the total number of hospitalizations (3). Any vascular access is of limited duration, and each patient has a limited number of sites for the creation of vascular access.

The concept of modern hemodialysis began in 1966 with the creation of direct arteriovenous dialysis fistula (4), which still represents the best form of vascular access for chronic hemodialysis. Many factors influence the survival of arteriovenous fistula in patients on chronic hemodialysis (5-10). In this study, we recorded early and late survival of primary arteriovenous fistula in 597 patients. We presumed that the identification of possible factors influencing the survival of the fistula might help to postpone its failure.

Patients and Methods

Patients and Setting

The study was carried out at five hemodialysis centers in Zagreb (Zagreb University Hospital Center, Dubrava University Hospital, Sisters of Mercy University Hospital, Holy Ghost General Hospital, and Sesvete Hemodialysis Center). The study included a total of 597 patients with end-stage renal disease whose primary arteriovenous fistula was used for hemodialysis. Informed consent was obtained from each patient.

The patients were prospectively followed-up for five years (January 1992 – December 1996), and retrospectively to the day of the fistula creation. Patients who underwent kidney transplantation or died during the follow-up period were followed up until the day of transplantation or day of death.

Risk Factors

The causes of end-stage renal disease in our patients were: glomerulonephritis, polycystic kidney disease, arterial hypertension, diabetes mellitus, chronic pyelonephritis, other (obstructive) uropathy, systemic lupus erythematosus, Alport's syndrome, Wegener's
The survival of arteriovenous fistula denoted time span (years) between the creation of the primary fistula and its first failure or until the end of the study period. Any revision or reanastomosis was considered a second arteriovenous fistula. Failure of the arteriovenous fistula function within a month from its creation was considered an early arteriovenous fistula failure (11,12) and after that period a late arteriovenous fistula failure. The term “low forearm fistula” denotes an anastomosis between the radial artery and cephalic vein, whereas “high forearm fistula” denotes an anastomosis between the radial artery and antebrachial anterio r vein in the segment next to the cubital artery bifurcation.

Impact of several prognostic factors on arteriovenous fistula survival was estimated. Values for all variables were recorded regularly during the follow-up period. Survival rates were calculated using the Kaplan-Meier procedure. The Mantel-Cox test and generalized Wilcoxon test were used to compute the differences in survival time between groups. The probability of fistula survival was determined by standard tables of survival (13-15). Logistic regression was used to determine the outcome of the fistula survival. Statistically significant probability level was set at 0.05.

Results

The median number of patients per hemodialysis center was 80 (range 58-161). Upon completion of the prospective five-year period, 134 (22%) patients were lost to follow-up, because they moved to other hemodialysis centers in Croatia or abroad due to the war in Croatia. The final analysis included 463 patients: 269 (58%) men and 194 (42%) women, with a median age of 58 (range 12-83) years.

Of these patients, 124 (27%) died and 21 (5%) underwent kidney transplantation. Arteriovenous fistula survival ranged from 0 to 253 (median 38) months at a rate of 73%, 63%, 52%, 44%, 36%, 10%, 3%, and < 1% after 1, 2, 3, 4, 5, 10, 15, and 20 years, respectively (Fig. 1). Early fistula failure was found in 63 (14%) out of 463 patients.

The survival of arteriovenous fistula was not affected by age (p=0.152), gender (p=0.178), cause of end-stage renal disease (p=0.237), cerebrovascular insult (p=0.758), myocardial infarction (p=0.304), smoking habit (p=0.682), body weight loss during hemodialysis session (p=0.762), administration of salicylates (p=0.24), coumarins (p=0.543), platelet count (p=0.306), or hematocrit level (p=0.847, Mantel-Cox test).

The rates of specific causes of end-stage renal disease are presented in Table 1. Period when statistical significance of factors relevant for arteriovenous fistula survival occurred is showed in Table 2.

