

Meta-analysis of total versus partial graft excision: Which is the better choice to manage arteriovenous dialysis graft infection?

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BACKGROUND: Arteriovenous graft infection (AVGI) is a major cause of hemodialysis access failure. Delayed diagnosis and inappropriate treatment may lead to increased morbidity (3-35%) and mortality up to 12%.

OBJECTIVES: Compare the postoperative outcomes of total graft excision (TGE) and partial graft excision (PGE) in the treatment of AVGI.

DESIGNS: Systematic review and meta-analysis

METHODS: The dataset was defined by searching PubMed, EMBASE, Google Scholar, and the Cochrane database for articles outlining the terms arteriovenous graft infection, infected dialysis graft, TGE and PGE published between 1995-2020. The data analysis evaluated the outcomes of TGE and PGE in the management of AVGI. The meta-analysis was performed using Review Manager Software version 5.4.1.

MAIN OUTCOME MEASURES: 30-day mortality, recurrent infection, and reoperation rate.

SAMPLE SIZE: Eight studies, including 555 AVGI, and 528 patients.

RESULTS: PGE showed a significant increase in recurrent graft infection rate (OR=0.23,95% CI=0.13–0.41, $P<.00001$) and re-operation rate for control of infection (OR=0.14,95% CI=0.03–0.58, $P<.007$). However, the 30-day mortality rate did not differ significantly between the groups (OR=0.92,95% CI=0.39–2.17, $P=.85$).

CONCLUSIONS: TGE remains a safe and effective surgical method for the management of AVGI. PGE is associated with a higher risk of graft infection and need for re-operation. As a result, PGE should only be considered in carefully selected patients.

LIMITATION: Risk of bias due to the differences in patient characteristics.

CONFLICT OF INTEREST: None.

According to data from the US Centers for Disease Control and Prevention, the number of people in the United States with end-stage renal disease (ESRD) increased by 93% between 1990 and 2016. However, the annual incidence among the population that received a kidney transplant remained approximately 2% throughout the period.¹ Thus, renal replacement therapy, which includes peritoneal dialysis and hemodialysis, is beneficial for increasing ESRD patient survival by 11% to 18%. The number of patients starting renal replacement therapy has increased at an exponential rate each year.²⁻⁴

Hemodialysis is the most commonly used renal replacement therapy modality in ESRD patients. As a result, a permanent vascular access for hemodialysis, such as arteriovenous fistula and arteriovenous bridge graft, is required. However, there are significant postoperative consequences after creating a dialysis access, such as bleeding, pseudoaneurysm formation, and infection. The incidence of vascular access site infection has been estimated to be between 0.5- 5% for autogenous arteriovenous fistula, but can rise to 20–35% for prosthetic arteriovenous bridge graft that is associated with repeated graft puncture and exposure at the graft site.^{5,6} Arteriovenous bridge graft infection (AVGI) usually presents with fever or local symptoms such as redness, warmth, tenderness, swelling, purulent discharge, and skin erosion. Duplex ultrasound may be used to diagnose complications by detecting perigraft fluid.⁷

The European Society for Vascular Surgery clinical practice guideline from 2018 recommended the surgical management option in AVGI as follows: total graft excision (TGE) should be considered in sepsis patients and perigraft fluid around the whole graft. Partial graft excision (PGE) may be considered in selected cases when a segment of the graft is well incorporated and appears to be uninfected. This method eliminates extensive arterial dissection and the risk of nerve injury.^{8,9}

Each surgical approach offers risks and benefits and there is no evidence to support which is the best option to control graft-related infection. We conducted a meta-analysis to compare postoperative outcomes such as 30-day mortality, recurrent graft infection, and re-operation rate between PGE and TGE in the treatment of AVGI.

METHODS

The electronic databases PubMed, Embase, Google Scholar, and the Cochrane database were accessed for literature searches. The search terms 'arteriovenous

graft infection,' 'infected prosthetic dialysis graft,' 'whole graft excision,' 'total graft excision,' and 'partial graft excision' were used to identify all relevant English-language articles published between 1995 and 2020.

The meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹⁰ The protocol of this meta-analysis was registered on PROSPERO (CRD42021252838; https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=252838)

The following were inclusion criteria: (1) English-language studies; (2) studies which used polytetrafluoroethylene (PTFE) as a hemodialysis arteriovenous bridge graft; (3) studies which compared outcomes of surgical treatment techniques between the TGE group and PGE group; and (4) outcomes must have evaluated mortality and postoperative complication rates. The TGE group was defined by the entire graft having been removed and defective arteries repaired by primary suture or autologous vein patch. The PGE group was defined as segmental resection of the infected prosthesis graft and leaving off the prosthesis material on arterial and venous ends or with immediate flow restoration by autologous or prosthesis graft. To prevent contamination of the new prosthesis during reoperation, subtotal graft excision was defined as segmental resection of the graft with the prosthetic cuffs remaining less than 5 millimeters on either the artery or vein. In this meta-analysis the authors decided to classify subtotal graft excision as a PGE group.

Mortality rate was defined as a death that occurred during the 30-day postoperative period. Finally, postoperative complication was defined as recurrent infection (including local graft infection, abscess formation, pseudoaneurysm formation with or without bleeding, and systemic sepsis) and where re-operation to control the infection was required. Non-English language publications, review articles, and non-comparative research were all excluded. The Newcastle-Ottawa scale was used to assess the quality of the studies that were included in the meta-analysis. The best methodological excellence was represented by a score of 9, which is the highest possible.¹¹

Author names, country of origin, year of publication, study design, number of patients, patient characteristics, surgical treatment modalities, and postoperative outcomes were all collected by the two reviewers independently from the selected studies. The extracted data was double-checked for accuracy before being placed into a computerized spreadsheet for analysis. The Cochrane Collaboration's Review

Manager software, version 5.4.1, was used to conduct the meta-analysis (Nordic Cochrane Center, Cochrane Collaboration, Copenhagen, Denmark). To measure between-study heterogeneity, the Cochrane chi-square-based Q-statistic test was used. The I^2 statistic was used to evaluate for heterogeneity among the included studies (significant heterogeneity was defined as $P < .05$).

The Mantel-Haenszel method was used to construct a pooled odds ratio (OR) with 95 percent confidence intervals (95 % CI) in order to assess the mortality and postoperative complications between the TGE and PGE groups. At the $P < .05$ level, the OR was judged statistically significant, and the 95 percent confidence interval (CI) did not include the value 1. Odds ratio (ORs) were calculated using the fixed-effect model. When considerable evidence of heterogeneity was discovered, a random effects model was used to assess levels of association using a weighted average of the effects reported in different studies. A funnel plot was used to measure publication bias, while Egger's linear regression test and the rank correlation test (Begg's test) were used to officially quantify asymmetry.

RESULTS

Of 117 potential articles identified during the initial search, eight studies were judged qualified for inclusion in the meta-analysis since they fit the researcher's requirements (Figure 1).¹²⁻¹⁹ The resulting dataset was unanimously approved by the two reviewers. A total of 555 arteriovenous dialysis prosthesis graft infections in 528 patients were included in the pooled studies, which were utilized to analyze the relationship between TGEs and PGEs with postoperative complication and mortality rates.

The average age of the patients in the eight studies was 60.4 years, with a 50:50 male:female ratio. The most common clinical symptoms included localized pus formation (11.7%-73.2%), bleeding (7.8%-23%), pseudoaneurysm formation (11%-47.3%) and graft exposure (4%-17.1%). The incidence of systemic sepsis in AVGI patients ranged between 5% and 32%. TGE was performed in 188 procedures (36.6%) and PGE was performed in 327 procedures (63.4%). All of the studies included in the meta-analysis scored moderate to good (6–8 stars) on the Newcastle-Ottawa scale (Table 1).

30-day mortality rates

Six observational studies (357 patients) reported the association between each surgical technique with 30-day mortality as an outcome. The overall mortality rate

was 6.2% (24/357), in which the 30-day mortality in the TGE and the PGE groups were 6.1% (8/132) and 7.1% (16/225), respectively.

