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Efficacy and safety of endovascular versus surgical arterio-venous fistula creation for hemodialysis

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VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Efficacy and safety of endovascular versus surgical arterio-venous fistula creation for hemodialysis

[Effektivitet och säkerhet för endovaskulärt jämfört med kirurgiskt anlagd arterio-venös fistel för hemodialys]

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Table of contents

1. Abstract 4
2. Svensk sammanfattning – Swedish summary 5
3. Summary of findings 7
4. Abbreviations/Acronyms 8
5. Background 9
6. Health Technology at issue: Endovascular arteriovenous fistula (AVF) creation 10
7. Focused question 11
8. Methods 12
9. Results 13
10. Ethical aspects 14
11. Organizational aspects 15
12. Economic aspects 15
13. Discussion 16
14. Future perspectives 17
15. Participants in the project 18

Appendix 1 Study selection, search strategies and references

Appendix 2 Included studies – design and patient characteristics

Appendix 3 Excluded articles

Appendix 4 Outcome tables

1. Abstract

Background
Chronic kidney disease (CKD) is often caused by hypertension or diabetes mellitus type 2. Patients with end-stage CKD need renal replacement therapy: hemodialysis, peritoneal dialysis, or kidney transplantation. In Sweden, the prevalence for any stage of CKD is 6%, and 3,200 patients (0.03% of the Swedish population) have end-stage CKD treated with hemodialysis. Long-term vascular access options for hemodialysis are arterio-venous fistula (AVF) or graft, and tunnelled central dialysis catheter (TDC). TDC carries a substantial risk for serious complications. The first choice is therefore a surgical AVF, but only 25% of patients start hemodialysis with an AVF due to, e.g., late referrals, long waiting time and time to maturation, i.e. the time until the AVF has adequate blood flow, vessel diameter, and vessel wall thickness to allow cannulation for dialysis. The novel endovascular AVF technique includes brachial artery and vein puncture, catheters positioned in the proximal ulnar artery and vein which are pulled together, followed by vaporisation of the tissue between the catheters. Endovascular AVF has been suggested to enable shorter waiting times and might thus have the potential to make a temporary TDC, with its associated risks, unnecessary.

Question at issue: Is percutaneous endovascular AVF creation more effective and safer compared with surgical AVF creation regarding patient survival, reinterventions, technical success, functional usability, patency, and health-related quality of life in adult patients with end-stage kidney disease in need of hemodialysis?

Method
In October 2020, systematic literature searches were conducted in Medline, Embase, and the Cochrane Library. The included articles were critically appraised, outcome data were extracted, and certainties of evidence were assessed using the GRADE approach.

Results
Thirteen studies were included, two non-randomised controlled studies (NRCT) and 11 case series. The non-randomised controlled studies used the WavelinQ device, and had some problems with directness, moderate to serious study limitations and problems with precision.
Two NRCT reported reintervention rates. One study reported numerically more whereas the other study reported significantly less reinterventions in the endovascular versus the surgical group. One NRCT reported primary patency after one year with n.s. difference between the intervention and control groups (56.5 vs. 44 %, p=0.63). One NRCT reported time from operation to cannulation with n.s. difference between the groups.
Conclusion: It is uncertain whether there is any difference in the frequency of reinterventions, primary patency, and time from operation to cannulation after endovascular compared with surgical AVF creation for hemodialysis in patients with end-stage kidney disease. Very low certainty of evidence (GRADE ⊕◯◯◯).
Two NRCT and eleven case series reported complications using the WavelinQ or the Ellipsys device. Reporting standards were heterogeneous, as complications were not predefined, or divided into major and minor complications, but complications were frequent, both after endovascular and after surgical AVF creation.
Conclusion: It is uncertain whether there is any difference in the frequency of complications after endovascular compared with surgical AVF creation (GRADE ⊕◯◯◯). Patient survival, technical adequacy for dialysis, cannulation success, technical success, vein length available for cannulation and health-related quality of life were not reported.

Concluding remarks
The novel technique endovascular AVF creation is poorly studied and comparisons with surgical AVF are very few. It is uncertain whether there is any difference in the frequency of reinterventions, primary patency and time from operation to cannulation after endovascular compared with surgical arteriovenous fistula creation for hemodialysis in patients with end-stage kidney disease (GRADE ⊕◯◯◯). Complications are frequent after endovascular as well as surgical AVF.

2. Svensk sammanfattning – Swedish summary

Bakgrund Kronisk njursjukdom orsakas ofta av högt blodtryck eller diabetes mellitus typ 2. Patienter med kronisk njursjukdom i slutstadiet behöver hemodialys, peritonealdialys eller njurtransplantation. I Sverige är prevalensen för kronisk njursjukdom 6% och 3200 patienter (0,03% av populationen) behandlas med hemodialys. Kärlaccess för hemodialys fås med en arteriovenös fistel (AVF) eller graft eller med en tunnelerad central dialyskateter (TDC). TDC medför risker för allvarliga komplikationer. Förstahandsval är därför en kirurgisk AVF, men endast 25% börjar hemodialys med en AVF främst på grund av sen remiss, lång väntetid till operation och till mognad av fisteln, vilket innebär tiden till att fisteln har tillräcklig diameter, väggtjocklek och blodflöde för dialysändamål. Den nya endovaskulära tekniken för AVF innefattar punktion av en artär och ven i armen, katetrar införs till proximala ulnarartären och artär och ven dras samman, varefter vävnaden mellan katetrarna bränns bort så att en förbindelse fås. Endovaskulär AVF kan troligen förkorta väntetiden till operation och skulle i så fall kunna ha potentialen att göra en temporär TDC onödig varigenom komplikationer till TDC skulle kunna undvikas.

Fokuserad fråga Är perkutant anlagd endovaskulär AVF effektivare och säkrare jämfört med kirurgiskt anlagd AVF vad gäller patientöverlevnad, reinterventioner, öppetstående av fisteln, lyckandefrekvens för operationen, funktion för dialys och hälsorelaterad livskvalitet hos vuxna patienter med kronisk njursjukdom i slutstadiet som behöver hemodialys?

Metod I oktober 2020 gjordes systematiska litteratursökningar i Medline, Embase och Cochrane Library. De inkluderade artiklarna granskades kritiskt, data extraherades och evidensläget bedömdes enligt GRADE.

Resultat Tretton studier inkluderades, två icke-randomiserade kontrollerade studier (NRCT) och 11 fallserier. De icke-randomiserade kontrollerade studierna använde WavelinQ för endovaskulär AVF och hade vissa problem med överförbarhet, medan studiebegränsningar och problem med precisionen var måttliga eller allvarliga. Två NRCT rapporterade reinterventioner. En studie rapporterade numeriskt fler, medan den andra studien rapporterade signifikant färre reinterventioner i den endovaskulära versus den kirurgiska gruppen. En NRCT rapporterade ingen signifikant skillnad i öppetståendefrekvens efter ett år mellan endovaskulär- respektive kirurgigruppen (56,5 vs. 44%, p = 0,63). En NRCT rapporterade ingen signifikant skillnad i tid från operation till kanylering för dialys mellan grupperna.

Slutsats Det är osäkert huruvida det föreligger någon skillnad i frekvensen av reinterventioner, öppetståendefrekvens och tid från operation till kanylering för dialys efter endovaskulärt jämfört med kirurgiskt anlagd AV-fistel för hemodialys hos patienter med kronisk njursjukdom i slutstadiet. Mycket låg tillförlitlighet (GRADE ⊕○○○). Två NRCT och elva fallserier rapporterade komplikationer med WavelinQ eller Ellipsys. Rapporteringsstandarden varierade, komplikationer var inte predefinierade eller indelade i allvarliga och mindre allvarliga komplikationer, men komplikationer var vanliga efter såväl endovaskulär som kirurgisk AVF. Det är osäkert huruvida det föreligger någon skillnad i frekvensen av komplikationer efter endovaskulärt jämfört med kirurgiskt anlagd AVF (GRADE ⊕○○○). Patientöverlevnad, funktion för dialys, funktionell användbarhet, lyckandefrekvens för operationen, tillgänglig venlängd för kanylering och hälsorelaterad livskvalitet var ej studerade.

Sammanfattande kommentar Den nya tekniken för endovaskulär AVF är otillräckligt studerad och jämförelser med kirurgiskt anlagd AVF är mycket få. Det är osäkert huruvida det finns någon skillnad i frekvensen av reinterventioner, primär öppenhet och tid från operation till kanylering efter endovaskulärt jämfört med kirurgiskt anlagd AVF (GRADE ⊕○○○). Komplikationer är vanliga efter såväl endovaskulärt som kirugiskt anlagd AVF.

The above summaries were written by representatives from the HTA-centrum. The HTA report was approved by the Regional board for quality assurance of activity-based HTA. The abstract is a concise summary of the results of the systematic review. The Swedish summary is a brief summary of the systematic review intended for decision makers and is ended with a concluding summary.

