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REVIEW

Radiocephalic Wrist Arteriovenous Fistula for Hemodialysis: Meta-analysis Indicates a High Primary Failure Rate

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Objective. *To improve the precision of the estimates of primary failure rates and primary and secondary 1 year patency of radial-cephalic arteriovenous fistulas (RCAVF) for hemodialysis.*
Design. *Meta-analysis.*
Materials and methods. *A Medline search was performed of the English language medical literature between January 1970 and October 2002. Key words that were searched included* radiocephalic fistula, arteriovenous shunt, Brescia-Cimino fistula *and* patency. *Primary failure, primary and secondary patency rates were analysed using the standard mixed effects model, which allows for variability between the different studies.*
Results. *Eight prospective and 30 retrospective studies were included. The analysis showed a pooled estimated primary failure rate of 15.3% (95% CI: 12.7–18.3%). In addition, the pooled estimated primary and secondary patency rates of 62.5% (95% CI: 54.0–70.3%) and 66.0% (95% CI: 58.2–73.0%), respectively, were calculated. Subgroup analysis concerning various study characteristics, including study year, gender and age, did not reveal statistically significant differences.*
Conclusion. *Although, the autogenous RCAVF is considered to be the primary choice for vascular access, this meta-analysis indicates a high primary failure rate and only moderate patency rates at 1 year of follow-up.*

Keywords: Radiocephalic wrist arteriovenous fistula; Meta-analysis; Patency; Primary failure; Vascular access; Hemodialysis.

Introduction

Use of the radiocephalic arteriovenous fistula (RCAVF) as an autologous vascular access for hemodialysis dates back to the mid 1960s.[1] Once established, it has the advantage of good long-term survival, and a low complication rate. Therefore, the RCAVF is considered the optimal first choice for an autologous hemodialysis fistula. However, the RCAVF suffers from a high incidence of primary failure, due to early thrombosis or failure to mature. Estimates of primary failure, primary patency and secondary patency vary considerably. An important source of that variability is the lack of precision in individual studies.

In the present study, we aggregated primary failure rates and primary and secondary patency data at 1 year of follow-up from various publications considering RCAVFs for hemodialysis, with the primary objective of improving the precision of the estimates of these parameters. The information derived will be incorporated in a future decision model, we are developing, to compare effects of various treatment strategies for patients who need a vascular access for hemodialysis. In addition to improving the precision, a meta-analysis offers the opportunity to explore questions that could not be answered by the original studies by determining the effect of particular study characteristics on the overall results. In the present

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analysis, we examined the effect of various study characteristics, including study year, gender and age, on outcome.

Methods

Data sources and data extraction

A Medline search was performed of the English language medical literature between January 1970 and October 2002. Key words that were searched included *radiocephalic fistula, arteriovenous shunt, Brescia-Cimino fistula* and *patency*. This electronic database search was supplemented by manual search of bibliographic reference lists in review articles and original articles.

Studies that reported patency or primary failure data of RCAVFs were included if: (1) the patient and study characteristics were reported in sufficient detail to allow for adjustment for the case mix and the reporting methods in the analysis and (2) if the RCAVF was created at the wrist. In instances in which more than one publication from the same institution was available, we included only the most recent publication from that institution, unless evidence was available that the patient population did not overlap. Because there are only a few prospective studies,[2–9] we also included retrospective studies in this meta-analysis.[10–39] Studies with insufficient information on the location of the constructed autogenous arteriovenous fistula were excluded. Also publications were excluded if the arteriovenous fistula was created in the anatomical snuff box, upper arm or in the antecubital fossa. In many of the studies that were included, the results of the RCAVFs were reported together with those of other types of autogenous arteriovenous fistulas. Only when it was possible to separate the results of the RCAVFs from those of the other types these studies were included.

The methodological quality of included trials was assessed independently by two reviewers, which resolved any discrepancies by discussion and consensus.

Nine prospective studies and 37 retrospective studies were identified as possible candidates for this meta-analysis. One prospective study and seven retrospective studies were excluded, so that eight prospective and 30 retrospective studies were included in this meta-analysis.

A standard form was used to extract the data from the articles, including characteristics of study design, reporting methods, study population, patency data.

