MEDICAL DEVICE MATERIAL PERFORMANCE STUDY

PTFE Safety Profile

Report Details

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Ed Margerrison, PhD

Director, Office of Science and Engineering Laboratories (OSEL)
Center for Devices and Radiological He
U.S. Food and Drug Administration

ECRI Corporate Governance

Michael Argentieri, MS
Vice President, Technology and Safety
Phone: (610) 316-2766
Email: margentieri@ECRI.org

Dheerendra Kommala, MD
Chief Medical Officer
Phone: (215) 341-5171
Email: dkommala@ECRI.org

Project Manager

Scott R. Lucas, PhD, PE
Principal & Director, Accident and Forensic Investigation
Phone: (804) 690-8542
Email: slucas@ECRI.org

If you have any questions or require additional information, please do not hesitate to call the Project Manager.

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Table of Contents

Table of Tables

Executive Summary

Key Points

1. Searches identified 1,782 citations; 52 articles were selected for inclusion.
2. The included studies most often found no difference in local responses, including patency, thrombosis, stenosis, or occlusion, when comparing a PTFE graft to a reference material or technique. The quality of evidence is low.
3. Studies indicate there is no difference in systemic responses, including mortality, myocardial infarction, and ischemia, when comparing a PTFE graft to other materials or techniques. The quality of evidence is low.
4. Studies of stent-grafts indicate PTFE stent-grafts yield better patency and stenosis results than percutaneous transluminal angioplasty (PTA). The quality of evidence is moderate, as this was reported in almost all human studies. Some studies found PTFE stent-grafts to have better patency than bare metal stents, but other studies found no difference.
5. The accident investigation and PRN data on PTFE devices was limited and generally involved a component braking or migrating resulting in a foreign body.
6. The PSO data included 4 reports of complication with associated harm scores indicating error, but no harm to the patient.
7. The healthcare technology alerts database returned the most relevant results (32 alerts). These consisted of IFU and labeling recalls, but also more serious hazards such as graft and stent component separation and graft tears.
8. Evidence gaps:
    a. Only 1 animal study met inclusion for PTFE as a material and reported inflammation, which could result in oxidative destruction of devices. Additional animal studies are indicated.
    b. The majority of studies included investigated the use of PTFE grafts, stents, and stent-grafts. There was relatively little on the use of PTFE for catheters, filters, and sutures.
    c. Multivariable controlled studies on grafts to confirm the trend of no differences between PTFE grafts and grafts made from other materials.
    d. RCTs on stents to confirm observed trend of low adverse events with PTFE stents relative to control groups.
    e. Research on outcomes other than occlusion and restenosis in PTFE stent-grafts compared to other materials.

Overview - Polytetrafluoroethylene (PTFE)

FDA engaged ECRI to perform a comprehensive literature search and systematic review to identify the current state of knowledge with regard to medical device material biocompatibility. Additionally, data derived from ECRI's Patient Safety Organization (PSO), accident investigations, Problem Reporting Network (PRN), and healthcare technology alerts were analyzed. This report focuses on answering 5 key questions provided by FDA and summarized below, regarding a host's local and systemic response to PTFE. If data did not exist to sufficiently address these questions, a gap was noted in this report. These gaps could represent areas of further research.

1. What is the typical/expected local host response to PTFE?

Patency, thrombosis, stenosis, and occlusion were the most investigated local responses among the studies included, which mostly addressed vessel repair or reconstruction. Pseudoaneurysm, re-exploration/reoperation, hematoma, and complication rate were also reported in several studies. The studies we reviewed most often found no difference in these responses when comparing a PTFE graft to a reference material or technique. Several studies report responses without a comparison to a reference material or technique. The available ECRI surveillance data were related, in part, to component separation or broken parts; however, it was unclear in the data whether this was related to material response due to insufficient biocompatibility or mechanical integrity and use of the device.

a. Can that response vary by location or the type of tissue the device is implanted in or near?

i. PTFE (Teflon) peripheral intravenous catheters (PICs) may have a higher rate of phlebitis than polyurethane PICs in adult patients. No inflammation or blockage was observed in a randomized control trial (RCT) of newborns.
ii. Evidence suggests PTFE stent grafts provide better patency rates than percutaneous transluminal angioplasty (3 RCTs).
iii. PTFE may provide better patency rates than a bare-metal stent. 1 RCT and 1 non-randomized controlled study (NRCS) found better, 1 RCT and 2 NRCSs found no difference.
iv. 1 systematic review (SR) and 1 RCT found PTFE to have worse patency rates than Dacron and bovine carotid artery graft, respectively.
v. Other studies reported PTFE to have similar or worse rates than polyurethane, autogenous grafts, and basilic vein transposition.

b. Over what time course does this local host response appear?

i. Signs of inflammation may appear within 24 to 48 hours.
ii. Other responses occurred within a few days to several years after implantation.

2. Does the material elicit a persistent or exaggerated response that may lead to systemic signs or symptoms – beyond known direct toxicity problems?