Christina Bergh, Professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden, March 31st 2021

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Svensson, Mikael	Health economist, Professor
Wallerstedt, Susanna	MD, Professor
Wartenberg, Constanze	Psychologist, PhD

DDS Doctor of dental surgery
MD Medical doctor
PhD Doctor of Philosophy
OD Odontology doctor
PT Physiotherapist
RN Registered Nurse
MSc Master of Science

3. Summary of findings

Outcomes	Study design Number of studies	Relative effect (95% CI)	Absolute effect	Certainty of evidence GRADE[1]
Patient survival	Not reported			
Reinterventions	2 NRCT n= 70 and n= 120	NA	NRCT 1 (Inston 2019) WavelinQ I: 0.4 per patient-year C: 0.3 per patient-year p=0.14 NRCT 2 (Yang, 2017) WavelinQ I: 0.5 per patient-year C: 1.8 per patient-year p<0.0001	Very low[1] ⊕◯◯◯
Primary patency at 1 year	1 NRCT	NA	NRCT 1 (Inston 2019) WavelinQ, I: 56.5 % C: 44.0 % p=0.63	Very low[2] ⊕◯◯◯
Time to cannulation	1 NRCT	NA	NRCT 1 (Inston 2019) WavelinQ I: 130 ± 86 days C: 141 ± 118 days p=0.66	Very low[2] ⊕◯◯◯
Technical adequacy for dialysis	Not reported			
Functional usability or cannulation success	Not reported			
Technical success	Not reported			
Vein length available for cannulation	Not reported			
Health-related quality of life	Not reported			

Footnotes: I= Endovascular AVF. C= Surgical AVF. NA = Meta-analysis not applicable for this outcome. NRCT = Non-randomised controlled study

[1] Downgraded from ⊕⊕◯◯ for NRCT due to serious study limitations, some inconsistency, uncertain precision. [2] Downgraded due to serious study limitations, some inconsistency, serious imprecision.

Certainty of evidence

High certainty ⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty ⊕⊕⊕◯	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty ⊕⊕◯◯	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty ⊕◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

4. Abbreviations/Acronyms

AVF	Arteriovenous fistula
BD	Becton, Dickinson and Company
CKD	Chronic kidney disease
CVC	Central venous catheter
FDA	Food and Drug Administration (USA)
F	French = 1/3 mm
GFR	Glomerular filtration rate
KDIQO	Kidney Disease: Improving Global Outcomes
NRCT	Non-randomised controlled study
SBU	Swedish Agency for Health Technology Assessment and Assessment of Social Services
SR	Systematic review
TDC	Tunneled dialysis catheter
VA	Vascular access
VGR	Region Västra Götaland

5. Background

End-stage chronic kidney disease

Chronic kidney disease (CKD) has become a global health problem, with hypertension and diabetes mellitus type 2 being the leading causes in developed countries. It is estimated that more than 37 million patients in the USA have CKD. Guidelines define CKD as abnormalities of kidney structure or function present for more than three months with health implications. Normal kidney function is 120 ml/min of glomerular filtration rate (GFR). Patients with low kidney function (around 10 ml/min) and symptoms of end-stage CKD (e.g., shortage of breath, edema, nausea, vomiting, tiredness) need renal replacement therapy. Renal replacement therapy is hemodialysis, peritoneal dialysis, or kidney transplantation. According to the Swedish kidney registry, six per cent of the Swedish population has any stage of CKD, and 3,200 (0.03% of the population) have end stage CKD and are currently treated with hemodialysis. In-hospital hemodialysis patients usually need dialysis for four hours, three times a week. One of the most important factors that affect dialysis quality is the type of vascular access.
In patients on hemodialysis, possible long-term vascular access (VA) options are arteriovenous fistula (AVF), arteriovenous graft, and tunnelled central venous catheter (TDC). Native AVFs, described by Brescia and Cimino in 1966 (Brescia et al., 1966), have the longest survival and the lowest frequency of complications among all current types of VA for hemodialysis, and should be the first choice whenever possible. Complications of TDC include infections and central venous stenosis or occlusions. According to the Swedish kidney registry, 66 percent of the hemodialysis patients have AVF as vascular access. However, only 25 percent start hemodialysis with a functioning AVF. The main reasons for this low proportion are late referrals to nephrology clinic, late referrals to surgery, long waiting time for surgical fistula creation, and long time for AVF maturation. New techniques for endovascular AVF creation might allow a shortening of the time from referral to AVF. Endovascular AVF creation could potentially make some temporary TDCs unnecessary, thereby avoiding the associated morbidity.

Prevalence and incidence

According to the Swedish kidney registry (2020), 3,231 patients were on hemodialysis in Sweden on December 30, 2019. Approximately 700 patients start hemodialysis in Sweden annually. Only 25 percent of these start hemodialysis with AVF. One-year mortality for patients on hemodialysis in Sweden is 18.2 percent.

Present treatment

Kidney Disease: Improving Global Outcomes (KDOQI) guidelines (Lok et al., 2020) and The Fistula First Initiative are programs to improve the use of AVF in the USA that have set goals for vascular access in hemodialysis patients. According to the Swedish kidney registry, 25 percent of patients start hemodialysis with an AVF, and 66 percent of all patients on hemodialysis have AVF as vascular access.

The standard method to achieve an AVF in Sweden is by surgical operation. All patients considered for surgical AVF creation undergo arterial and venous doppler ultrasound of both arms before surgery. Surgical AVF creation is done by a surgeon in an operation room and includes connection of an artery and a vein in the forearm or upper arm. The operation takes approximately one hour, usually under local or regional anesthesia.

After surgery, patients stay a few hours for observation and are then discharged from the hospital. Postoperative controls of fistula maturation, i.e. the time from creation of the AVF until the AVF has adequate blood flow, vessel diameter, and vessel wall thickness to allow cannulation for dialysis, are performed in the nephrology clinic. In the United States, the time from AVF creation until first use averages 133 days, or approximately 4 months (Saran et al., 2017).

The typical pathway through the healthcare system and current wait time for medical assessment/treatment

Patients with CKD and GFR < 30 ml/min are referred to a nephrology clinic to start treatment for CKD. Those patients who have CKD progression (GFR around 15 ml/min) and are considered for hemodialysis then undergo appropriate vascular access assessment. Patients in good clinical condition and with adequate vessel anatomy and diameter are referred for AVF surgery. Wait time from referral to surgery is commonly six to eight weeks.

Number of patients per year who undergo current treatment regimen

Approximately 700 patients start hemodialysis annually in Sweden, of which 120 patients in Region Västra Götaland (VGR).

Present recommendations from medical societies or health authorities

Guidelines from KDOQI suggest AVF in preference to a central dialysis catheter in most predialysis patients as well as in patients already on hemodialysis due to less frequent vascular access-related adverse events (mainly infection, thrombotic and nonthrombotic complications).

6. Health Technology at issue: Endovascular arteriovenous fistula (AVF) creation

There are two commercially available systems for endovascular creation of AVFs. The WavelinQ™ EndoAVF System (Becton, Dickinson and Company (BD); formerly EverlinQ, TVA Medical) and the Ellipsys® device (Avenu Medical). The WavelinQ™ EndoAVF System uses two 6F, or 4F (1 F = 1/3 mm) catheters in the newer variant, to create the AVF (Figure 1). Only the WavelinQ device is currently commercially available in Sweden.

Figure 1. Catheters for endovascular creation of AVF

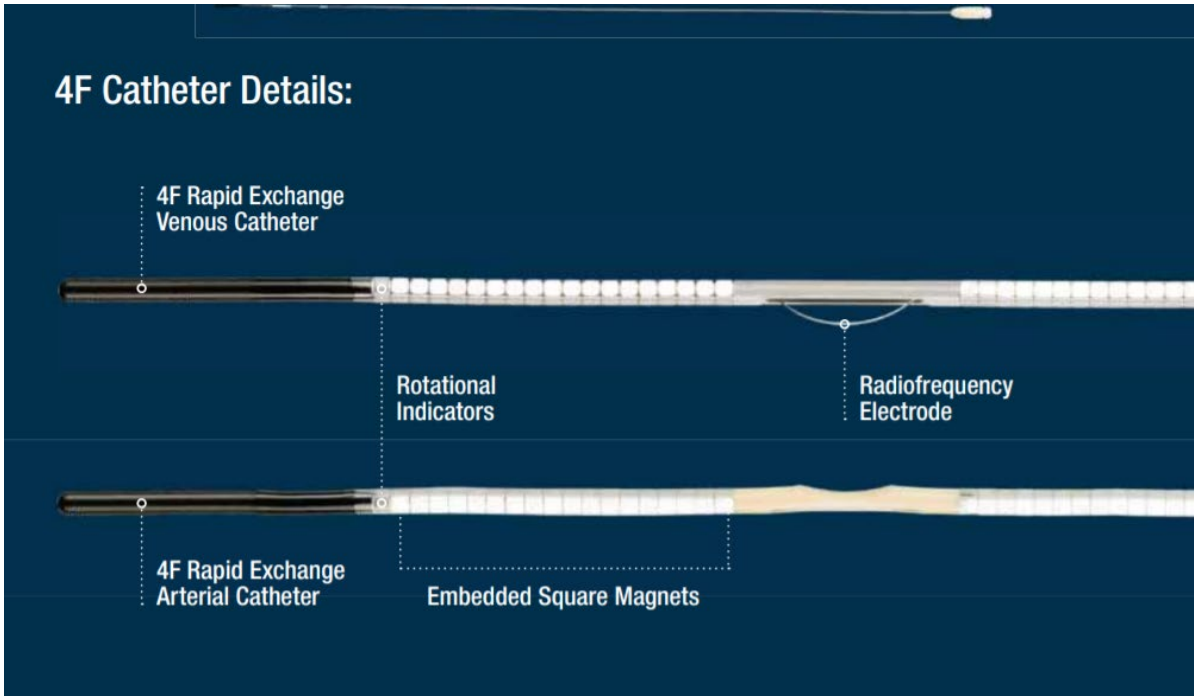

Figure with permission from BD company

After brachial artery and vein punctures, catheters are positioned in the proximal ulnar artery and vein under fluoroscopic control. The catheters are aligned to each other and pulled together with rare-earth magnets. After that, a short, high-energy pulse is sent through the radio-frequency heating electrode in the venous catheter, vaporizing the tissue between the catheters and creating a 1 mm x 5 mm fistula. The smaller 4F device offers greater flexibility regarding access and fistula creation site making distal radial and ulnar vessel puncture and retrograde catheterisation possible. After fistula creation, proximal brachial vein embolization is performed routinely to promote flow from deep veins to the superficial venous system (Figure 2).