Table 1. Specific causes of chronic renal failure in 463 dialyzed patients

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. (%) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glomerulonephritis</td>
<td>130 (28)</td>
</tr>
<tr>
<td>Polycystic renal disease</td>
<td>49 (11)</td>
</tr>
<tr>
<td>Nephroangiosclerosis</td>
<td>24 (5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>14 (3)</td>
</tr>
<tr>
<td>Chronic pyelonephritis</td>
<td>62 (13)</td>
</tr>
<tr>
<td>Other</td>
<td>38 (8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>146 (32)</td>
</tr>
<tr>
<td>Total</td>
<td>463 (100)</td>
</tr>
</tbody>
</table>

Diabetes mellitus was found in 28 (6%) patients: in 14 patients as a cause of end-stage renal disease and in 14 as a concomitant disease. It had no effect on the fistula survival (p=0.127, generalized Wilcoxon test). After exclusion of 10 patients with early fistula failure from the analysis, arteriovenous fistula survival was significantly reduced in diabetic patients (p=0.009, generalized Wilcoxon test). Insulin dependence (11 patients) had no effect on arteriovenous fistula survival (p=0.614, Mantel-Cox test). However, the fistula survival was considerably reduced in 5 patients on oral anti diabetic therapy (p=0.004, Mantel-Cox test).

In 393 patients, arteriovenous fistula was created at one of the five study hospitals in Zagreb, in 68 patients at another institution in Croatia or abroad, and for two patients the exact information was not available. Significant difference in arteriovenous shunt survival was observed with respect to the institution where the fistula had been created (p<0.001, Mantel-Cox test, Fig. 2). This difference disappeared upon exclusion of the patients with early shunt failure from the analysis (p=0.192, Mantel-Cox test).

The survival of the “high forearm fistulas” (23 patients) was better than that of the “low forearm fistulas” (p=0.047, Mantel-Cox test).
The mean systolic and diastolic pressure measured before the start of hemodialysis was 155±22.47 mm Hg and 87 ±11.24 mm Hg, respectively. There was no effect of either systolic (p=0.235) or diastolic (p=0.09) blood pressure before dialysis on arteriovenous fistula survival (Mantel-Cox test). A difference in survival for both systolic (p=0.034) and diastolic (p=0.037) pressure appeared upon exclusion of patients with early fistula failure from the analysis (generalized Wilcoxon test). The lowest mean systolic and diastolic pressure measured during hemodialysis procedure was 137±22.15 mm Hg and 80±9.97 mm Hg, respectively. The lowest systolic pressure had no effect on fistula survival (p=0.624), unlike the lowest diastolic pressure (Fig. 3), which had a significantly negative influence (p=0.045, Mantel-Cox test).

During the same 10 consecutive hemodialysis sessions at least one episode of arterial hypotension was observed in 401 (86%) patients but with no effect on fistula survival (p=0.155, Mantel-Cox test).

The institution at which hemodialysis was carried out showed no influence on failure of arteriovenous fistula (p=0.062) until we excluded patients with early fistula failure from the analysis (p=0.037, Mantel-Cox test).

At least one episode of arterial hypotension during 10 consecutive hemodialysis sessions was recorded in 218 (47%) patients. The negative effect of these sporadic episodes of hypotension on arteriovenous fistula survival was found only after exclusion of patients with early fistula failure from the analysis (p=0.002, generalized Wilcoxon test). However, during the same 10 consecutive hemodialysis sessions at least one episode of arterial hypertension was observed in 401 (86%) patients but with no effect on fistula survival (p=0.155, Mantel-Cox test).

A significantly longer arteriovenous fistula survival was found in 329 (71%) patients who were undergoing hemodialysis ≥12 h per week than in 134 (29%) patients who were undergoing hemodialysis <12 h per week (p=0.022, Mantel-Cox test, Fig. 4). However, arteriovenous shunt survival was worse in patients who were undergoing less than 3 hemodialysis sessions per week (p=0.007, Mantel-Cox test, Fig. 5).

The total dose of heparin used per hemodialysis session was ≥5000 IU in 13 (3%) and <5000 IU in 439 (95%) patients, whereas in 12 (2%) patients no heparin was used. Upon exclusion of patients with early fistula failure from the analysis, significantly lon-
Arteriovenous fistula survival was recorded in heparinized patients (p=0.004, generalized Wilcoxon test).

