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Original Investigation

Preemptive Correction of Arteriovenous Access Stenosis: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Background: Preemptive correction of a stenosis in an arteriovenous (AV) access (fistula or graft) that is adequately providing hemodialysis (functional AV access) may prolong access survival as compared to waiting for signs of access dysfunction to intervene (deferred salvage). However, the evidence in support of preemptive intervention is controversial. We evaluated benefits and harms of preemptive versus deferred correction of AV access stenosis.

Study Design: Systematic review and meta-analysis of randomized controlled trials.

Setting & Population: Adults receiving hemodialysis by a functional AV access.

Selection Criteria for Studies: We searched the Cochrane Kidney and Transplant Specialised Register and EMBASE to October 15, 2015.

Intervention: Active access surveillance (flow measurement and Doppler or venous pressure) and preemptive correction of a newly identified stenosis versus routine clinical monitoring and deferred salvage, or preemptive correction of a known stenosis versus deferred salvage.

Outcomes: Access loss (primary outcome) and thrombosis (overall and by access type), infection, mortality, hospitalization, and access-related procedures.

Results: We included 14 trials (1,390 participants; follow-up, 6-38 months). Relative to deferred salvage, preemptive correction of AV access stenosis had a nonsignificant effect on risk for access loss (risk ratio [RR], 0.81; 95% CI, 0.65-1.02; $I^2 = 0\%$) and a significant effect on risk for thrombosis (RR, 0.79; 95% CI, 0.65-0.97; $I^2 = 30\%$). Treatment effects were larger in fistulas than in grafts for both risk for access loss (subgroup difference, $P = 0.05$) and risk for thrombosis (subgroup difference, $P = 0.002$). Results were heterogeneous or imprecise for mortality, rates of access-related infections or procedures, and hospitalization.

Limitations: Small number and size of primary studies limited analysis power.

Conclusions: Preemptive stenosis correction in a functional AV access does not improve access longevity. Although preemptive stenosis correction may be promising in fistulas, existing evidence is insufficient to guide clinical practice and health policy.

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INDEX WORDS: Hemodialysis access; vascular access; arteriovenous fistula; arteriovenous graft; access screening; access surveillance; access thrombosis; pre-emptive stenosis correction; access salvage; access angioplasty; access loss; patency; renal replacement therapy; systematic review.

A reliable access to the bloodstream by a vascular access is necessary for hemodialysis, the most common form of therapy for end-stage kidney failure. The native arteriovenous (AV) fistula (a direct link between an artery and a vein in the arm) is considered the best type of access, followed by the AV graft (in which graft material is used for the AV communication),[1,2] based on large studies showing associations with reduced risk for all-cause mortality, fatal infections, and cardiovascular events in people using an AV access compared with those using central venous catheters.[3] However, stenosis and thrombosis of the

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AV access are a leading cause of hospitalization and health care resource consumption among hemodialysis patients.[4] About 50% of fistulas require additional procedures in the year following creation (1.45-3.3 procedures/access-year) and revisions are often necessary in the long term to maintain patency (0.17-0.57 procedures/access-year).[5] Vascular access–related morbidity has profound social and psychological consequences for the patient.[6]

Optimal access function is routinely assessed during hemodialysis to ensure that the access is adequate to provide sufficient dialysis dose (functional access). Routine clinical monitoring involves examination of access thrill and bruit, hemostasis time after needle removal, and hemodialysis parameters, including hemodialysis circuit blood flow (Q_b), arterial and transmembrane pressures, or dialysis adequacy indexes. During clinical monitoring, evidence of access dysfunction (eg, reduced Q_b or prolonged bleeding upon needle removal) prompts access-related procedures to correct the underlying cause of access dysfunction (usually a stenosis or narrowing) and thereby prevent thrombosis and access loss (deferred salvage interventions). Because stenosis of the AV access reduces blood flow in the AV access (Q_a) and consequently increases the risk for access thrombosis, different noninvasive methods of active surveillance of Q_a have been proposed to determine earlier whether a functional access is at risk for dysfunction.[7,8] These involve direct measurements of Q_a; indirect measures, including dynamic or static venous dialysis pressure (venous pressure to systolic blood pressure ratio); and duplex ultrasound, which provides both blood flow and anatomical information. Guidelines recommend access imaging and preemptive correction of stenoses $>$ 50% when critical Q_a values are present regardless of the access ability to provide adequate hemodialysis (preemptive correction of access stenosis).[7-12] These guideline recommendations assume that a reduction in Q_a identifies a treatable stenosis before the access becomes dysfunctional, and that preemptive correction of the stenosis will maintain the functional AV access, prevent thrombosis, and prolong longevity of the access use as compared to deferred salvage. However, a previous systematic review found no benefits from access screening in grafts and uncertain benefits in fistulas.[13]