Figure 2. WavelinQ device for creation of AVF

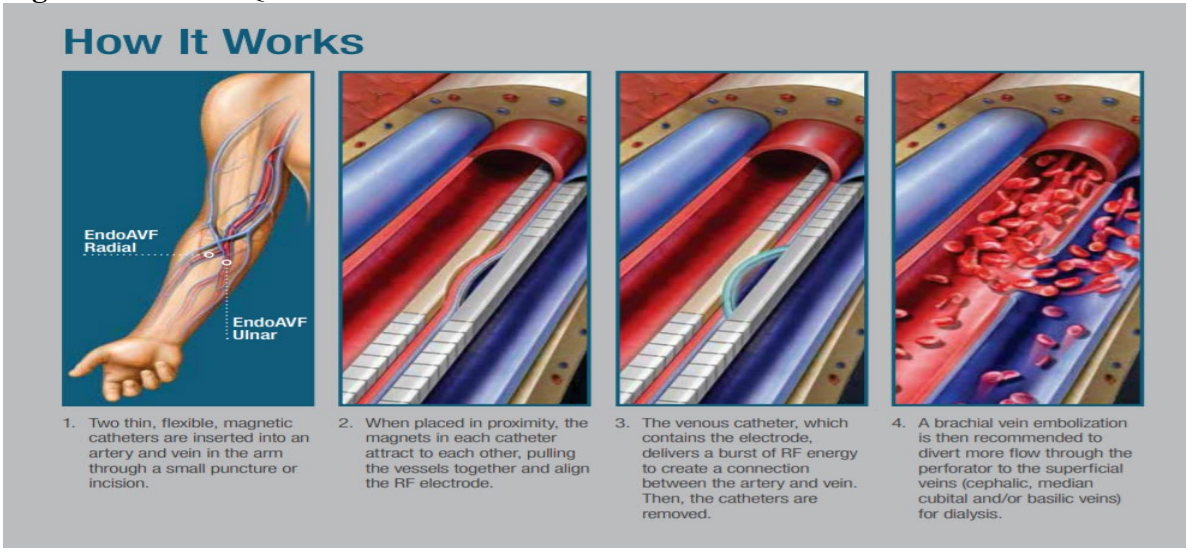

Figure with permission from BD company

The Ellipsys® device (Avenu Medical) is a 6F single catheter system. Under ultrasound guidance, a 21-gauge needle is used to puncture the median cephalic or median basilic vein. The needle is advanced into the radial artery allowing placement of a guidewire into the artery. The needle is removed and the Ellipsys catheter is advanced over a guidewire until the tip is positioned in the radial artery and the catheter capture the arterial and venous vessel walls. The catheter is closed and activated, which creates a fistula through pressure and thermal resistance energy.

The same preoperative assessment and postoperative care as for standard surgical AVF are used for endovascular AVF creation. An interventional radiologist or a vascular surgeon will perform the endovascular AVF creation.

7. Focused question

Is percutaneous endovascular AVF creation more effective and safer compared with surgical AVF creation regarding patient survival, patency, time to cannulation, technical adequacy for dialysis, functional usability, need for re-intervention, technical success, available vein length for cannulation and health-related quality of life in adult patients with end-stage kidney disease in need of hemodialysis?

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

P: Adult patients with end-stage kidney disease who are candidates for AVF operation

I: Percutaneous endovascular creation of AVF

C: Surgical creation of AVF

O:

Outcomes critical for decision-making

Patient survival

Re-intervention (endovascular/surgical)

Patency: primary (= without any reintervention), primary-assisted (= treated for failure but not to the level of occlusion), secondary (= reintervention for occlusion), primary-functional (= no occlusion, and functioning for hemodialysis), primary-functional assisted = treated for failure but not to the level of occlusion, and functioning for hemodialysis)

Functional usability:

time to cannulation (cannulation type: 1- or 2 needle or central venous catheter (CVC) assisted outflow)

-technical adequacy* for dialysis (*e.g. Physiological suitability: defined as brachial flow > 500mL/min and diameter >4mm)

-cannulation success i.e., dialysis w/ 2 needles.

Complications

Outcomes important for decision-making

Technical success

Functional usability: vein length available for cannulation

Health-related quality of life

8. Methods

Systematic literature search (Appendix 1)

In October 2020, two authors (TS, LB) performed systematic literature searches in Medline, Embase, and the Cochrane Library. Reference lists of relevant articles were scrutinised for additional references. Search strategies, eligibility criteria, and a graphic presentation of the selection process are presented in Appendix 1. These authors conducted the literature searches, selected studies, and independently of one another assessed the obtained abstracts and made a first selection of full-text articles for inclusion or exclusion. Relevant systematic reviews were included in the primary selection. Any disagreements were resolved in consensus. The remaining articles were sent to all the authors. All authors read the articles independently of one another, and it was finally decided in a consensus meeting which articles should be included in the assessment.

Critical appraisal and certainty of evidence

Included studies and their design and patient characteristics are presented in Appendix 2. Excluded studies and the reasons for exclusion are presented in Appendix 3. The included non-randomised controlled studies (NRCT) were critically appraised using modified checklists for quality assessment from the Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU). Certainty of evidence was assessed using the GRADE approach (Atkins et al., 2004; GRADE Working group). Data extraction was performed by one author and checked for accuracy by another. The results of each article were tabulated per outcome in Appendix 4. A summary result per outcome and the associated certainty of evidence are presented in a Summary-of-findings table (page 7).

Ongoing research

A search in Clinicaltrials.gov (2021-01-08) using the search terms *(percutaneous OR endovascular) AND (renal OR kidney OR dialysis OR hemodialysis OR haemodialysis) AND (fistula OR endoAVF OR endo-AVF OR ellipsys OR everlinq OR wavelinq OR AV-fistula OR AVfistula)* identified 95 studies.

9. Results

Search results and study selection (Appendix 1)

The literature search identified 715 articles after the removal of duplicates. After reading the abstracts, 673 articles were excluded. Another 16 articles were excluded by two authors after reading the articles in full text. The remaining 26 articles were sent to all authors, and 15 articles (two SRs, two NRCTs and 11 case series) were after a consensus discussion finally included in the assessment (Appendix 2). After final assessment of the available literature, it was decided to exclude the two SRs. Hence, 13 articles (two NRCTs and 11 case series) were finally included.

Included studies

Thirteen studies were included, two NRCTs and eleven case series (Appendix 2). No RCTs were identified. Both RCTs used the WavelinQ device and the surgical AVF comparator was radiocephalic AVF in one NRCT, while the other NRCT did not define the level for the surgical AVF. Two NRCTs reported data from the same control group from the NEAT study (open single-arm study, Lok et al., 2017). Another NRCT compared two endovascular systems (Ellipsys vs. Wavelin Q) without any surgical control group and is included as a case series (Franco et al., 2020). The included NRCTs had some problems with directness and moderate to serious study limitations and problems with precision, such as different criteria for re-interventions, a retrospective collection of data in the control group, few included patients, and many dropouts.

Results per outcome

Outcomes, critical for decision-making

Reinterventions

Two NRCTs reported reintervention rates (Appendix 4.1) after AVF creation. The studies had some problems with directness and serious study limitations, some inconsistency and uncertain precision. In one study (Inston et al., 2019) there were numerically more reinterventions in the endovascular group (0.4 versus 0.27 reinterventions per patient year, p=0.14), whereas in the other study (Yang et al., 2017) there were significantly fewer reinterventions in the endovascular compared with the surgical group (0.46 versus 1.77 reinterventions per patient year, p<0.001).

Conclusion: It is uncertain whether there is any difference in the frequency of reinterventions after endovascular compared with surgical arteriovenous fistula creation for hemodialysis in patients with end-stage kidney disease.

Very low certainty of evidence (GRADE ⊕◯◯◯).