Mortality, myocardial infarction, and ischemia are the most investigated systemic responses among the studies included. The studies indicate there is no difference in these responses when comparing a PTFE graft to other materials or techniques.

a. What evidence exists to suggest or support this?

i. Several studies reported no difference in mortality between PTFE and Dacron (1 SR), bare-metal stent (4 RCT, 3 NRCS), or autologous vein (2 NRCS).
ii. Studies reported no difference in major cardiac events between PTFE and bare-metal stent (2 RCT), or vein graft (3 NRCS).
iii. Studies investigated ischemia were mostly single-arm studies.

b. What are the likely systemic manifestations?

Studies indicate there is no difference in systemic responses, including mortality, myocardial infarction, and ischemia, when comparing a PTFE graft to other materials or techniques.

c. What is the observed timeline(s) for the systemic manifestations?

Systematic responses occurred within a few days to several years after implantation.

d. Have particular cellular/molecular mechanisms been identified for such manifestations?

5 non-randomized studies investigated cytokines and white blood cell response, but did not specify a specific mechanism for manifestation of systemic response.

3. Are there any patient-related factors that may predict, increase, or decrease the likelihood and/or severity of an exaggerated, sustained immunological/systemic response?

Most studies did not report any patient-related factors regarding a systemic response. One study reported atrial fibrillation was a significant risk factor for patient mortality.[1] One study reported hepatic encephalopathy was influenced by albumin, and survival was influenced by total bilirubin, albumin, and model for end-stage liver disease score.

4. Are there any material-related factors that may predict, increase, or decrease the likelihood and/or severity of an exaggerated, sustained immunological/systemic response?

The included studies did not strongly indicate any associations between material-related factors and systemic responses.

5. **What critical information gaps exist and what research is needed to better understand this issue?**

   All gaps listed here could benefit from future research.

   a. Only 1 animal study met inclusion for PTFE as a material and reported inflammation, which could result in oxidative destruction of devices. Additional studies are indicated.
   b. The majority of studies included investigated the use of PTFE grafts, stents, and stent-grafts. There was relatively little on the use of PTFE for catheters, filters, and sutures.
   c. Multivariable controlled studies on grafts to confirm the trend of no differences between PTFE grafts and grafts made from other materials.
   d. RCTs on stents to confirm observed trend of low adverse events with PTFE stents relative to control groups.
   e. Research on outcomes other than occlusion and restenosis in PTFE stent-grafts compared to other materials.

Project Overview

FDA engaged ECRI to perform a comprehensive literature search and systematic review to identify the current state of knowledge with regard to medical device material biocompatibility. Specific materials or topics were selected by FDA based on current priority. For the first quarter of 2021, the following six topics were chosen:

1. Magnesium (Mg)
2. Complications associated with Polypropylene Mesh in Pre-, Peri-, and Post-Menopausal Women
3. Polytetrafluoroethylene (PTFE)
4. Acrylics 1: PMMA,
5. Acrylics 2: pHEMA
6. Acrylics 3: Cyanoacrylates

The systematic review was guided by key questions mutually agreed upon by FDA and ECRI. Data were extracted from literature articles and ECRI surveillance databases accordingly.

Key Questions

1. What is the typical/expected local host response to PTFE?

   a. *Can that response vary by location or type of tissue the device is implanted in or near?*
   b. *Over what time course does this local host response appear?*

2. Does the material elicit a persistent or exaggerated response that may lead to systemic signs or symptoms – beyond known direct toxicity problems?

   a. *What evidence exists to suggest or support this?*
   b. *What are the likely systemic manifestations?*
   c. *What is the observed timeline(s) for the systemic manifestations?*
   d. *Have particular cellular/molecular mechanisms been identified for such manifestations?*

3. Are there any patient-related factors that may predict, increase, or decrease the likelihood and/or severity of an exaggerated, sustained immunological/systemic response?

4. Are there any material-related factors that may predict, increase, or decrease the likelihood and/or severity of an exaggerated, sustained immunological/systemic response?

5. What critical information gaps exist and what research is needed to better understand this issue?

If data did not exist to sufficiently address these questions, a gap was noted in this report. These gaps could represent areas of further research.

Safety Profiles were written for the six materials listed above to include the summary of key findings from the systematic review and surveillance search and are included in this report.

Literature Search and Systematic Review Framework

The ECRI-Penn Evidence-based Practice Center (EPC) conducts research reviews for the Agency for Healthcare Research and Quality (AHRQ) Effective Health Care (EHC) Program. ECRI's scientific staff within our Center for Clinical Excellence has authored hundreds of systematic reviews and health technology assessments on 3,500+ technologies/interventions for ECRI's public- and private-sector clients. In addition to this work, ECRI staff have coauthored several methods papers on evidence synthesis published on the AHRQ Effective Health Care website and in peer-reviewed journals.