Because of the substantial morbidity associated with access complications, as well as the resource implications of both preemptive and deferred interventions and their unclear benefits and harms based on the limited power of previous knowledge synthesis,[13] we did a systematic review of randomized controlled trials (RCTs) comparing a strategy of preemptive correction of AV access stenosis versus a strategy of deferred salvage in people with a functional AV access.

METHODS

Study Design, Interventions, and Outcomes

We conducted a systematic review and meta-analysis of RCTs according to a published peer-reviewed protocol[14] and followed recommended guidelines for reporting.[15]

We included RCTs and quasi-RCTs (RCTs in which allocation to treatment was obtained by predictable methods such as alternation, use of alternate medical records, or date of birth) evaluating the benefits and harms of a preemptive strategy to correct AV access stenosis in adults with end-stage kidney failure treated with hemodialysis, regardless of the duration of dialysis therapy. These studies could be of any follow-up duration and reported in any language. Participants had to have an AV access (either fistula or graft) that was adequately providing hemodialysis (functional AV access) without suspected or known stenoses (primary prophylaxis) or a functional AV access with a known or suspected stenosis (secondary prophylaxis). Studies of primary prophylaxis evaluated the effects of any method for measuring Q_a (flow measurement, Doppler, or venous pressure; active surveillance) to identify and preemptively correct stenosis (preemptive correction) in addition to or instead of a strategy for routine physical examination or monitoring of hemodialysis parameters (clinical monitoring) and interventions prompted by access dysfunction (deferred salvage). Studies of secondary prophylaxis evaluated the effects of preemptive correction of a documented stenosis in a functional access versus deferred salvage. We excluded studies in which participants used a central venous catheter for hemodialysis and studies comparing different approaches to treat a dysfunctional AV access (an access that was not adequately providing hemodialysis) or a clotted access.

In primary prophylaxis studies, the intervention could be any method for access surveillance followed by preemptive correction of a newly identified stenosis, including surgical or imaging-assisted procedures. In secondary prophylaxis studies, the intervention was any preemptive correction procedure. In primary prophylaxis studies, the comparator was either a strategy based on routine clinical monitoring and deferred correction of a stenosis (inactive comparator) or another active surveillance method for preemptive stenosis correction (active comparator). Deferred correction procedures included surgical interventions or imaging-assisted procedures. In secondary prophylaxis studies, the intervention was any deferred correction procedure.

The primary outcome was access loss (permanent loss of access patency leading to access abandonment). Secondary outcomes were AV access thrombosis (temporary loss of patency leading to access dysfunction, or inability to adequately provide hemodialysis, and prompting an access procedure), mortality, rates of infection, access-related procedures and hospitalization, health costs, and quality of life.

Study Searches, Selection, and Data Extraction

We searched the Cochrane Kidney and Transplant Specialised Register and EMBASE to October 15, 2015, without language restriction (Table S1, available as online supplementary material).

Two authors (P.R. and D.J.K.) independently screened the citations retrieved by searching by title and abstract, then by reviewing the full text, to identify studies that fulfilled the inclusion criteria. Any study considered potentially eligible by at least 1 reviewer was retrieved for further review.

The same 2 authors extracted data for study population characteristics, interventions, nonrandomized cointerventions, and risks of reporting bias into a purpose-built database. Each author double-checked data extraction and data entry independently, and