Primary patency at 1 year

One NRCT (Inston et al., 2020) reported primary patency rates (Appendix 4.2) one year after AVF creation. The NRCT had serious study limitations and imprecision. There was no significant difference between the intervention and control groups (56.5 vs. 44 %, p=0.63).

Conclusion: It is uncertain whether there is any difference in the primary patency one year after endovascular compared with surgical arteriovenous fistula creation for hemodialysis in patients with end-stage kidney disease.

Very low certainty of evidence (GRADE ⊕◯◯◯).

Time to cannulation
One NRCT (Inston et al., 2020) reported time from operation to cannulation of the AVF for hemodialysis **(**Appendix 4.3**)**. The NRCT had serious study limitations and imprecision. There was no significant difference between the groups (130 ± 86 versus 141 ± 118 days, p=0.66).
Conclusion: It is uncertain whether there is any difference in the time to cannulation after endovascular compared with surgical arteriovenous fistula creation for hemodialysis in patients with end-stage kidney disease.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Complications
Two NRCTs and eight case series reported complications (Appendix 4.4). In one study (Yang et al., 2017) complications in the control (surgery) group had been registered retrospectively. Reporting standards were heterogeneous, as complications were neither predefined, nor divided into major and minor complications. Common complications after endovascular AVF included thrombosis of the AVF in 9.4 – 19% of cases in six case series and stenosis of the AVF, which was reported in 3–43% of the cases, in three separate case series. Different endovascular techniques, Ellipsys and WavelinQ, have been evaluated. In the NRCTs, most complications after endovascular as well as after surgical AVF were treated by angioplasty and embolization.
Conclusion: Complications are frequent after endovascular as well as after surgical AVF creation. There is considerable heterogeneity in reporting standards for complications in the different studies. It is uncertain whether there is any difference in complication rates after endovascular and surgical creation of AVF, respectively (GRADE ⊕◯◯◯).

10. Ethical aspects

Since tunnelled central dialysis catheters are associated with high infection rates, it is advisable to refer patients with end-stage renal disease for AVF creation well in advance of the commencement of dialysis. International and Swedish guidelines strongly recommend AVF as the first and best choice for vascular access in hemodialysis patients. Despite these clear recommendations, an unacceptably high number of patients start hemodialysis with a central dialysis catheter. The cost of the equipment for endovascular AVF creation is very high. There is currently no evidence demonstrating that endovascular AVF creation is more effective, cost-effective, or safer in comparison with surgical AVF creation. Long-term effectiveness is largely unknown. Introducing a novel technique which may lead to short-term cost increases without evidence of superiority or non-inferiority is ethically questionable. The included NRCTs and case series did not report unusually high reintervention or complication rates following endovascular AVF creation, but these results must be interpreted with care. As a new technique, operators may have selected only patients with optimal chances to succeed when receiving an endovascular AVF, leading to selection bias.

If reintervention and complication rates for endovascular AVF and standard surgical AVF would be equivalent, use of the endovascular method might lead to better availability and accessibility of AVF creation. If the waiting time to AVF creation could be shortened by endovascular instead of surgical AVF creation, some unnecessary insertions of a TDC and the associated adverse events could be avoided. This remains to be proven, however. There is no data suggesting a shorter time to AVF maturation by endovascular versus surgical AVF creation. Maturation makes up a large portion of the time until an AVF is in use. Long-term results for the endovascular technique are unknown, and there may be a risk of late complications and lower patency rate with the endovascular method.

11. Organizational aspects

Time frame for the putative introduction of the new health technology

If a decision to start endovascular AVF creation would be taken, it would be possible for us to introduce the technique in April 2021 as a complementary method to the standard surgical procedure. Possibly eligible patients would undergo a preoperative Doppler ultrasound and then be assessed for an endovascular intervention. Interventional radiologists would perform the endovascular AVF creation, and there is no need for extra resources. The plan would be to utilize the endovascular method as an outpatient procedure in an interventional radiology suite without a need for regional anesthesia or an operating theatre.

Present use of the technology in other hospitals in Region Västra Götaland

None.

Consequences of the new health technology for personnel

Since endovascular creation of AVF at the Sahlgrenska University Hospital would be performed at the Department of radiology by interventional radiologists, there would be more time and ORs for other types of surgery. One or two interventional radiologists interested in endovascular AVF will need training in this new technique. If the use of endovascular AVF would start with 10 to 15 endovascular procedures per year, no extra staff or equipment would be needed for the radiology department. The endovascular approach does not change current patient pre- and postoperative care.

Consequences for other clinics or supporting functions at the hospital or in the Region Västra Götaland

The introduction of the endovascular technique for creating AVFs might result in slightly reduced need for TDC catheters. These could open time from TDC insertions to AVF fistula endovascular operations. In hospitals where such endovascular interventions would be performed in an interventional radiology suite by an interventional radiologist, the use of endovascular AVF creation would probably slightly increase the availability of surgeons and ORs for other operations, provided that the long-term complication rate is not increased. The availability of interventional radiologists will probably decrease marginally. However, in other hospitals, such endovascular interventions may be performed by vascular surgeons in an interventional OR.

12. Economic aspects

Present costs of currently used technologies

Based on the Swedish cost per patient database (KVÅ-code: VEH58) the mean intervention cost for creating surgical AVF is 60,840 Swedish kronor (SEK) per patient. The mean intervention cost varies substantially within patients, and e.g. 5% of all intervention costs are higher than 130,000 SEK.

Expected costs of the new health technology

The list price for the only currently available endovascular AVF technology in Sweden (WavelinQ) is 48,500 SEK per catheter set. Assuming similar intervention time and staff use as with surgical creation of AVF, the total cost per patient of percutaneous endovascular creation of AVF is assumed to be about 109,000 SEK.

Total change in costs

Assuming similar intervention and staff time between the two technologies compared, percutaneous endovascular creation of AVF comes with an increased cost of 48,500 SEK per patient. If we assume 66% (AVF access) of 120 patients per year in VGR, this translates to about 3.85 million SEK per year.
If the two treatment alternatives have different post-procedure consequences, e.g., related to reinterventions, the cost differences could sway in both directions (since such post-procedure events have high associated costs). However, considering the lack of clear evidence of differences in reintervention rates in this report we do not assume that such related costs will differ.

Possibility to adopt and use the new technology within the present budget

Percutaneous endovascular creation of AVF can most likely not be adopted within the present budget. It would instead most likely require additional funding to the healthcare sector and/or imply that other healthcare services are displaced.

Available economic evaluations or cost advantages/disadvantages

Three papers on the costs and cost-effectiveness of percutaneous endovascular creation of AVF compared to surgical creation of AVF were identified in the literature searches. Two of the studies were from the US health care context and assessed the post-procedure costs between the two treatment alternatives (i.e., costs associated with post-creation procedures) among US Medicare patients (Yang et al. 2017, Arnold et al. 2018). The US-based studies found that percutaneous endovascular creation of AVF had significantly lower post-procedure costs (between $11,240 to $16,500 lower) due to less post-procedure events. The study from the Italian National Health Service perspective was based on a decision-analytic model with data from a systematic literature review that identified less post-procedure events with endovascular creation of AVF. The model results showed that the percutaneous endovascular strategy both reduced costs and was associated with better health-related quality of life outcomes (Rognoni et al. 2020). Using other assumptions on post-procedure events, i.e., assuming no difference, would have led to other model results.

13. Discussion

The percutaneous endovascular method for AVF creation was introduced in 2015 and approved by the U.S. Food and Drug Administration in 2018. No RCTs comparing these new methods with surgical techniques for AVF creation have been published so far. We could only identify two NRCTs that compared any of the predefined, clinically important outcomes and complication rates with those of surgical AVF creation. Due to study limitations and poor precision, it is uncertain whether this novel technique is associated with improved results and fewer complications (GRADE ⊕◯◯◯, regarding the reported outcomes). Regarding directness, end-stage CKD populations may vary between countries.

Two NRCTs included in this HTA report showed numerically less and slightly higher reintervention rates respectively, compared with surgical AVF creation. Due to missing data in one of these studies, meta analysis was not possible. One NRCT showed numerically similar primary patency at one year and time to cannulation with endovascular versus surgical AVF creation. The surgical AVF comparator was radiocephalic AVF in one of the NRCTs, while the level for the surgical AVF was undefined in the second NRCT. The endovascular AVF technique creates an AVF at a more proximal level than the classical surgical distal radial AVF.
Complications were frequent after both endovascular and surgical AVF creation. Considerable heterogeneity in reporting standards for complications in the different studies made comparisons difficult, and it is uncertain whether there is any difference between the complication rates after endovascular and surgical creation of AVF.
A previous systematic review (SR) and meta-analysis (Yan Wee et al., 2020) of the efficacy and safety of endovascular AVF creation included seven case series, four of which were prospective, and three retrospective. All the included case series lacked a comparative analysis with surgical AVF creation.