The meta-regression was performed to assess adjusted differences in patient characteristics; there were no significant differences between patient groups (coefficient 0.1406, standard error 0.272, 95 percent confidence interval (95% CI)=0.025-0.975, $P=.627$). The 30-day mortality rates were not significantly different between the two surgical therapy groups (OR=0.92, 95% CI=0.39 - 2.17, $P=.85$), according to the pooled analysis. Between studies, there was no significant heterogeneity ($I^2=0\%$, $P=.96$). Figure 2 shows no association between TGE and PGE and 30-day mortality rates. Egger's test ($P=.490$) and the rank correlation test ($P=.573$) revealed no evidence of publication bias. The symmetrical distribution in the funnel plot indicates no difference in 30-day mortality (Figure 3).

Recurrent graft infection

In eight studies, recurrent graft infection was observed in 4.8 percent (9/188) of TGE patients and 26.6 percent (87/327) of PGE patients, respectively. A recurrent graft infection developed within a few days to 12 weeks after initial surgery. The PGE group had a significantly increased incidence of recurrent infection (OR=0.23, 95% CI=0.13–0.41, $P=.00001$), according to the

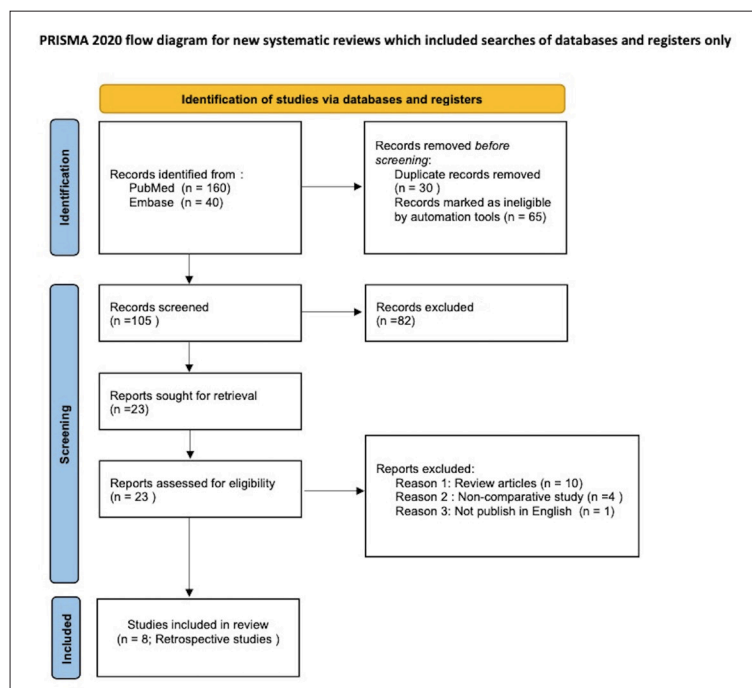


Figure 1. Selection process of studies for inclusion in the meta-analysis.

Table 1. Characteristic of the eight included studies in the meta-analysis regarding total versus partial graft.

Study	Country	Year	Study design	Number of patient	Number of graft infection	Location of graft
Deneuille ¹²	France	2000	Retrospective	19	19	Upper extremity
Kim et al ¹³	Korea	2017	Retrospective	47	50	Upper extremity Lower extremity (1 cases)
Li et al ¹⁴	Taiwan	2020	Retrospective	41	41	Upper extremity
Schutte et al ¹⁵	USA	2007	Retrospective	90	111	Upper extremity Lower extremity (23 cases)
Tabbara et al ¹⁶	USA	1995	Retrospective	52	57	Upper extremity Lower extremity (3 cases)
Walz et al ¹⁷	USA	2005	Retrospective	84	77	Upper extremity
Liu et al ¹⁸	USA	2020	Retrospective	177	122	Upper extremity
Ryan et al ¹⁹	USA	2004	Retrospective	45	51	