For this project, the clinical and engineering literature was searched for evidence related to biocompatibility of each material. Searches of PubMed/Medline and Embase were conducted using the Embase.com platform. Scopus was used initially to search nonclinical literature; however, it was determined that the retrieved citations did not meet inclusion criteria and that database was subsequently dropped from the search protocol. Search limits included publication dates between 2010 and 2020 and English as the publication language. ECRI and FDA agreed on appropriate host and material response search concepts as follows:

- **Material Response**
  - Strength
  - Embrittlement
  - Degradation
  - Migration
  - Delamination
  - Leaching

- **Host Response**
  - Local
    - Inflammation
    - Sensitization
    - Irritation
    - Scarring/fibrosis
      - *Keloid formation*
      - *Contracture*
    - Ingrowth
    - Erosion
  - Systemic
    - Cancer
      - Lymphoma
    - Inflammation
    - Immune Response
    - Fatigue
    - Memory Loss
    - Rash
    - Joint Pain
    - Brain Fog

Search strategies were developed for each concept and combined using Boolean logic. Several search approaches were used for comprehensiveness. Strategies were developed for devices of interest as indicated by FDA as well as the material-related strategies. Each of these sets were combined with the material and host response strategies. Detailed search strategies and

contextual information are presented in Appendix B. Text mining, logistic regression, and a search for "random" and "systematic" in titles and abstracts were used to prioritize only the top 35%-40% of the identified literature. This subset was screened against the inclusion criteria, first by title/abstract review, and then by full article review. An evidence prioritization scheme was used to ensure the inclusion of approximately 50 studies. Data were extracted from the resulting articles.

ECRI Surveillance Search Strategy

There are four key ECRI sources for medical device hazards and patient incidents. These databases were searched by key terms and device models. Relevant data were extracted to address the key questions agreed upon by FDA and ECRI. Patient demographics were extracted when available. All data presented were redacted and contain no protected health information (PHI).

ECRI surveillance data comprise ECRI Patient Safety Organization (PSO) event reports, accident investigations, problem reporting network (PRN) reports, and alerts. The PSO, investigations, and PRN reports included in this report include mostly acute patient events. We rarely find chronic conditions or patient follow-up reports, which are more prevalent in the clinical literature. Complications are reported directly by clinical staff, thus reports vary greatly in the level of detail provided.

ECRI Patient Safety Organization (PSO)

ECRI is designated a Patient Safety Organization by the U.S. Department of Health and Human Services and has collected more than 3.5 million serious patient safety events and near-miss reports from over 1,800 healthcare provider organizations around the country. Approximately 4% of these reports pertain to medical devices. Most of these reports are acute (single event) reports and do not include patient follow-up. These data were filtered by complication, and relevant reports were included in the analysis. "Harm Score" refers to the National Coordinating Council Medication Error Reporting and Prevention (NCC MERP) taxonomy of harm, ranging from A to I with increasing severity (see Figure 1). The entire PSO database was included in the search, with reports ranging from year 2004 through January 2021, unless otherwise noted.

Category A (No Error)

Circumstances or events that have the capacity to cause error.

Category B (Error, no harm)

An error occurred, but the error did not reach the patient (an "error of omission" does reach the patient).

Category C (Error, no harm)

An error occurred that reached the patient but did not cause patient harm.

Category D (Error, no harm)
An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm.

Category E (Error, harm)

An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention.

Category F (Error, harm)

An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization.

Category G (Error, harm)

An error occurred that may have contributed to or resulted in permanent patient harm.

Category H (Error, harm)

An error occurred that required intervention necessary to sustain life.

Category I (Error, death)
An error occurred that may have contributed to or resulted in patient's death.

Definitions

Harm: Impairment of the physical, emotional, or psychological function or structure of the body and/or pain resulting therefrom.
Monitoring: To observe or record relevant physiological or psychological signs.
Intervention: may include change in therapy or active medical/ surgical treatment.
Intervention Necessary to Sustain Life: includes cardiovascular and respiratory support (e.g., CPR, defibrillation, intubation)

Figure 1. NCC MERP "harm score," which is now regularly used by patient safety organizations.

Accident Investigation

ECRI has performed thousands of independent medical-device accident investigations over more than 50 years, including on-site and in-laboratory investigations, technical consultation, device testing and failure analysis, accident simulation, sentinel event and root-cause analyses, policy and procedure development, and expert consultation in the event of litigation. Our investigation files were searched by keywords, and the search was limited to the past 10 years unless we found landmark investigations that are particularly relevant to biocompatibility.

Problem Reporting Network (PRN)

For more than 50 years, ECRI's Problem Reporting Network (PRN) has gathered information on postmarket problems and hazards and has been offered as a free service for the healthcare community to submit reports of medical device problems or concerns. Each investigation includes a search and analysis of the FDA MAUDE database for device-specific reports. Based on our search findings, we may extend our analysis to all devices within that device's FDA-assigned product code. The PRN database was searched by keywords, and the search was limited to the past 10 years.

Healthcare Technology Alerts

We regularly analyze investigation and PRN data to identify trends in use or design problems. When we determine that a device hazard may exist, we inform the manufacturers and encourage them to correct the problem. ECRI publishes the resulting safety information about the problem and our recommendations to remediate the problem in a recall-tracking management service for our members. The Alerts database contains recalls, ECRI exclusive hazard reports, and other safety notices related to Medical Devices, Pharmaceuticals, Blood Products, and Food Products. This database was searched by keywords and specific make and model, and the search was limited to the past 10 years.