Six and 12-months patency was 92 and 85.7 percent, respectively. The procedure-related complication rate was 5.5 percent. However, given the lack of comparison with the surgical technique and the small sample size (300 patients), the results presented in the quoted SR should be interpreted with caution. ´real-world´ results were presented in a non-systematic review by Illig et al. (2020), showing only 50 percent primary maturation rate and a 37 percent failure rate. By contrast, excellent technical success (88-100 percent) and a one-year patency rate of 87 percent was reported in another non-systematic review (Jones et al., 2018) including six case series. Thus, there is significant heterogeneity across the published studies. One explanation to this might be heterogeneity regarding included patients and staff ‘s experience with this novel technique.

If this novel technique whould be introduced into routine clinical practice, appropriate selection of patients and adequate training of interventional radiologists and/or vascular surgeons would be important. Potential benefits of the endovascular, minimally invasive approach to AVF creation includes no scars after fistula creation and probably unimpaired opportunities for later conversion to surgical AVF creation, should the endovascular AVF fail. If these interventions would be performed in an interventional radiology suite, there might be a potential to slightly improve early access to AVF since, typically, no general anesthesia or OR would be needed.

This HTA report is the first SR that included NRCTs and provided an overview of complication rates across the included studies. In conclusion, there is a lack of high-quality head-to-head studies comparing endovascular with surgical AVF creation.

14. Future perspectives

Scientific knowledge gaps

The efficacy and safety of percutaneous compared with surgical AVF are uncertain, and cost-effectiveness is unknown. It is essential to perform randomized controlled trials that compare surgical and endovascular AVF in patients representative of the current dialysis patient population, with increasing age and comorbidity. Furthermore, it is essential to study how endovascular methods can complement existing surgical techniques for AVF creation in complex clinical settings. Cost-effectiveness and the availability of resources are also important. Furthermore, comparative studies, preferably RCTs, should be performed in hospitals with significant experience in endovascular techniques and in adequately selected patient groups. Such studies should include clinically relevant outcomes and long-term follow-up periods.

Ongoing research

A search of ongoing trials identified 95 studies, 16 of which studied endovascular AVF. Two of the 16 studies have already published results in the NEAT and EASE studies (Lok et al., 2017 and Berland et al., 2019). One study (NCT04404985) from the University of Alabama plans to randomize 80 patients to compare outcomes of endovascular and surgical AVF creation. Primary outcomes are AVF blood flow and diameter, and secondary outcomes are clinical maturity of the fistula and fistula survival. The remaining 13 studies are endovascular AVF case series.

15. Participants in the project

The question was nominated by
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Declaration of interests
None.

Project time
The HTA was accomplished during the period of October 1st, 2020 – March 31st, 2021.
Literature searches were made in October 2020.

Components of this Health Technology Assessment

- ☑ Description of methods
- ☑ PICO
- ☑ Full literature search
- ☑ Flowchart
- ☑ Selection based on relevance
- ☑ Quality assessment
- ☑ Data tabulation
- ☑ Evidence synthesis
- ☐ Meta-analysis
- ☑ Certainty of evidence by GRADE
- ☑ Summary
- ☑ Economical aspects
- ☑ Organisational aspects
- ☑ Ethical aspects
- ☑ Ongoing studies
- ☑ Excluded articles
- ☑ Participation of experts
- ☑ External review
- ☑ Knowledge gaps identified
- ☑ Conflict of interest reported

Appendix 1: PICO, study selection, search strategies, and references

Question at issue:
Is percutaneous endovascular AVF creation more effective and safer compared with surgical AVF creation regarding patient survival, patency, time to cannulation, technical adequacy for dialysis, functional usability, need for re-intervention, technical success, available vein length for cannulation and health-related quality of life in adult patients with end-stage kidney disease in need of hemodialysis?

PICO: (*P=Patient I=Intervention C=Comparison O=Outcome*)

P: Adult patients with end-stage kidney disease who are candidates for AVF operation
I: Percutaneous endovascular creation of AVF
C: Surgical creation of AVF
O:

Outcomes critical for decision-making

Patient survival
Re-intervention (endovascular/surgical)
Patency: primary (= without any reintervention), primary-assisted (= treated for failure but not to the level of occlusion), secondary (= reintervention for occlusion), primary-functional (= no occlusion, and functioning for hemodialysis), primary-functional assisted = treated for failure but not to the level of occlusion, and functioning for hemodialysis)
Functional usability:
-time to cannulation (cannulation type: 1- or 2 needle or central venous catheter (CVC) assisted outflow)
-technical adequacy* for dialysis (*e.g. Physiological suitability: defined as brachial flow > 500mL/min and diameter >4mm)
-cannulation success i.e., dialysis w/ 2 needles.
Complications

Outcomes important for decision-making

Technical success
Functional usability: vein length available for cannulation
Health-related quality of life

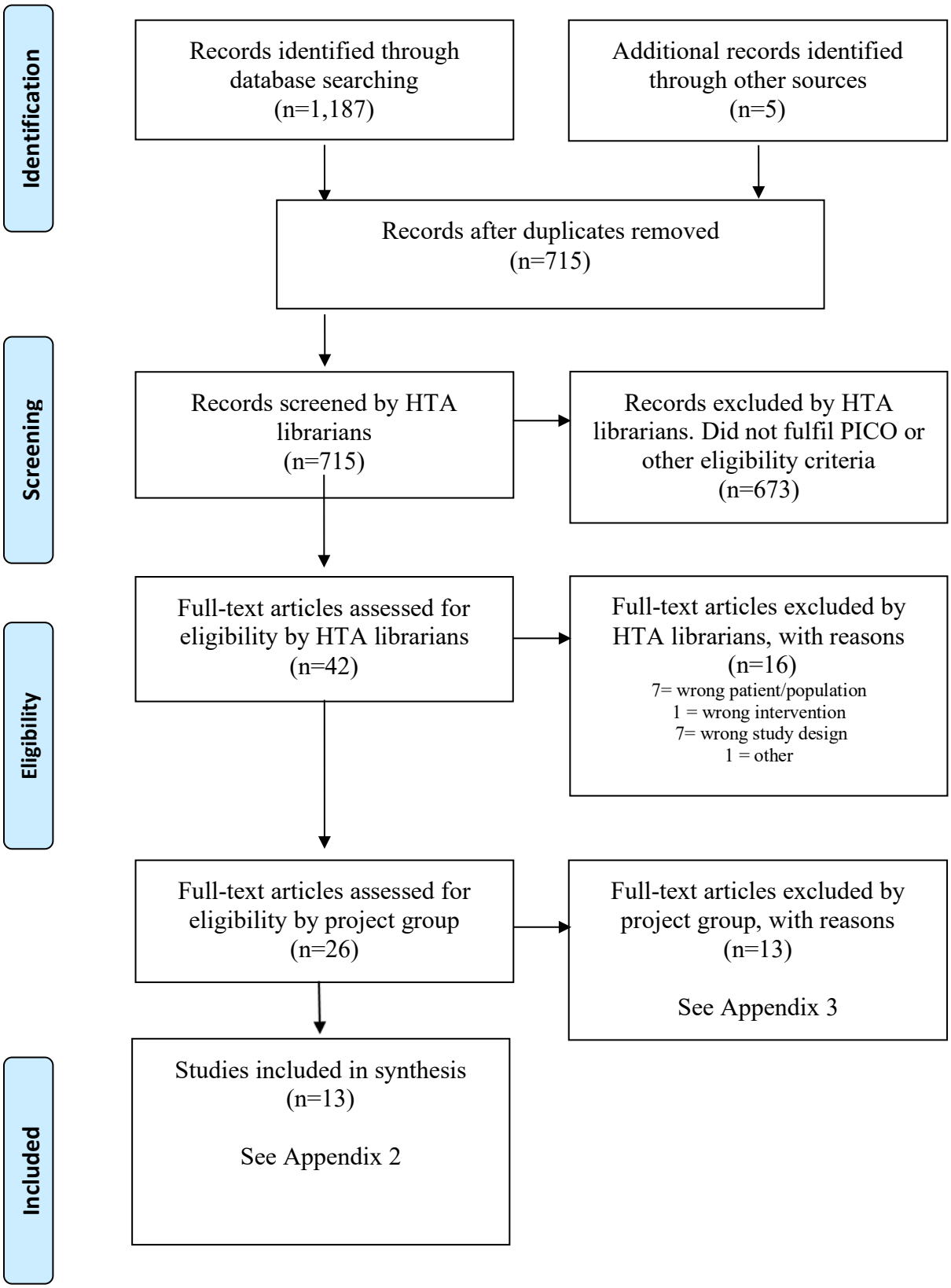
Eligibility criteria

Study design:
Randomised controlled trials
Non-randomised controlled trials
Case series etc. if ≥ 10 patients

Language:
English, Swedish, Norwegian, Danish

Publication date: 2015-

Selection process – flow diagram



Modified from Moher et al., 2009

Search strategies

Database(s): Ovid MEDLINE(R) ALL 1946 to October 13, 2020 (OvidSP)
Date:15 Oct 2020
No. of results. 561