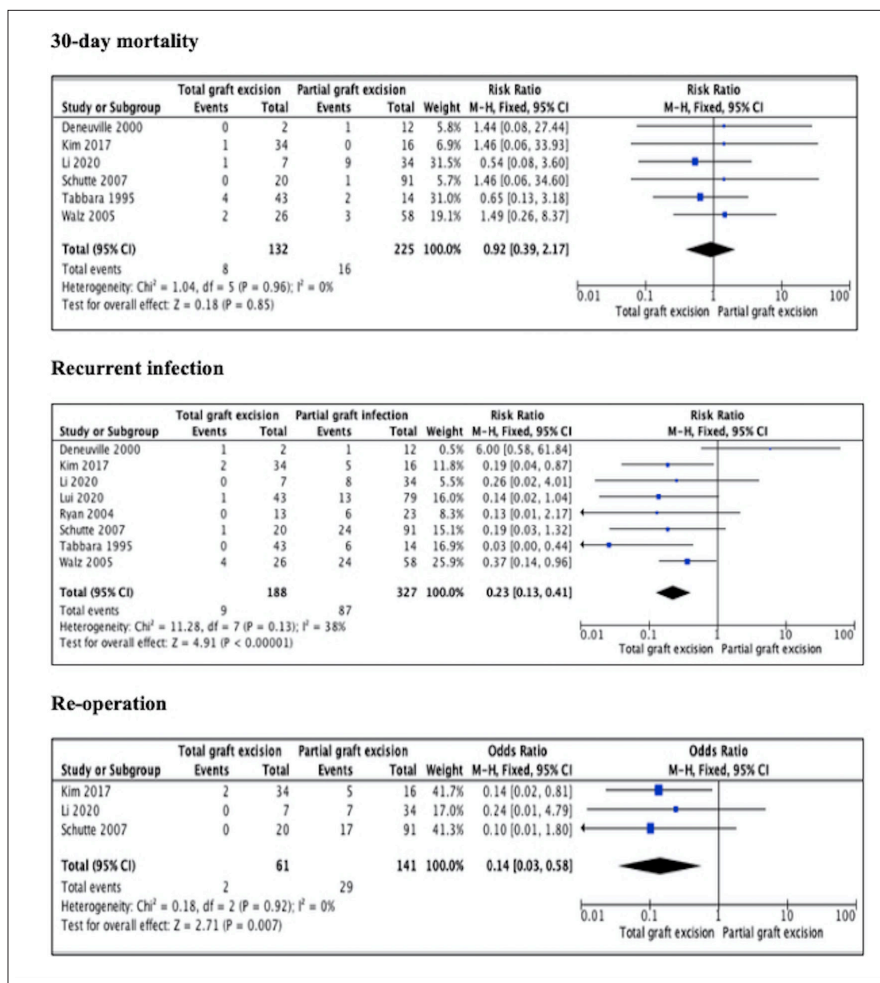


Figure 2. Forest plot displaying the association between total and partial graft excision with the postoperative outcomes.

Table 1 (cont.). Characteristic of the 8 included studies in the meta-analysis regarding total versus partial graft.

Study	Method for Diagnosis for AVGI	Site of AVGI infection	Pathogen	Matching	Newcastle Ottawa score
Deneuville ¹²	- Clinical diagnosis - Doppler ultrasound	- Anastomosis - Puncture site - Graft Tunnel	<i>Staphylococcus aureus</i>	a, b, c, d, e	7
Kim et al ¹³	- Clinical diagnosis - Doppler ultrasound	- Puncture site - Previous incision - Unused graft	<i>Staphylococcus aureus</i> <i>Pseudomonas aeruginosa</i> <i>Serratia marcescens</i>	a, b, c, e, f	8
Li et al ¹⁴	Clinical diagnosis	- Puncture site - Anastomosis - Other sites	<i>Staphylococcus aureus</i> <i>Pseudomonas aeruginosa</i> Fungi	a, b, c, e, f	8
Schutte et al ¹⁵	Clinical diagnosis	N/A	N/A	a, b, c,	6
Tabbara et al ¹⁶	Clinical diagnosis	N/A	<i>Staphylococcus</i> species <i>Streptococcus</i> species Gram negative bacteria Fungi	a, b, c, e, f	7
Walz et al ¹⁷	Clinical diagnosis	N/A	<i>Staphylococcus aureus</i> <i>Pseudomonas aeruginosa</i> <i>Streptococcus faecalis</i>	a, b, e, f	6
Liu et al ¹⁸	Clinical diagnosis	N/A	<i>Staphylococcus aureus</i> <i>S epidermidis</i> Gram negative bacteria	a, b, c, e, f	8
Ryan et al ¹⁹	Clinical diagnosis	- Incision - Graft body - Puncture site	<i>Staphylococcus aureus</i> <i>Pseudomonas aeruginosa</i> <i>Streptococcus</i> species	a, b, c, e	7