Safety Profile - Polytetrafluoroethylene (PTFE)

Full Name: Polytetrafluoroethylene
CAS Registry Number: 9002-84-0

Safety Brief - Systematic Review Results

The systematic review included clinical and engineering literature on biocompatibility (i.e., host response and material response) of polytetrafluoroethylene (PTFE) used in medical devices. In addition to fundamental material biocompatibility, we focused on specific devices known to be made of PTFE. The devices in **Error! Reference source not found.** were identified in the ECRI literature search and acknowledged by FDA to be within scope. These guided ECRI in review of this literature and ECRI's surveillance data. In the latter, only those devices listed in **Error! Reference source not found.** were included.

Table 1: Medical Devices Containing PTFE provided by FDA to Guide ECRI Searches

Regulatory Description	Product Code	Class
Diagnostic Intravascular Catheter	DQO	2
Percutaneous Catheter	DQY	2
Catheter, Intravascular Occluding, Temporary	MJN	2
Prosthesis, Vascular Graft, Of 6mm And Greater Diameter	DSY	2
Prosthesis, Vascular Graft, of less than 6mm Diameter	DYF	2
System, Endovascular Graft, Aortic Aneurysm Treatment	MIH	3
System, Endovascular Graft, Arteriovenous (Av) Dialysis Access Circuit Stenosis Treatment	PFV	3
Iliac Covered Stent, Arterial	PRL	3
Suture, Surgical, Nonabsorbable, Expanded, Polytetraflouroethylene	NBY	2
Nonabsorbable Expanded Polytetrafluoroethylene Surgical Suture For Chordae Tendinae Repair Or Replacement	PAW	2
Stent, Carotid	NIM	3
Stent, Superficial Femoral Artery	NIP	3
Coronary Covered Stent	NIV	HDE/3
Cardiovascular intravascular filter	DTK	2
Shunt, Portosystemic, Endoprosthesis	MIR	3

The Safety Brief summarizes the findings of the literature search on toxicity/biocompatibility of PTFE. Inclusion/exclusion criteria and quality of evidence criteria appear in Appendix A in the Appendices document. Quality of evidence ratings reflected a combination of the quality of comparative data (study designs), quantity of evidence (number of relevant studies),

consistency of evidence, magnitude of effect, directness of evidence, and evidence for a dose response or response over time. The search strategy appears in Appendix B, and a flow diagram documenting inclusion/exclusion of studies appears in Appendix C. Summary evidence tables with individual study data appear in Appendix D, and a reference list of studies cited in the Safety Brief appears in Appendix E.

A summary of our primary findings is shown in **Error! Reference source not found.**. We then turn to a detailed discussion of research on PTFE as a material as well as research on the various device categories.

Table 2: Summary of Investigated Responses from the Systematic Review

Application	Local Host Responses/Device Events	Quality of Evidence (local responses)	Systemic Responses	Quality of Evidence (systemic responses)
PTFE as a material (1 animal study)	Foreign Body Response	Very low	No studies	Very low (no evidence)
Catheters (2 human studies)	Phlebitis	Low	No studies	Very low (no evidence)
Filters (2 human studies)	Thrombosis	Low	Death Myocardial infarction Pulmonary embolism Stroke	Low
Grafts (22 human studies)	Patency, Thrombosis, Occlusion, Hematoma, Overall complications, Pseudoaneurysm, Displacement, Re-exploration/Re-operation, Small-for size syndrome, Conduit events, Non-maturation, Early allograft dysfunction, Bile leak, Edema, Stenosis, Extrusion, Biliary stricture, Acute cellular rejection, Inflammation, Granuloma	Low	Death, Pneumonia, Renal failure/insufficiency, Congestive heart failure, Mycardial infarction, Hypertension, Arrythmia, Respiratory complications, Skin rash, Sepsis, Diarrhea, Delirium, Hypovolemic shock, Ileus, Inflammation	Low
Stents (9 human studies)	Restenosis, Patency, Shunt dysfunction, Hepatic encephalopathy, Variceal rebleeding, Hepatic function decline, Thrombosis,	Low	Mortality, major cardiac events, myocardial infarction, Hospitalization, Respiratory failure/embolism, Dialysis,	Low

Application	Local Host Responses/Device Events	Quality of Evidence (local responses)	Systemic Responses	Quality of Evidence (systemic responses)
	Pericardial effusion, Tissue ingrowth, Granulation tissue, Stent migration, Recoarctation, Pseudoaneurysm		Hypertension, Distal embolization	
Stent Grafts (15 human studies)	Primary patency, Restenosis, Occlusion, Thrombosis, Embolism, Hematoma, Stent fracture, Endoleak, Migration, Target vessel failure, Hemorrhage, Pseudoaneurysm,	Moderate for Occlusion and Restenosis Low for other local responses	Post-implantation syndrome, Inflammatory markers, Hepatic encephalopathy, Mortality	Low
Sutures (1 human study)	Granuloma, Preseptal cellulitis, Abscess	Low	No Studies	Very low (no evidence)

PTFE as a Material

1 animal comparative study.[2] For further information see Table 1 in Appendix D.