We repeated the analysis for subgroups defined by characteristics that might be of additional influence on the primary failure and patency rates. For example, we examined whether patency rates reported in studies, which were performed before 1981, differ from studies reported from 1981 up to 1991 or differ from studies started after 1991. Other characteristics that were examined in subgroup analyses include the average age of the study population ($\leq$50 years versus $>$50 years) and the percentage of women in the study ($\leq$40 versus $>$40%). Both cut-off points are median values of all studies combined.

Outcome measures

The primary outcome measures were primary failure, primary patency and secondary patency at 1 year of follow-up. For the purpose of this analysis, primary patency was defined as the interval from the time of RCAVF creation until any intervention designed to maintain or re-establish patency, fistula thrombosis, or the time of measurement of patency. Secondary patency was defined as the interval from the time of RCAVF creation until access abandonment, thrombosis, or the time of patency measurement including intervening manipulations (surgical or endovascular interventions) designed to re-establish functionality in thrombosed access.[40] Primary failure was defined as fistula thrombosis, or failure to mature resulting in inadequate functioning for hemodialysis at 6 weeks.

Data analysis

Primary failure, primary and secondary patency rates were analysed using the standard mixed effects model, which allows for true variability between the studies.[41] The estimated percentages and standard errors were transformed to the logit scale, then the analysis was carried out using SAS Proc Mixed,[42] before retransformation of data. The method allowed the specification of covariates (meta-regression) in order to search for the effect of possible explanatory variables. To assess publication bias, funnel plots were derived, accompanied by the linear regression test on symmetry.[43] Throughout this report, two sided p-values are reported, except for between study variances. A p-value of <0.05 was considered to be statistically significant.

Results

Nine prospective studies and 37 retrospective studies were identified as possible candidates for this meta-

analysis. Following application of inclusion criteria, eight prospective and 30 retrospective studies remained. Patient characteristics of the included prospective studies, ordered by calendar year, in which the study started and finished, are given in Table 1.

During the search for candidate studies for this meta-analysis, we noticed that most studies, which report on patency rates of RCAVFs, were retrospective. Therefore, these studies were included in the analysis separately, and in a subgroup analysis, we carefully examined whether their results differed from the prospective group. Patient characteristics of the retrospective studies, ordered by calendar year, in which the study started and finished, are given in Table 2.

Primary failure rates and the primary and secondary patency rates at 1 year as reported in the prospective studies are presented in Table 3. In all prospective studies, a primary failure rate was reported. Only one study reported a secondary patency rate at 1 year, and another study also reported a primary patency rate at 1 year. Two studies reported both primary and secondary patency rates. Primary failure rates differ significantly among these studies, from Wetzig *et al*. reported a low primary failure rate of 9.4%[3] to Dixon *et al*. reported a very high primary failure rate of 31.5%.[5]

Primary failure rates and the primary and secondary patency rates at 1 year from the various retrospective studies are reported in Table 4. In all but six retrospective studies, primary failure rate was reported. Four studies reported also primary patency at 1 year and 11 studies reported also secondary patency at 1 year. Only in two studies, both primary and secondary patency at 1 year was reported.

In all eight prospective studies, and in 30 retrospective studies a primary failure rate was reported. The estimated mean primary failure rate, based on the data from the prospective studies, does not differ statistically from that based on the retrospective studies (16.9 versus 14.7%; $p=0.51$). Therefore, we pooled the data of the 38 studies, and the overall mean primary failure rate was estimated as 15.3% (95% CI: 12.7–18.3%). There was very significant ($p<0.0001$) heterogeneity between the studies, the range covering 95% of the study specific primary failure rate was estimated as 6–34%.

The estimated primary patency rate at 1 year, based on the retrospective studies, did not differ significantly from that based on the data from the retrospective studies (64.6 versus 61.5%; $p=0.73$). The pooled primary patency rate at 1 year based on the retrospective studies together with the prospective studies was 62.5% (95% CI: 54.0–70.3%). Again the between study heterogeneity was very significant ($p<0.0001$), resulting in an estimated 95% range for the study specific primary failure of 39–82%. Further, no statistically significant difference was found between the estimated secondary patency at 1 year based on the prospective studies and that based on the retrospective studies (68.5 versus 65.5%; $p=0.75$). The pooled estimated secondary patency at 1 year was 66.0% (95% CI: 58.2–73.0%). The between study heterogeneity was very significant ($p<0.0001$), resulting in an estimated 95% range for the study specific primary failure of 36–87%.