Abbreviations: AVGI=arteriovenous graft infection, N/A: not available, a=age, b=sex, c= patient comorbidity, d=timing of surgery, e=bacteriologic culture, f=mortality

pooled analysis (**Figure 2**). There was no evidence of heterogeneity between studies ($I^2=38\%$, $P=.13$). Both Egger's test ($P=.902$) and the rank correlation test ($P=.805$) found no evidence of publication bias.

Re-operation rate

Three studies reported the association between the re-operation rate and surgical options. The incidence

of re-operation to control infection was 3.3% (2/61) and 20.6% (29/141) in the TGE and PGE groups, respectively. Reoperation for the management of a postoperative complication was performed between two weeks and several months after the initial operation. The PGE group had a significantly higher re-operation rate (OR=0.14, 95% CI=0.03–0.58, $P=.007$), with no evidence of heterogeneity between studies ($I^2=0\%$,

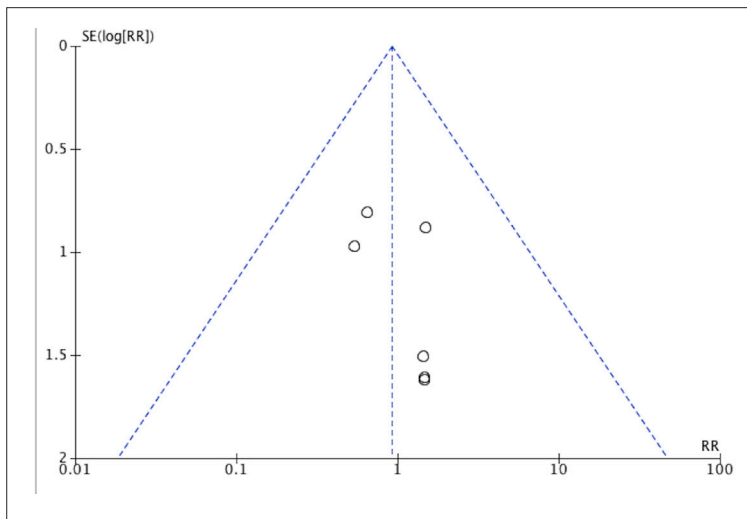


Figure 3. Funnel plot of the association of total and partial graft excision with the 30-day mortality.

$P=.92$). Egger's test ($P=.720$) and the rank correlation test ($P=.602$) (**Figure 2**) revealed no evidence of publication bias.

The patency of dialysis access following partial graft excision

Patients with AVGI who underwent TGE were given temporary dialysis access via the central venous catheters. After confirming the absence of bacteremia, 52.9% of patients had a new permanent vascular access created within 90 days of surgery, with a 100% patency rate after 10 months of follow-up. The long-term patency rate of the remaining dialysis graft in the PGE group was reported to be 90% at 12 months and 30% at 24 months after surgery, respectively. However, long-term patency (>24 months) was documented in both groups. Compared to TGE groups, only 12.5-23% of PGE patients require temporary dialysis via central venous catheters due to recurrent graft infection. Furthermore, the results from two included studies demonstrated that PGE with immediate graft reconstruction using the prosthetic interposition with the previous access was associated with a greater rate of recurrent graft infection than PGE without immediate graft reconstruction. (46.7%-57.1% versus 12.7%-14.3%).