Local Host Responses (human studies):

We did not identify any human studies reporting local host responses.

Local Responses (animal studies)

1 animal study (15 rats) reported whether there were local host reactions related to PTFE (Ovcharenko et al.).[2] At 2 weeks, a loose, 69 µm thick, collagen-based fibrous capsule was observed around the sample, indicating the end of the inflammatory process. Implantation sites demonstrated no foreign-body giant cells (FBGCs) or lymph nodes at two weeks. At 2 months, dense connective tissues 78 µm thick with evident collagen fibers were observed. FBGCs were present in the fibrous capsule. Such FBGCs can potentially contribute to oxidative damage and destruction of implanted devices. There were visible calcific deposits at the tissue/implant interaction.

Systemic Responses (human studies)

We did not identify any studies reporting systemic responses.

Overall Quality of Evidence

This summary was based on 1, small animal study, so the quality of evidence was very low.

Catheters

2 human studies (1 systematic review[3] and 1 randomized controlled trial[RCT][4]). For further information see Table 2 in Appendix D.

Local Responses/Device Events (human studies)

A systematic review of 35 studies concluded PTFE (Teflon) peripheral intravenous catheters (PICs) had a higher phlebitis incidence rate (33%, 95% CI: 25%, 41%) vs polyurethane Vialon (27%, 95% CI 21–32%).[3] Three of the studies included in

the review identified PTFE (Teflon) catheter use as a risk factor for the development of phlebitis. The mean patient age in this systematic review was 57 yrs.

An RCT of PIC use in newborns found no venous inflammation or blockage using either PTFE or PUR PICs.[4] Rates of catheter removal due to extravasation were similar between PTFE and PUR PIC's.

Local Responses/Device Events (animal studies)

We did not identify any animal studies reporting local host responses.

Systemic Responses

We did not identify any studies reporting systemic responses.

Overall Quality of Evidence

The occurrence of phlebitis/inflammation during the use of PTFE PICs was inconsistent, although that inconsistency may be related to the difference in age of the patients considered in each study. Overall, given the small amount of evidence, the quality of evidence supporting phlebitis/inflammation is low. Since systemic responses were not investigated in any study, the quality of evidence for systemic responses is very low.

Filters

Two human single-arm studies.[5,6] For further information see Table 3 in Appendix D.

Local Host Responses (human studies)

A single-arm study of embolic filters with a PTFE mesh observed thrombus in or near the filter in 9 out of 125 cases. No signs of filter migration or fracture were observed.[6]

Local Host Responses (animal studies)

We did not identify any animal studies reporting local host responses.

Systemic Responses

A single-arm study of an embolic filter with PTFE mesh found a major adverse event rate of 4%, including 2 deaths, 7 strokes, and 1 myocardial infarction out of 250 patients.[5] Another study reported 13 cases of lower-limb deep vein thrombosis and 5 cases of definitive or suspected pulmonary embolism in 125 patients who received an inferior vena cava filter.[6]

Overall Quality of Evidence

The evidence for thrombus is based on a single, moderately-sized, single-arm study. Therefore, the quality of evidence for thrombus is low. Similarly, each of the system responses is based on a single, moderately-sized, single-arm study. Therefore, the quality of evidence for systemic responses is also low.

Grafts

Twenty-one studies (22 human studies and 0 animal studies)

The human studies included 4 SRs,[7-10] 2 RCTs,[11,12] 14 non-randomized comparative studies,[1,13-25] and 2 single-arm studies.[26,27] For further information, see **Error! Reference source not found.**in Appendix D.

Local Host Responses (human studies)

The five most commonly investigated local responses were patency, thrombosis, occlusion, hematoma, and overall complication rate. The studies we reviewed most often found no difference in these responses or that the rate of these responses was less favorable using a PTFE graft compared to another graft material or technique. Several studies reported responses without a comparison to a reference material.

Below we detail some of the important findings from the SRs, RCTs, and prospective comparative studies. For all study results, see **Error! Reference source not found.**in Appendix D.

Medialization laryngoplasty: One SR (9 studies) from 2019 examined medialization laryngoplasty using **GORE-TEX** with or without arytenoid adduction.[8] Three studies reported no complications associated with Gor-Tex. Among the other 6 studies, there were 11 complications including 6 cases of extrusion into the lumen, 3 cases of persistent inflammation with granulation formation requiring removal of the **GORE-TEX** implant, and 2 cases of displacement. This review included studies with more than 10 cases of medialization laryngoplasty using GT, which contained information regarding complications and all reported series and case reports of patients with extrusion complications.[8]

Based on an in-depth review of 12 extrusions, voice function after removal of GT implant was reported in 7 cases. The consequences of these 7 removals were no substantive deterioration (1), speech/voice remained altered (1), injection of autologous fat was required to remedy glottal insufficiency (1), all symptoms resolved (1), voice not changed significantly (1), voice recovered (1), and MPT and perceptual vocal evaluation revealed slight deterioration (1). Details about the other 5 removals were not reported. The reports of extrusion included a follow-up period ranging from 1 month to 10 years.[8]