Arteriovenous fistula survival was significantly reduced in patients taking dipyridamole (5 patients) vs those who did not (p=0.007, Mantel-Cox test).

Malignant neoplasm was detected in 7 patients (skin tumor in three, larynx tumor in two, and kidney and breast tumor each in a patient). In these patients the survival of arteriovenous fistulas was worse than in other patients (p=0.003, generalized Wilcoxon test). However, the significance of difference disappeared upon exclusion of patients with early fistula failure from the analysis (p=0.562, generalized Wilcoxon test).

Logistic regression analysis showed that only the number of hemodialysis hours per week had a significant influence on the survival of arteriovenous fistula, when the results of the total number of 463 patients (p=0.045) were compared with the results of 400 patients without early fistula failure (p=0.028).

Figure 4. Survival of arteriovenous fistula in patients on chronic hemodialysis per week. Closed circles – <12 h of dialysis per week (134 patients), open circles – ≥12 h of dialysis per week (329 patients); p=0.022 (Mantel-Cox test).

Figure 5. Survival of arteriovenous fistula in patients on chronic hemodialysis sessions per week. Closed circles – <3 hemodialysis sessions per week (21 patients), open circles – ≥3 hemodialysis sessions per week (375 patients); p=0.007 (Mantel-Cox test).

Discussion

Primary arteriovenous fistula survival in our patients ranged from 0 to 253 (median 38) months, which was almost identical to the results reported by Burger et al (12) and Zibari et al (8), better than that found by Sands and Miranda (16), and poorer than that described by Chazan et al (17). These authors investigated a smaller number of patients in a single dialysis center. Early fistula failure occurred in 63 (14%), whereas arteriovenous fistula survival of less than a year was recorded in 130 (28%) patients. This is consistent with other research findings reporting 5-28% of early fistula failure (12,18-20) and by far better than 58% of one-year fistula failure reported by Elfstrom (21). If the patients with early fistula failure had been excluded from the analysis, the five-year survival would have been significantly longer, 49% instead of 36%.

As reported by Eggers (22), an ever-increasing proportion of patients aged >60 were also recorded in our study. Our results did not show that arteriovenous fistula survival depended on either age or gender, which is consistent with some (11) and opposite to other reports (6,9,23).

Opposite to the results of a USA study (24), where type II diabetes mellitus and arterial hypertension were the most frequent causes of end-stage renal disease, we observed high predominance of glomerulonephritis in our patients. Although preponderance of elderly type II diabetes mellitus in Croatia may be the main reason, there is no simple explanation for very low percentage of diabetics in our study. However, the cause of end-stage renal disease remained unknown in as many as 146 (32%) patients due to inadequate number of renal biopsies.

Published work points to an increased mortality of uremic patients from acute myocardial infarction (25,26) or cerebrovascular accident (27), but we were not able to find them significant for survival of arteriovenous fistula in our patients. However, in our patients with malignant neoplasm blood coagulation impairment (28,29) may have been the main cause of shorter survival of arteriovenous fistula.

In our study, the mean systolic and diastolic pressure measured before the start of hemodialysis had no effect on arteriovenous fistula survival. The lowest mean systolic pressure, measured in our patients during hemodialysis session had no effect on the fistula survival but the lowest mean diastolic pressure had negative effect. The effect of diastolic pressure should be of major importance compared with systolic pressure merely due to its lower levels (sometimes lower than 30 mm Hg). These crises of hypotension (systolic and diastolic) affected the arteriovenous fistula survival after exclusion of patients with early fistula failure from the study.

Similar to some reports (9,11), heparinization during hemodialysis session significantly prolonged arteriovenous fistula survival in our patients. The significant role of heparin in arteriovenous fistula sur-
vival increased even more upon exclusion of patients with early fistula failure from analysis. This finding is consistent with the opinion that the inappropriate surgical procedure for fistula creation is primarily responsible for early fistula failure (30).