#	Searches	Results
1	Endovascular Procedures/	19384
2	(percutaneous or endovascular).ab,kf,ti.	207834
3	1 or 2	212162
4	Arteriovenous Fistula/	13786
5	Arteriovenous Shunt, Surgical/	10626
6	(arteriovenous and fistula$).ab,kf,ti.	19803
7	(ellipsys or everlinq or wavelinq).ab,kf,ti.	22
8	(endo-AV$ or endoAV$).ab,kf,ti.	17
9	(AV-fistul$ or AVfistul$).ab,kf,ti.	1214
10	4 or 5 or 6 or 7 or 8 or 9	32533
11	exp Renal Insufficiency/	174561
12	renal dialysis/ or hemodiafiltration/	93461
13	(dialysis or renal or kidney or h?emodialysis or h?emo-dialysis).ab,kf,ti.	981770
14	11 or 12 or 13	1009755
15	3 and 10 and 14	1632
16	limit 15 to yr="2015 -Current"	586
17	**limit 16 to (danish or english or norwegian or swedish)**	**561**

Database(s): **Embase** 1974 to 2020 October 14 (OvidSP)
Date:15 Oct 2020
No. of results. 545

#	Searches	Results
1	endovascular surgery/	25515
2	(endovascular or percutaneous).ab,kw,ti.	294742
3	1 or 2	300219
4	arteriovenous fistula/ or kidney arteriovenous fistula/	22196
5	arteriovenous shunt/	7257
6	(arteriovenous and fistula$).ab,kw,ti.	22337
7	(ellipsys or everlinq or wavelinq).ab,kw,ti.	43
8	(endo-AV$ or endoAV$).ab,kw,ti.	46
9	(AV-fistul$ or AVfistul$).ab,kw,ti.	2331
10	4 or 5 or 6 or 7 or 8 or 9	36408
11	exp kidney failure/	368723
12	hemodialysis/ or continuous hemodialysis/	109871
13	exp hemodialysis patient/	28910
14	(dialysis or renal or kidney or h?emodialysis or h?emo-dialysis).ab,kw,ti.	1245195
15	11 or 12 or 13 or 14	1339535
16	3 and 10 and 15	2220

17	limit 16 to (embase or medline)	1636
18	limit 17 to yr="2015 -Current"	595
19	**limit 18 to (danish or english or norwegian or swedish)**	**545**

Database(s): **Cochrane library**
Date:15 Oct 2020
No. of results. 81
Cochrane reviews: 1
Trials: 80

ID	Search	Hits
#1	MeSH descriptor: [Endovascular Procedures] this term only	435
#2	(percutaneous or endovascular):ti,ab,kw (Word variations have been searched)	22882
#3	#1 OR #2	22882
#4	MeSH descriptor: [Arteriovenous Fistula] this term only	124
#5	MeSH descriptor: [Arteriovenous Shunt, Surgical] this term only	283
#6	((arteriovenous and fistula*)):ti,ab,kw (Word variations have been searched)	1101
#7	(ellipsys or everlinq or wavelinq):ti,ab,kw (Word variations have been searched)	3
#8	(endo-AV* or endoAV*):ti,ab,kw (Word variations have been searched)	1
#9	((AV-fistul* or AVfistul*)):ti,ab,kw (Word variations have been searched)	150
#10	#4 OR #5 OR #6 OR #7 OR #8 OR #9	1239
#11	MeSH descriptor: [Renal Insufficiency] explode all trees	8988
#12	MeSH descriptor: [Renal Dialysis] this term only	4179
#13	MeSH descriptor: [Hemodiafiltration] this term only	242
#14	((dialysis or renal or kidney or h*emodialysis or h*emo-dialysis)):ti,ab,kw (Word variations have been searched)	81800
#15	#11 OR #12 OR #13 OR #14	81813
#16	#3 AND #10 AND #15	154
#17	(clinicaltrials or trialsearch):so	333045
#18	**#16 NOT #17 with Cochrane Library publication date Between Jan 2015 and Dec 2020**	**81**

Reference lists
A comprehensive review of reference lists brought 5 new records

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Project: HTA - Efficacy and safety of endovascular versus surgical AV fistula creation for hemodialysis
Appendix 2: Characteristics of the included studies

Author, Year, Country	Study Design	Study Duration (years)	Study Groups; Intervention vs control	Patients (n)	Mean Age (years)	Men (%)	Outcome variables (related to PICO)
Inston, 2020, UK	NRCT	3 years	I=endoAVF WavelinQ C=sAVF	n=70	I=57 C=54	I=83.3 CI=72.5	Scope: The aim of the study was to compare a matched cohort of endovascular arteriovenous fistula with surgical radiocephalic arteriovenous fistulas. Outcome variables: Primary patency and secondary patency Time to cannulation Re-interventions Complications
Yang, 2017, USA	NRCT	1 year	I= endoAVF EverlinQ C= sAVF	n=120	I=60.0 C=61.1	I=65 CI= 61.7	Scope: To compare AVF- post-creation procedures and their associated costs in patients with SAVF with patients with a new endovascular created AVF (endoAVF) Outcome variables: Re-interventions Complications
Berland, 2019, USA	Case series	6 months	I=endoAVF EverlinQ	n=32	51	96.8	Scope: Multioperator single-arm prospective study to evaluate safety and efficacy of endoAVF through 6 months of follow. Outcome variable: Complications
Hebibi, 2019, France	Case series	14 months	I=endoAVF Ellipsys	n=34	62	58,8	Scope: The aim of this study was to report clinical experience using a percutaneous arteriovenous fistula(pAVF) which was created with the Ellipsys vascular access system Outcome variable: Complications

Hull, 2017, USA	Case series	1 year	I=endoAVF Ellipsys	n=26	45.5	38.4	Scope: To evaluate the safety and efficacy of arteriovenous fistula creation with pAVF Outcome variable: Complications
Hull, 2018, USA	Case series	1 year	I=endoAVF Ellipsys	n=107	56.7	73	Scope: To evaluate safety and efficacy of arteriovenous fistula created with pAVF Outcome variable: Complications
Hull, 2020, USA	Case series	6 months	I=endoAVF Ellipsys	n=60	64	56.7	Scope: A prospective study to evaluate the maturation of the endovascular arteriovenous fistula system for 2 needle cannulations Outcome variable: Complications
Lok, 2017, Canada, Australia, New Zealand	Case series	1 year	I=endoAVF EverlinQ	n=60	59.9	65	Scope: Prospective single arm and multicentre study to study the safety and efficacy of using an endovascular technique to create an arteriovenous fistula suitable for dialysis Outcome variable: Complications
Mallios, 2019, France	Case series	1 year	I=endoAVF Ellipsys	n=14	58	50	Scope: Retrospective study to report the results of early cannulation in patients who had an pAVF Outcome variable: Complications
Mallios, 2020a, France	Case series	1 year	I=endoAVF Ellipsys	n=234	64	63	Scope: Retrospective study to report midterm results of percutaneous arteriovenous fistula (pAVF) creation Outcome variable: Complications

Rajan, 2015, Paraguay	Case series	6 months	I=endoAVF EvelinQ	n=33	51	61	Scope: Prospective study to evaluate safety and efficacy of a percutaneous system Outcome variable: Complications
Shahverdyan, 2020, Germany, USA	Case series	1 year	I1=endo AVF WavelinQ I2=endoAVF Ellipsys	n=100	64.1	69	Scope: The aim of the study was to compare the clinical outcomes of Ellipsys with those of WavelinQ Outcome variables: Complications
Zemela, 2020, USA	Case series	Mean follow up 73 day	I=endoAVF WavelinQ	n=32	60.2	72	Scope: The aim of the study was to evaluatea single center´s success rates and short term follow up using the WavelinQ to create arteriovenous fistulas. Outcome variables: Complications

NRCT: Non-randomised controlled study. Incident patients: patients who did not start with hemodialysis,. Prevalent patients: patients on hemodialysis

Project: HTA - Efficacy and safety of endovascular versus surgical AV fistula creation for hemodialysis
Appendix 3. Excluded studies

Author, Year	Reason for exclusion
Arnold, 2018	Duplicate data with Yang, 2017
Beathard, 2020	Case series with no information on complications
Dawoud, 2020	Non-systematic review
Franco, 2020a	Case series with no information on complications
Franco 2020b	Cohort study, does not have PICO outcome
Illig,2020	Non-systematic review
Mallios, 2020b	Case series with too few patients.
Mallios, 2018	Duplicate publication with Mallios, 2020a
Mallios, 2020c	Duplicate publication with Mallios, 2020a
Radosa, 2017	Case series with too few patients.
Rognoni, 2020	Systematic review, included in the primary selection, which was excluded after final assessment since it was decided to use only original studies
Sultan, 2020	Case series with too few patients.
Yan Wee, 2020	Systematic review, included in the primary selection, which was excluded after final assessment since it was decided to use only original studies

Project: HTA - Efficacy and safety of endovascular versus surgical AV fistula creation for hemodialysis
Appendix 4.1 Outcome variable: Reinterventions

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients	Withdrawals - dropouts	Results Reinterventions		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Inston, 2019, UK	NRCT	n=70 I=30 C=40	I=0 C=0	0.4 per patient-year p=0.14	0.27 per patient-year	Did not included catheter placement in event rates (reinterventions).	?	?/-	+/ ?
Yang, 2017, USA	NRCT	n=120 I=60 C=60	I=10 (Kidney transplant n=1, Withdrew consent n=1, Death n= 3, Transfer to PD n=1, Occlusion of AVF n=1 Technical failure n=2, Palliative care n=1) C= 0	0.456 per patient-year p<0.0001	1.767 per patient-year	Prospective data collection in intervention group. Retrospective data collection in control group. Intervention patients from Australia, New Zealand and Canada. Control patients from USA. Adjusted for catheter placement and infections.	?	+/?	?