Several subgroup analyses were performed. The pooled results from the studies that included 40% or fewer women were very similar to those from studies with more than 40% women. The estimated primary failure rate was 16.3 versus 15.9% ($p=0.09$). Also the estimated primary patency rate at 1 year (53.1 versus 69.1%; $p=0.07$) and the estimated secondary patency rate at 1 year (60.9 versus 64.8%; $p=0.66$) did not differ significantly between these two groups. The median age of patients in all studies was 50 years. Therefore, we investigated in a subgroup analysis if there was a difference in primary failure rate and in patency rates between the studies with a mean age of ≤ 50 years and the studies with a mean age of >50 years. The estimated primary failure rate among studies with a mean age above 50 years was higher than for studies

Table 1. Prospective studies regarding the outcome of RCAVFs for hemodialysis

Author	Study years	Number of patients	Number of RCAVFs	Male %	Mean age (years)	Age range (years)
Reilly *et al*.[2]	1976–1981	145	145	–	–	–
Wetzig *et al*.[3]	1979–1983	85	100	48	50.5	16–69
Wedgwood *et al*.[4]	1981–1983	71	71	68	–	–
Dixon *et al*.[5]	1992–1998	73	73	82	51.6	–
Golledge *et al*.[6]	1993–1996	107	107	68	63	–
Malovrh[7]	1993–1997	116	116	47	51.4	15–81
Lin *et al*.[8]	1994–1995	176	176	45	57.8	20–86
Wong *et al*.[9]	1996	60	60	62	58.4	17–77

Table 2. Retrospective studies regarding the outcome of RCAVFs for hemodialysis

Author	Study years	Number of patients	Number of RCAVFs	Male %	Mean age (years)	Age range (years)
Cohen *et al.*[10]	1966–1967	19	22	59	–	18–58
Röhl *et al.*[11]	1966–1967	30	30	–	–	–
Kinnaert *et al.*[12]	1966–1975	202	202	62	–	16–69*
Tellis *et al.*[13]	1968–1971	59	59	59	–	14–55
Zerbino *et al.*[14]	1968–1974	160	160	99*	–	19–77*
Thompson *et al.*[15]	1970–1972	77	77	–	–	–
Cheek *et al.*[16]	1970–1973	84	84	–	–	–
Lindfors *et al.*[17]	1970–1973	45	45	67	42	18–67
Paruk *et al.*[18]	1971–1974	108	108	–	–	–
Tordoir *et al.*[19]	1971–1981	114	129	47	48.5	16–75
Burger *et al.*[20]	1971–1991	208	208	56*	46*	7–80*
Thomsen *et al.*[21]	1972–1978	191	191	56	49.1	7–74
Alm *et al.*[22]	1972–1974	67	67	48	48	12–67
Rohr *et al.*[23]	1973–1976	126	126	–	49*	14–82
Fernström *et al.*[24]	1975–1985	71	83	73	50	22–73
Kherlakian *et al.*[25]	1977–1983	106	106	61	50	17–80
Simoni *et al.*[26]	1979–1989	248	248	54	53	19–83
Enzler *et al.*[27]	1980–1992	412	412	55*	43.9*	7–81*
Cassioumis *et al.*[28]	1981–1992	173	173	–	55*	13–85*
Al-Mohoya *et al.*[29]	1983–1988	112	112	60	–	13–75
Sparks *et al.*[30]	1983–1993	147	147	58*	53.8*	18–79*
Nazzal *et al.*[31]	1988–1989	85	85	61*	37*	7–70*
Leapman *et al.*[32]	1989–1994	144	150	73	50.1	19.2–87.5
Prischl *et al.*[33]	1989–1994	123	123	63*	54.2*	17–85*
Miller *et al.*[34]	1990–1994	41	41	45*	64.4*	33–90*
Bender *et al.*[35]	1993	56	56	56*	62*	7–83*
Lin *et al.*[36]	1994–1995	126	126	44	–	20–83
Zeebregts *et al.*[37]	1995–1999	150	153	63	56	17–80
Ascher *et al.*[38]	1996–1999	47	47	54*	69*	28–95*
Hingorani *et al.*[39]	1997–2001	206	206	–	68*	29–94*

* Based on all patients reported in the study, including patients with other procedures.