In spite of the well-known effect of acetylsalicylic acid and coumarin anticoagulants on blood coagulation (31,32), we did not find that their regular administration had any statistically significant impact on arteriovenous fistula survival. At the same time, our analysis indicated reduced arteriovenous fistula survival in patients receiving dipyridamole. We believe that this finding calls for further investigation because of the small number of patients who were receiving the drug.

It is believed that blood viscosity influences the arteriovenous fistula survival rate. Human recombinant erythropoetin increases blood viscosity (33,34). A number of thrombosed arteriovenous fistulas found in patients treated by human erythropoetin (35) and abnormalities of blood rheology after successful renal transplantation (36) confirm that theory. In our patients, hematocrit as a parameter of blood viscosity did not affect arteriovenous fistula survival, which is consistent with Shand's report (34).

Comparable to findings by Erdem et al (37), platelet count did not have any major effect on arteriovenous fistula survival in our patients.

Our results showed that arteriovenous fistula survival was directly dependent on either the number of hours or the number of hemodialysis sessions per week. An unexpected finding was that neither increased number of vascular cannulations (regular, repeated intimal lesions with all pathophysiological implications) nor local compressions of the fistula (hemostatic bandage placed at the cannulation site) had negative effect on fistula survival. A similar effect (reduced risk of the arteriovenous fistula failure) was found in patients with more hours of hemodialysis per week, which may be explained hypothetically by a favorable effect of enhanced flow during hemodialysis in terms of dilation of the fistula and prolonged patient’s heparinization (shown as statistically significant for fistula survival). Our results partially differ from those reported by Culp et al (11), who could not confirm the fistula survival to depend on the duration of hemodialysis session. This difference could be accounted for by the fact that their group of patients was smaller than our group (267 vs 463) and followed-up for only one year.

In our study, proximal forearm fistula survived significantly longer than distal one, which is consistent with some studies (11,38) and opposite to others (39). We presume that a wider vessel lumen, higher flow rate, and easier surgical approach to fistula creation were the most important advantages of the proximal over the distal forearm arteriovenous fistula.

The so-called center effect was clearly indicated by the analysis of fistulas survival according to the institutions where they were created. Arteriovenous fistulas created at the hospital had significantly longer lifespan, presumably because of the advanced surgical skills of the staff due to their experience with a large number of operations (138 of 463 fistula creations). However, the center effect disappeared after the exclusion of the patients with early fistula failure from analysis, which probably means that during the first month after fistula creation, prolonged heparinization and enhanced blood flow during the hemodialysis sessions counterpoised the factors favoring early fistula failure, such as inappropriate surgical technique, perioperative care, tissue handling, premature use of the fistula for hemodialysis, hypotensive episodes, blood hypercoagulability, and increased viscosity.

Finally, our data analysis showed some risk factors (malignant neoplasm, oral antidiabetics, dipyridamole, fistula location, heparin, and diabetes) to have significant influence on arteriovenous fistula survival. Other risk factors (hypertension, myocardial infarction, cerebrovascular accident, acetylsalicylic acid, coumarins, platelet count, hematocrit) were not found significant for arteriovenous fistula survival. Although previous reports by Peto et al (14,15) might allow us to compare very small subgroups of patients with a large control group and draw some relevant conclusions, we hesitated to accept those results. In our opinion, those results would be more reliable if the patient population had been larger because that way it would probably result in larger subgroups of followed-up patients.

In conclusion, the comparison of end results obtained by analysis of parameters observed in the total of 463 patients with those recorded in patients free from early arteriovenous fistula failure (400 patients) showed that the number of hemodialysis sessions and total hours of hemodialysis per week were the factors with significant positive effect, whereas the lowest diastolic pressure during hemodialysis procedure and oral antidiabetic agents (ie, type II diabetes mellitus) were the factors with significantly negative effect on arteriovenous fistula survival in both groups of patients. In addition, our experience underscores the significant role of surgical skills and technique of fistula creation in early failure of arteriovenous fistula.

References
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