NRCT=Non-randomised controlled study

Project: HTA - Efficacy and safety of endovascular versus surgical AV fistula creation for hemodialysis
Appendix 4.2 Outcome variable: Primary patency at 1 year

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients	Withdrawals - dropouts	Results Primary patency at 1 year		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Inston 2019 UK	NRCT	n=70 I=30 C=40	I=0 C=0	56.5 % p=0.63	44 %		**?**	?/ -	+/?

NRCT=Non-randomised controlled study.

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Appendix 4.3 Outcome variable: Time to cannulation

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients	Withdrawals - dropouts	Results Time to cannulation		Comments	Directness*	Study limitations *	Precision *
				Intervention	Control				
Inston 2019 UK	NRCT	n=70 I=30 C=40	I=0 C=0	130 ± 86 days p=0.66	141 ± 118 days		**?**	?/ -	+/?

NRCT=Non-randomised controlled study.

Project: HTA - Efficacy and safety of endovascular versus surgical AV fistula creation for hemodialysis

Appendix 4.4 Outcome variable: Complications

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results Complications		Comments	Directness *	Study limitations *	Precision *
				Endovascular AV fistulas	Surgical AV fistulas				
Yang, 2018, USA and Canada	NRCT	I=60 C=60	I=10 (Kidney transplant; n=1 Withdrew consent; n=, 3 Death; n= 1 Transferred to PD; n=1 Occlusion; n=2 Technical failure; n=1 Transferred for palliative care; n=1) C= 0	Event rate/patient year Infection, outpatient care: 0 Infection, inpatient care: 0.019	Event rate/patient year Infection, Out-patient care: 0.967 Infection, inpatient care: 0.267	In both groups: Incident cases; n=27 Prevalent cases; n=33 Only registry data for the surgical AVF. No data about vessel diameter and no information about what type of surgical AVF (Forearm or upperarm) WavelinQ technique	?	?/-	+/?
Berland, 2019, Paraguay	Case series	32	8 (Dead; n=5 Technical failure; n=2 Lost to follow up; n=1)	Number of events (%) Bleeding; n=1 (3) Thrombosis; n=3 (9,4) Stenosis; n=1 (1)		The patient that was converted to surgical AVF was one of those with thrombosis Mean age 51 years, Mean BMI 26 kg/m^2 WavelinQ device			
Hull, 2017, USA	Case series	26	14 (Dead; n=5 Technical failure; n=3 Thrombosis; n=5 Lost to follow up; n=1)	Number of events (%) Hematoma; n=1 (4) Thrombosis; n=5 (19) Tract fistula; n=1 (4)		Mean age 45.5 years, Diabetes and obesity 65% Total 38 procedures Technical success n=23 Ellipsys device			
Hull, 2018, USA	Case series	107	26 (Dead; n=7 Technical failure; n=4 Thrombosis; n=4 Lost to follow up; n=11 AVF not created; n=1)	Number of events (%) Bleeding; n=3 (3) Thrombosis; n=15 (16) Stenosis; n=46 (43) Cannulation injury; n=13 (12) Steal syndrome; n=1 (1) Venous hypertension; n=3 (3) Neuropathy, =1 (1) Vein rupture; n=1 (1) Epitaxis; n=1 (1)		Incidence patients; n=39, Prevalence patients; n=64 Mean age 56.7 years, Obesity 50% Diabetes (65%) Total 205 procedures 360d Follow up time Ellipsys device			

Hull, 2020, USA	Case series	62	10 (Dead; n=7 Technical failure; n=2 Thrombosis; n=2 Lost to follow up; n=1	Number of events (%) Hematoma; n=6 (10) Embolisation; n=24 (39) Thrombosis; n=8 (13) Stenosis; n=7 (11) Cannulation injury; n=5 (8) Steal syndrome; n=1 (2) Venous hypertension; n=1 (2) Neuropathy; n=1 (2)		Incidence patients; n=16 (27%), Prevalence; n=46 (73%) Mean age 64 year, Mean BMI 30.7 kg/m^2 Diabetes 93% Total 70 procedures 180d Follow up time Ellipsys device			
Lok, 2017, Canada, Australia, New Zeeland	Case series	60	10 (Kidney transplant; n=1 Withdrew consent; n=, 3 Death; n= 1 Transferred to PD; n=1 Occlusion of AVF;n=2 Technical failures; n=1 Transferred for palliative care; n=1)	Number of events (%) Embolism; n=2 (3) Dissection; n=1 (2) Pseudoaneurysm; n=2 (3) Steal syndrome; n=1 (2) Thrombosis; n=2 (3) Neuropathy/Swelling, n=1(2)		The NEAT study. Same patient material in the endo AVF group as in Yang et al. Incident cases; n=27 Prevalent cases; n=33 Mean age 60.1 year, Obesity 65% Diabetes 61% One year follow up time WavelinQ device.			
Rajan, 2015, Paraguay	Case series	33	7 (Withdrew consent; n= 1 Death; n= 4 Technical failures; n=1 Lost to follow up; n=1)	Number of events (%) Hematoma; n=2 (6) Pseudoaneurysm; n=2 (6) Thrombosis; n=1 (3) Tip of the catheter detachment; n=1 (3) Cannulation injury; n=2 (6)		Incident cases; n=97 (46%) Prevalent cases; n=137 (54%) Mean age 51 year, Obesity 30% Diabetes 58% WavelinQ device. Technical success n =32			
Shahverdyan, 2020, Germany, USA	Case series (NRCT comparing two endovascular techniques)	WavelinQ n=35 Ellipsys n=65	?	Number of events (%) *WavelinQ device* Bleeding; n=1 (3) Coil migration; n=1 (3) Pseudoaneurysm; n=1 (3) *Ellipsys device* Hematoma; n=1 (1.5)		Retrospective analysis Incident cases; n=46 (46) Prevalent cases; n=54 (54) Mean age 64.2 year, Mean BMI 27.2 kg/m^2 Diabetes 37% Average follow up time 187 day			
Zemela, 2020, USA	Case series	35	3 (Lost to follow up; n=3)	Number of events (%) Hematoma; n=3 (9) Extravasation of contrast; n=1 (3) Vessel spasm; n=1 (3)		Retrospective analysis Incident cases; n=23 (66%) Prevalent cases; n=12 (35%) Mean age 60.2 year, Diabetes 60% Mean BMI 32.5 kg/m^2 WavelinQ device.			

NRCT=Non-randomised controlled study.

* + No or minor problems
? Some problems
- Major problems

Project: Efficacy and safety of endovascular versus surgical AV fistula creation for hemodialysis

Appendix 4.4 Outcome variable: Complications (Reinterventions)

Author, year, country	Study design	Number of patients n=	Withdrawals - dropouts	Results Reinterventions		Comments	Directness *	Study limitations *	Precision *
				Endovascular AV fistulas	Surgical AV fistulas				
Yang, 2018, USA and Canada	NRCT	I = 60 C = 60	I=10 (Kidney transplant n=1 Withdrew consent; n=, 3 Death; n= 1 Transferred to PD; n=1 Occlusion n=2 Technical failure n=1 Transferred for palliative care,n=1) C= 0	Event rate/patient year Angioplasty=0.038 Thrombolysis=0.019 Thrombectomy=0.038 Embolisation/ligation=0.133 Thrombin injection=0.038 Distal revascularization =0.019 Revision=0.038 Catheter placement=0.114 AVG creation=0.019 Surgical AVF creation=0.114	Event rate/patient year Angioplasty=0.933 Thrombolysis=0 Thrombectomy=0.20 Embolisation/Ligation=0.1 Thrombin injection=0 Distal revascularization=0 Revision=0.167 Catheter placement=0.433 AVG creation=0.067 Surgical AVF creation=0.3	In both groups: Incident cases; n=27 Prevalent cases; n=33 Only registry data for the surgical AVF. No data about vessel diameter and no information about what type of surgical AVF (Forearm or upper arm) WavelinQ technique	+/?	?	+/?
Inston, 2020, UK	NRCT	I = 30 C = 40	I=0 C=0	Number of events (%) Angioplasty; n=6 (20) Thrombolysis n=1 (3) Stent placement; n=1 (3) Coiling; n=4 (13) Transposition/revision,n=6 (20) Balloon assisted maturation; n=0	Number of events (%) Angioplasty; n=11 (28) Thrombolysis; n=2 (5) Stent placement; n=1(2,5) Coiling; n=0 Transposition/revision,n=0 Balloon assisted maturation; n=1 (2.5)	Same inclusion and exclusion criteria for both C and I groups. Not matched for diabetes and peripheral artery disease between C and I groups WavelinQ technique	+	?/-	?/-
Berland, 2019 Paraguy	Case series	32	I=8 (Dead; n=5 Technical failure; n=2 Lost to follow up; n=1)	Number of events (%) Surgical AVF; n=1 (1)		The patient that was converted to surgical AVF was one of those with thrombosis Mean age 51 years, Mean BMI 26 kg/m^2 WavelinQ device			
Hebibi, 2019, France	Case series	34	?	Number of events (%) Angioplasty; n=11 (32) Ligation; n=1 (3) Surgical AVF; n=2 (6) Transposition; n=2 (6) Valvulotomy; n=1(3)		Mean age 62 years, Diabetes and obesity 35% Ellipsys device Technical success n=33			