As for factors predicting response, the authors report "Use of excessively large implants in women and occurrence of postoperative hematoma followed by infection are factors that may cause complications. "There was no significant difference in the incidence of GT extrusion between patients with a preserved perichondrium (2 in 286) and those without a preserved perichondrium (4 in 269)."[8]

Hemodialysis: One 2019 SR examined Flixene and Acuseal early cannulation grafts and reported mean time to first cannulation was 2 to 21 days for Flixene and 1.3 to 15 days for Acuseal. Primary patency rates (43.3% and 43.6%) and secondary patency rates (73.4% and 70.5%) at 12 months were similar for Flixene and Acuseal, respectively. The rate of steal syndrome (0 to 8% and 0 to 11%) was also similar for Flixene and Acuseal, respectively. The percent of patients with access thrombosis was lower in those treated with Flixene (11 to 29%) compared with Acuseal (17 to 41%). Pseudoaneurysm was also slightly lower in the Flixene group (0 to 6% vs. 0 to 15%). Although this SR attempted to include RCTs and observational studies, mainly small retrospective cohorts were included. Follow-up was 9 to 36 months.[7]

This SR reported the same data for polycarbonate urethane for Avflo and polyurethane Vectra grafts. Time to first cannulation was for Avflo was 7 days; all patients cannulated within 48 hours. For Vectra, the range was 1 to 19 days. Primary and secondary patency rates at 12 months were 58.2% and 79.2%, respectively, for the Avflo graft. For Vectra the corresponding rates were 63.7% and 85.8%. Avflo had no cases of pseudoaneurysm and access thrombosis ranged from 16% to 42%. Steal syndrome was not reported. Vectra had a rate of 0 to 3.5% for steal syndrome, 23 to 37% access thrombosis, and 0 to 17% pseudoaneurysm.[7]

A second SR from 2015, reviewed the evidence for the Hemodialysis Reliable Outflow (HeRO) graft in complex hemodialysis patients. This review included both RCTs and nonrandomized studies. Follow-up ranged from 7 to 18.5 months. Primary and secondary pooled patency rates were 21.9% (9.6 to 37.2%) and 59.4% (39.4 to 78%), respectively. The authors reported that the rate of interventions required to maintain HeRO patency ranged from 1.5 to 3 procedures per year and the rate of dialysis access associated steal syndrome was 6.3% (range 1 to 14.7%).[9]

A 2015 single-arm study also examined PTFE for hemodialysis. The authors evaluated standard ePTFE graft or a heparin-bonded ePTFE graft for hemodialysis access.[27] They reported primary patency was 35% and 14% for heparin-bonded grafts and 29% and 12% for standard ePTFE grafts at 6 and 12 months, respectively. Assisted primary patency was 54%, 41%, and 27% for heparin-bonded grafts and 41%, 30%, and 23% for standard grafts at 12, 24, and 36 months, respectively. Secondary patency was 83%, 83%, and 81% for heparin-bonded grafts and 81%, 73%, and 68% for standard grafts at 12, 24, and 36 months, respectively. All the grafts were ready for cannulation between 2 and 4 weeks postoperatively with no difference between the groups.[27]

There were significantly fewer thromboses at 1 month in the heparin-bonded group compared with standard grafts. Six heparin-bonded grafts (8%) occluded in the first month compared with 16 standard grafts (20%). An anatomic cause for occlusion in the first month could be found in 5 (83%) of the 6 heparin-bonded grafts compared with only 8 (50%) of the 16 standard grafts (p=0.18). There were also significantly fewer thromboses in heparin-bonded grafts during the first 5 months. Fifty out of 80 heparin-bonded grafts thrombosed during the follow-up period and required 119 thrombolytic treatments (range 0-8) compared with 57/80 standard grafts, which required 145 thrombolytic treatments (range 0-8). Mean time to first thrombosis was 9.7±10 months in the heparin-bonded group and 7.8±10.6 months in the standard group.[27]

Bleeding complications, graft abandonment and intervention rates were similar in both groups. There were no differences between upper and lower arm accesses and between the two graft types in the upper arm and the two graft types in the lower arm. No patients developed heparin-induced thrombocytopenia. Steal syndrome occurred in 1 patient in each group.[27]

A 2011 RCT, mean follow-up 33 months, compared standard cuffed ePTFE graft (Venaflo) to the bovine carotid artery (BCA) graft (Artegraft) for permanent hemodialysis access. Although there was no significant difference in secondary patency rates, primary and assisted primary patency rates were significantly higher in BCA than in the ePTFE grafts (60.5% vs. 10.1% and 60.5% vs. 20.8% at 1 year, respectively). Total number of interventions per patient year needed to prolong patency was 1.45±0.19 in the BCA group and 1.99±0.25 in the ePTFE group. The most common intervention used to achieve this secondary patency was percutaneous angioplasty. There were 1.19±0.18 angioplasties per patient year compared to 1.86±0.24 in the BCA and ePTFE groups, respectively.[11]