with a mean age of 50 or less, but this difference was not significant (15.5 versus 19.7%; $p=0.25$). Also the estimated primary patency rate at 1 year (59.4 versus 64.9%; $p=0.50$) and the estimated secondary patency rate at 1 year (66.4 versus 65.8%; $p=0.94$) were not different according to the age grouping. Finally a subgroup analysis was performed concerning publication period. We divided the studies in three different groups; studies performed before 1981, between 1981 and 1991, and performed after 1991. There were higher estimated primary failure rate for studies performed after 1991, however, this difference was not significant (13.5 versus 13.0 versus 18.0%; $p=0.14$). The estimated primary patency rate at 1 year (60.0% versus 62.7 versus 62.9%; $p=0.85$) and the estimated secondary patency rate at 1 year (55.7 versus 66.8 versus 67.7%; $p=0.62$) did not differ significantly between these two groups.

No indication for publication bias in the primary and secondary patency rates was observed. However, there was a clear indication of publication bias for the primary failure rates ($p=0.001$) (Fig. 1). Points in the

Table 3. Primary failure rates and primary and secondary patency rates at 1 year as reported in the prospective studies

Author	Primary failure rate (%)	Primary patency rate at 1 year (%)	Secondary patency rate at 1 year (%)
Reilly *et al.*[2]	11	–	80
Wetzig *et al.*[3]	9.4	78	–
Wedgwood *et al.*[4]	9.9	–	–
Dixon *et al.*[5]	31.5	44	52
Golledge *et al.*[6]	18	69	70
Malovrh[7]	19.8	–	–
Lin *et al.*[8]	13.6	–	–
Wong *et al.*[9]	29.6	–	–

Table 4. Primary failure rates and primary and secondary patency rates at 1 year as reported in the retrospective studies

Author	Primary failure rate (%)	Primary patency rate at 1 year (%)	Secondary patency rate at 1 year (%)
Cohen *et al.*[10]	13.6	–	–
Röhl *et al.*[11]	10	–	–
Kinnaert *et al.*[12]	8.6	–	–
Tellis *et al.*[13]	23.7	–	32.2
Zerbino *et al.*[14]	8.8	–	–
Thompson *et al.*[15]	13.0	–	–
Cheek *et al.*[16]	3.6	–	–
Lindfors *et al.*[17]	15.6	–	–
Paruk *et al.*[18]	15.7	–	75.9
Tordoir *et al.*[19]	10	–	80*
Burger *et al.*[20]	6.3	53	79
Thomsen *et al.*[21]	26	–	37
Alm *et al.*[22]	29.9	–	–
Rohr *et al.*[23]	–	60*	–
Fernström *et al.*[24]	29	45*	55*
Kherlakian *et al.*[25]	12	–	71
Simoni *et al.*[26]	–	75.5	–
Enzler *et al.*[27]	–	–	74
Cassioumis *et al.*[28]	–	–	79.1
Al-Mohaya *et al.*[29]	2.7	–	–
Sparks *et al.*[30]	12.2	–	–
Nazzal *et al.*[31]	–	–	72
Leapman *et al.*[32]	13	–	56
Prischl *et al.*[33]	22.8	–	48
Miller *et al.*[34]	12.2	–	–
Bender *et al.*[35]	9	–	76
Lin *et al.*[36]	23.8	–	–
Zeebregts *et al.*[37]	27.5	55*	–
Ascher *et al.*[38]	25	–	–
Hingorani *et al.*[39]	–	75	–

* Data taken from figure.

lower region of the plot have low precision and correspond to small studies, and the variability between studies is, therefore, larger than in the upper region where the spread is smaller. If there is no publication bias, the scatter should be symmetric around the vertical line, independent of the precision.

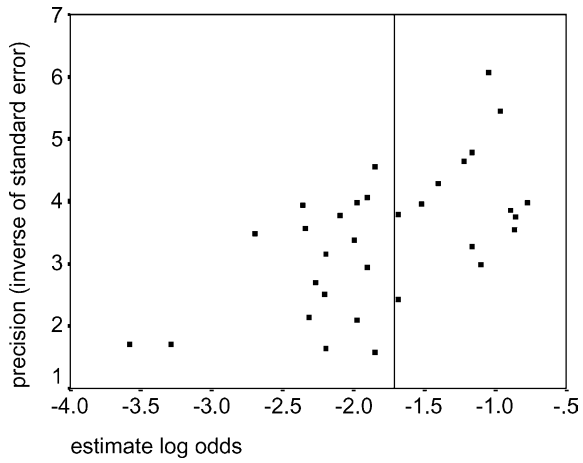

Fig. 1. Funnel plot indicating publication bias for primary failure rates. The vertical reference line denotes the estimated overall log odds.