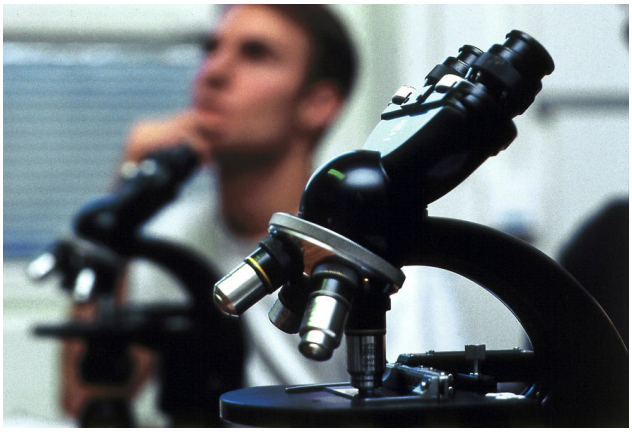
Hull, 2017, USA	Case series	26	I=14 (Dead; n=5 Technical failure; n=3 Thrombosis; n=5 Lost to follow up; n=1)	<u>Number of events (%)</u> Angioplasty; n=20 (77) Brachial vein Embolisation; n=6 (25) Ligation; n=4 (15) Transposition; n=7 (27) Valvulotomy; n=1 (4)		Mean age 45.5 years, Diabetes and obesity 65% Total 38 procedures Technical success n=23 Ellipsys device			
Hull, 2018, USA	Case series	107	I=26 (Dead; n=7 Technical failure; n=4 Thrombosis n;=4 Lost to follow up; n=11 AVF not created; n=1)	Number of events (%) Angioplasty; n=164 Embolisation; n=92 (86) Ligation; n=33 (31) Transposition; n=28 (26) Stent placement; n=8 (7)		Incidence patients; n=39, Prevalence patients; n=64 Mean age 56.7 years, Obesity 50% Diabetes (65%) Total 205 procedures 360d Follow up time Ellipsys device			
Hull, 2020, USA	Case series	62	I=10 (Dead; n=7 Technical failure; n=2 Thrombosis; n=2 Lost to follow up; n=1	<u>Number of events (%)</u> Angioplasty; n=63 (102) Thrombectomy; n=5 (8) Embolisation; n=24 (39) Ligation; n=18 (29) Valvulotomy; n=2 (3) Stent placement; n=2 (3)		Incidence patients; n=16 (27%), Prevalence; n=46 (73%) Mean age 64 year, Mean BMI 30.7 kg/m^2 Diabetes 93% Total 70 procedures 180d Follow up time Ellipsys device			
Mallios, 2020a, France	Case series	234	?	<u>Number of events (%)</u> Angioplasty; n=94 (40) Transposition; n=25 (11)		Retrospective analys Incident cases; n=97 (46%) Prevalent cases; n=137 (54%) Mean age 64 year, Obesity 35% Diabetes 55% Average follow up time 302 days Ellipsys device. Technical success n =232			
Rajan, 2015, Paraguay	Case series	33	I=7 (Withdrew consent; n=, 1 Death; n= 4 Technical failures;n=1 Lost to follow up; n=1)	<u>Number of events (%)</u> Angioplasty; n=3 (9) Thrombin injections; n=2 (6) Surgical AVF; n=1 (3)		Incident cases; n=97 (46%) Prevalent cases; n=137 (54%) Mean age 51 year, Obesity 30% Diabetes 58% WavelinQ device. Technical success n =32			

Shahverdyan, 2020, Germany, USA	Case-series	WavelinQ; n=35, Ellipsys; n=65	?	Number of events (%) *WavelinQ device:* Coiling; n=26 (74) Stent placement; n=1 (3) Surgical AVF; n=1 (3) *Ellipsys; n=65* Angioplasty; n=65 (100) Revision; n=1 (1.5)		Retrospective analysis Incident cases; n=46 (46) Prevalent cases; n=54 (54) Mean age 64.2 year, Mean BMI 27.2 kg/m^2 Diabetes 37% Average follow up time 187 days			
Zemela, 2020, USA	Case-series	35	I=3 (Lost to follow up; n=3)			Retrospective analysis Incident cases; n=23 (66%) Prevalent cases; n=12 (35%) Mean age 60.2 year, Diabetes 60% Mean BMI 32.5 kg/m^2 WavelinQ device.			

NRCT=Non-randomised controlled study

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

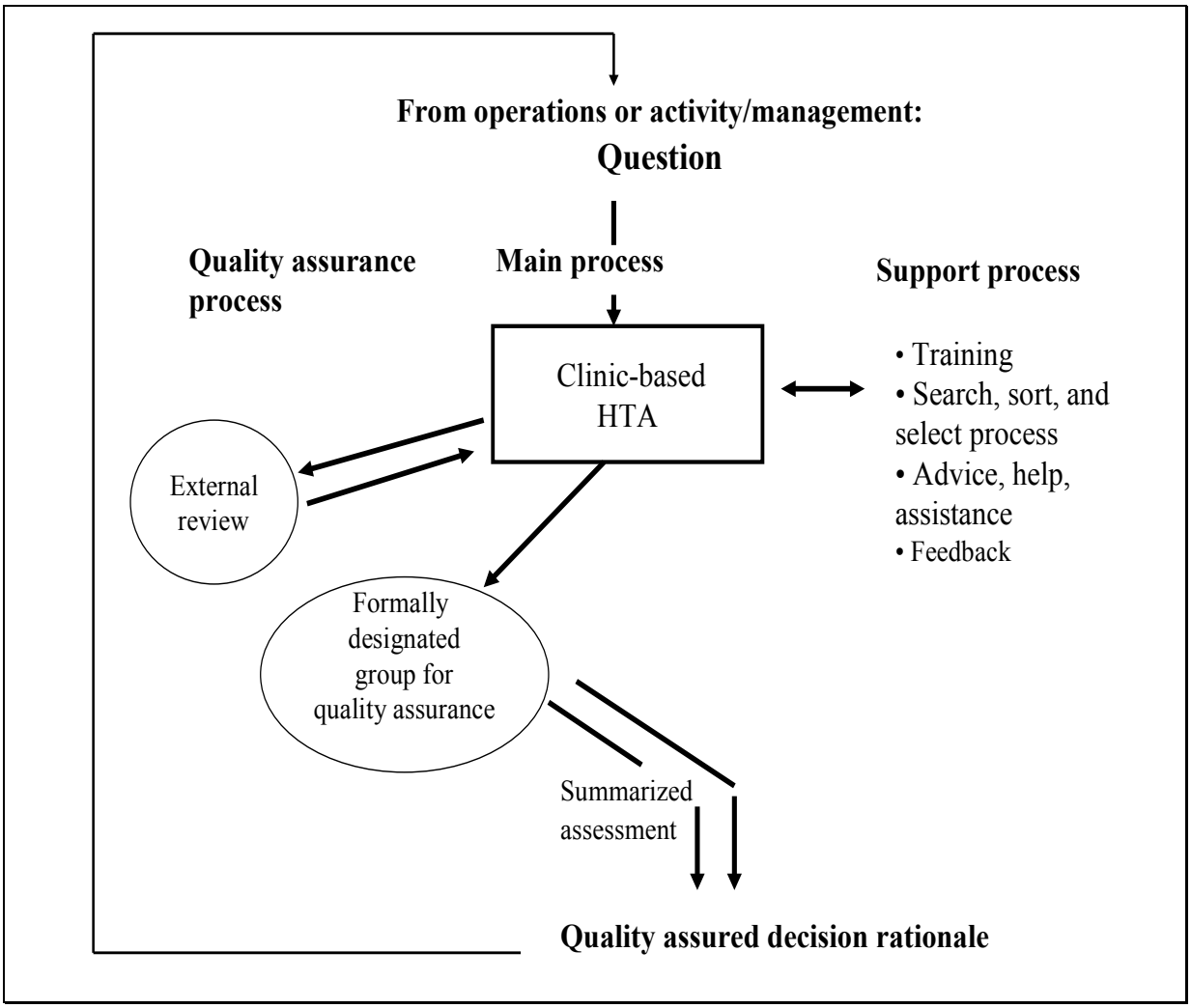
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the certainty of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High certainty of evidence	= (GRADE⊕⊕⊕⊕)
Moderate certainty of evidence	= (GRADE ⊕⊕⊕O)
Low certainty of evidence	= (GRADE ⊕⊕OO)
Very low certainty of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh
Professor, MD
Head of HTA-centrum


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

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