DISCUSSION

Hemodialysis by means of arteriovenous graft is one of the ultimate forms of renal replacement therapy in patients with end-stage kidney disease, especially in cases in which native arteriovenous fistula cannot be established. However, the long-term patency of an arteriovenous bridge graft is limited by graft-related

infection with a reported incidence of 11%-35%. Furthermore, delays in diagnosis and inappropriate surgical management may lead to increased morbidity (3%-35%) and mortality up to 12%.²⁰⁻²²

Management of AVGI includes use of a broad-spectrum intravenous antibiotic and proper graft resection for eradicating infection. Traditionally, TGE refers to the total removal of the entire prosthesis for adequate infection control, which is indicated as follows: 1) infection involving anastomoses or anastomotic bleeding; 2) systemic sepsis; and 3) the majority of the graft body and graft tunnel were involved by infection. The major disadvantages of TGE include the need for temporary dialysis access through the central venous catheter and increased overall morbidity up to 36.2% (with 26% of non-graft related complications), which consequently raised 90-day postoperative mortality up to 2.1%.^{23,24} However, in this study, a meta-regression analysis was performed to adjust for differences in patient characteristics, and there were no significant differences between each patient group.

In an attempt to reduce morbidity in TGE cases, TGE, partial excision of the infected prosthesis segment was conducted in selected situations; for instance, in cases of localized graft infection without life-threatening septic conditions. This surgical technique provides infection control (with a clinical success rate of 60%-80%), eliminates the need for temporary dialysis access, and preserves vascular access, especially when superficial veins are unsuitable for creating new dialysis access. Nevertheless, this remains controversial due to a high recurrent graft-infection rate of 35.3%, resulting in the need for subsequent TGE or repeat PGE to control the infection.^{25,26}

The present meta-analysis evaluated postoperative outcomes by comparing each surgical method, including postoperative complication and mortality rate. The pooled results indicate that PGE is associated with a significantly higher rate of recurrent graft infection than TGE, which led to a considerable increase in the rate of reoperation for correction of postoperative complications. Even though patients who had a subtotal graft excision were excluded from the analysis, their results were similar in terms of mortality, recurrent infection, and reoperation rate (data not shown). Several studies show increasing recurrent infections and need for re-operation as found in the present study.^{27,28}

In contrast to the studies in our meta-analysis, Sgroi et al reported that the recurrent infection rate in PGE was 22%, which was not statistically different from the TGE group.²⁹ Furthermore, there was no mortality in Sgroi et al, which might be explained by graft

reconstruction was not immediately performed and only 1-5 millimeters of the grossly uninfected graft remained at the anastomosis to facilitate adequate closure. Sepsis and failure to control infection were a major cause of early death in AVGI in the studies in this meta-analysis. To the contrary, even patients in the PGE group had a higher recurrence or graft infection rate, but the result of the meta-analysis demonstrated no effect on the 30-day mortality rate.

The strengths of this meta-analysis were: 1) the high quality of the selected studies; 2) the clear statistical analysis methods to account for differences in variables that affected the significance level of the research studies; and 3) the absence of heterogeneity, which increased the reliability of the results. However, the results are somewhat limited due to the risk of publication bias because all the included studies were observational retrospective studies, only PTFE graft was used for hemodialysis access, and almost all the AV access was constructed in the upper extremities.

Additionally, 30-day mortality was calculated from the survival curves in three studies, which can affect the accuracy of the pooled analysis. Evidence of heterogeneity between the studies was not observed in

this meta-analysis, even though there were differences in patient populations, age, comorbidities, timing between graft implantation to graft infection, and timing for surgery in each study.

Given that this study focused exclusively on studies where TGE or PGE was performed in the infected PTFE dialysis prosthesis graft, it may be beneficial for future studies to examine the association between surgical methods and the treatment outcomes based on the infected early cannulation graft. In addition, further studies should investigate additional procedures such as brachial artery ligation or negative wound pressure therapy, which may help to improve the treatment outcome.

In conclusion, the present report suggests that TGE remains a safe and effective surgical method for the management of AVGI, especially when associated with life-threatening septic complications. PGE is an alternative surgical option that has been shown to benefit dialysis access preservation without affecting mortality. Because of the increased risk of graft infection and the need for a re-operation for infectious control, PGE should only be considered in carefully selected patients.

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