It is obvious that symmetry is violated. There should be more small studies with large primary failure rates. Therefore, small studies with worse primary failure rates are underrepresented.

Discussion

The aim of this study was to aggregate primary patency, secondary patency and primary failure data from multiple sources, representing more than three decades of experience with the use of RCAVFs for hemodialysis across the world. The meta-analysis technique that we used allowed quantification of the variability between studies. A huge heterogeneity between studies was found in primary failure rates, primary patency and secondary patency. There are many potential causes of heterogeneity. An important (partly) explanation might be the heterogeneity between studies in the definitions of primary failure and primary/secondary patency. Only a few authors provided an explicit definition of the patency criterion they used. When criteria were specified, many different definitions were used. A very minor part of

the heterogeneity might be related to the fact that in some studies the patency data were given in the text but presented in patency curves in figures. In some instances, this allowed subjective interpretations of these data, which may have resulted in larger variability. However, the patency data were derived independently by two different investigators, and did not differ markedly.

The effect of sex on primary patency, secondary patency and primary failure rates has been examined in many studies.[6,33,44] For example, Allon *et al.* found that female sex was the only independent predictor of decreased likelihood of fistula maturation.[44] Colledge *et al.* reported results from 107 patients (73 men, 43 women) with a first RCAVF; they found that fistula failure was more common in women and primary and secondary patency were better in men.[6] In contrast, Prischl *et al*. found no significant differences in access survival between 80 men and 43 women on hemodialysis with a first RCAVF.[33] The different findings of these studies, perhaps can be explained by the small sample sizes and the fact that the populations were derived from single centres. In the present study, no significant relation was found between the gender ratio and primary patency, secondary patency or primary failure rates. With regard to age and access patency several reports have failed to find any association between age and access complications,[45–47] although others reported a significant effect of age appearing after 6 months of follow-up. In this meta-analysis, we found no relation between age and primary or, secondary patency and primary failure rates.

Finally our subgroup analysis showed a tendency towards a higher primary failure rate of fistulas constructed after 1991, however, this difference was not significant. Possible explanations were that the mean age of this subgroup was higher than in the other two groups, and the more liberal selection criteria for creation of a RCAVF, in recent years. In addition, the chronic dialysis population is more likely to have diabetes with various co-morbidities, including peripheral arterial obstructive disease and coronary artery sclerosis. Many of these patients appear to have poor vessels for construction of autogenous fistulas. Further, the Dialysis Outcome Quality Initiative (DOQI) published by the National Kidney Foundation in 1997 advocated intensive efforts to increase the use of RCAVF among these difficult dialysis patients. There are two possible explanations for the fact that there is no decrease in RCAVF patency over the years. The first explanation is that co-morbidity, like diabetes, has no significant influence on fistula patency. This explanation is supported by several studies, in which no difference in fistula maturation rates among diabetic and non-diabetic patients were found.[44,45,48] The other possible explanation is the increased recognition of adequate pre-operative vessel mapping and the value of fistula surveillance and elective intervention with percutaneous angioplasty of stenosed AVFs. However, as a result of this pre-operative vessel mapping, one could expect a decrease of primary failure rates and an increase of RCAVF patency rates.

This study showed that differences in primary failure, primary patency and secondary patency cannot be attributed to patient demographics, such as sex and age. Therefore, other factors must be taking into account, such as vessel diameter and quality. In a report of surgically created AVFs, Reilly *et al.* found that vein size was a significant predictor of subsequent fistula survival, while sex was not.[2] A more recent study also found that vessel size predicted fistula failure in the first 3 months after surgery.[9]

Conclusion

The current analysis aggregates primary failure and primary and secondary 1-year patency rates from multiple studies regarding autogenous wrist RCAVFs for hemodialysis. The analysis showed a pooled estimated primary failure rate of 15.3%. In addition the pooled estimated primary and secondary patency rates of 62.5 and 66.0%, respectively, were calculated.

Although, the autogenous RCAVF is considered to be the primary choice for vascular access, it appears to have a high primary failure rate and only moderate patency rates at 1 year of follow-up.

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