The most common complication was graft thrombosis which occurred 0.77±0.16 times per patient year in the ePTFE group compared to 0.34± 0.09 times per patient year in the BCA group. In the BCA group, 4 patients underwent 7 interventions before the first episode of thrombosis, which was not significantly different from the ePTFE group (5 patients underwent 6 interventions). There was no significant difference found for pseudoaneurysm and steal syndrome between groups.[11]

The BCA graft survival advantage was most profound in the upper arm grafts with significantly higher primary and assisted patency rates. There was no statistically significant difference in the rate of thrombosis, pseudoaneurysm formation, or arterial steal syndrome between the BCA and ePTFE groups within either graft location subset.[11]

Another 2011 RCT compared frozen saphenous vein with synthetic **GORE-TEX** vascular graft for treating arteriovenous fistulas. At the end of the 12 month follow-up period, 70.50% of the saphenous vein group and 72% of the **GORE-TEX** group were still being dialyzed from their shunts. Flowmetry showed that at the end of the year, 41.66% of the **GORE-TEX** group had good flow, 41.66% had moderate flow, and 16.66% had poor flow. In the saphenous vein group, 40% had good flow, 50% had moderate flow, and 10% had poor flow, which did not show significant differences. One patient died from complications of renal insufficiency. Auscultatable murmur rates were similar with 75% in the saphenous vein group and 76.66% of the **GORE-TEX** group. There was no significant difference in thrill sensation between the two groups in any of the follow-up visits, and 71.42% of the saphenous vein group and 73.33% of the **GORE-TEX** group had sensible thrill on their fistulas at the end of the year. The overall thrombosis rates of the fistulas were also similar at the end of the follow-up period, with 25% in the saphenous vein group and 20% in the **GORE-TEX** group.[12]

One of the nonrandomized comparative studies, published in 2015, assessed AVG made of PTFE GORE-TEX vs. tunneled cuffed catheters (TCCs)for hemodialysis through 24 months follow-up. The rate of loss of vascular access was 54.8% with PTFE graft and 44.6% with TCC during a 1-year follow-up. At the 24-month follow-up, loss of the vascular access was observed in 71% in the PTFE graft group and in 58.9% in the TCC group. Median survival of PTFE grafts at 24 months was 8.7 ± 3.4 months, whereas TCC survival was 14.1 ± 3.1 months.[1]

Vascular access thrombosis caused vascular access loss in 64.5% of patients with a PTFE graft and in 7.1% of patients with TCC, a significant finding. The mean time interval between vascular access placement and the onset of these major complications was 7.5 ± 7.9 months in the PTFE group and 13.0 ± 14.9 months in the TCC group (p=ns). The time between vascular access placement and the diagnosis of thrombosis was 7.1 ± 8.1 months in the PTFE group and after 1.8 ± 1.2 months in the TCC group. The overall infectious and thrombotic complications of vascular access during the follow-up (any complication) were more frequent in the PTFE graft group compared with the TCC group: 41.9% vs 12.5%.[1]

One out of 31 patients with PTFE graft (3.2%) and 20/56 of TCC patients (35.7%) died during the 12-month follow-up (p=0.001). In adjusted Cox regression analyses at 12 months, the TCC group patients had a 10.2 times higher likelihood of death than the PTFE group. At 24 months, the same observations were confirmed: 5/31 (16.1%) patients in the PTFE group had died versus 28/56 (50%) patients in the TCC group. In the PTFE group, 3 patients died from cardiovascular diseases and 2 from sepsis. In the TCC group, 8 patients died from cardiovascular diseases, 7 from sepsis, 4 from cachexia, 3 from gastrointestinal disease, 2 from malignant neoplasm, and in 4 cases, the cause of death was not known. The Cox regression analysis revealed that TCC patients had a 3.2 times higher risk of death than the patients with PTFE graft.[1]

Multivariate analysis adjusted for age, gender, type of vascular access, number of previously created arterial venous fistulae, diabetes, atrial fibrillation, and cigarette smoking found diabetes and all thrombotic and infectious complications of vascular access to be significant independent predictors of access survival. After 12 months, nondiabetic patients experienced a vascular access survival 2.2 times higher than diabetic patients. Vascular access survived in 62.1% of nondiabetic patients, whereas it survived in 44.4% of diabetic patients during a 12-month follow-up. Moreover, patients experiencing any infectious or thrombotic complications had a 2.7 times higher risk of vascular access failure than those not experiencing complications. At the 24-month follow-up, only diabetes maintained its role as a risk factor for vascular access survival. Patients without

diabetes had a 1.9 times higher probability of vascular access survival than that of diabetic patients independently of the type of vascular access. Vascular access survival was 27.8% in diabetic patients and 43.1% in nondiabetic patients.[1]

Abdominal aortic aneurysm: One non-randomized comparative study compared the Anaconda, Zenith Excluder and Endurant grafts for the treatment of abdominal aortic aneurysm in a 2013 publication. Follow-up was through day 30. The authors found that mean blood loss during surgery did not differ among the 4 groups. Endografts were successfully implanted in all patients. There were no open conversions, no deaths, and no major perioperative complications. There was no postoperative increase in troponin levels. Minor complications included local hematomas in femoral incisions in 3 patients (1 each in Anaconda, Zenith and Excluder), who were treated conservatively.[24]

Mural thrombus classification in this study was as follows: 0%, 9 cases (10%); 0% to 25%, 31 cases (36%); 25% to 50%, 9 cases (10%); >50%, 38 cases (44%). No statistically significant association was recorded among classification of mural thrombus and different types of endografts. At 1-month follow-up, endoleaks were recorded in 17.9% of Anaconda patients, 11.5% of Zenith patients, 13.0% of Excluder patients, and in 10% of Endurant-treated patients. No statistically significant differences were found for endoleak, operative time, and contrast volume administered intraoperatively among the graft groups.[24]

The Anaconda group showed the highest mean value of IL-10 at 24 hours and differed significantly from the Excluder and Endurant groups. The Zenith group also showed higher mean values than the Excluder group. Comparisons among the groups of endograft types at 48 hours showed that mean values in patients treated with Anaconda endografts were higher compared with Endurant and Excluder endografts, whereas mean values in patients treated with Zenith endografts were significantly higher compared with Endurant and Excluder endografts.[24]

Patients treated with Anaconda endografts also showed the highest IL-6 mean values at 24 hours postoperatively. Comparisons at 48 hours showed significant differences for Anaconda vs. Excluder, Anaconda vs. Endurant, Zenith vs. Excluder, and Zenith vs. Endurant. With regard to IL-8, although patients treated with Anaconda endografts showed the highest mean values at 24 hours and 48 hours postoperatively, no statistical differences were observed among the patients treated with different types of endografts. Patients in the Excluder group showed statistically lower mean values at 24 hours and 48 hours postoperatively.[24]

Higher mean values of white blood cells were recorded after 24 hours in patients treated with the Anaconda endograft compared with the Excluder and Zenith endografts and the Endurant endograft compared with the Excluder and Zenith endografts. After 48 hours, statistically significant differences were observed among Anaconda and every other graft group as well as for the Endurant vs. Excluder and Zenith vs. Excluder groups. No statistically significant differences were observed among the different endograft types concerning platelet values at 24 hours and 48 hours postoperatively. No statistically significant correlation was found between the categories of the amount of clot in the abdominal aortic aneurysm (AAA) before repair and any marker of postimplantation syndrome. The group of patients had no clinical adverse events related to postimplantation inflammatory syndrome.[24]

No differences in the mortality and morbidity rates were observed among the 4 groups.[24]

Femoropopliteal artery bypass: One SR, conducted in 2014, compared Dacron to PTFE grafts for above-knee femoropopliteal artery bypass. The maximum study follow-up was 10 years. Data from 6 RCTs found that primary and secondary patency rates at 12 months were not significantly different for the 2 materials. However, at 24-, 36-, and 60-months primary patency rates were significantly better with Dacron compared with PTFE grafts (relative risk [RR] 0.79; p=0.003; RR 0.80; p=0.03; RR 0.85; p=0.02). Higher secondary patency rates were also found for Dacron at 24 months (RR, 0.75; p=0.02) and 60 months (RR 0.76-0.77; p=0.03-0.27). Although primary patency was similar between grafts (28% vs. 28%; p=0.12), secondary patencies were better with Dacron at 10 years (49% vs. 35%; p=0.01). There was no difference in amputation, overall morbidity, or mortality rates between the 2 surgical graft populations.[10]

One non-randomized comparative study, published in 2014, compared PTFE to saphenous vein graft for femoropopliteal bypass surgery for lower limb ischemia at 12 months mean follow-up. PTFE had a lower graft patency rate than saphenous vein grafts but the difference did not reach statistical significance.[22]

Local Host Responses (animal studies)

We did not identify any animal studies reporting local host responses.

Systemic Responses

Mortality and ischemia were the most investigated systemic responses among the studies included. Pneumonia, limb salvage, renal insufficiency, and cardiac events were also investigated in several studies. The studies we reviewed most often found no statistically significant difference in these responses when comparing the use of a PTFE graft to another graft material or technique, but a lack of statistical significance does not imply that the risks are similar. Several studies report responses without a comparison to a reference material.

Femorofemoral crossover: One 2018 retrospective comparative study found no statistically significant difference in the frequency of skin rashes at the 30-day follow-up visits for PTFE (4.5%) and femoral veins (3.3%) (autologous and cryopreserved).[15]

Hemodialysis: One prospective comparative study, published in 2015, on chronic hemodialysis patients reported mortality rates at up to 24 months follow-up. One out of 31 patients with PTFE graft (3.2%) and 20/56 of TCC patients (35.7%) died during the 12-month follow-up (p=0.001). In adjusted Cox regression analyses at 12 months, the TCC group patients had a 10.2 times higher likelihood of death than the PTFE group. At 24 months, the same observations were confirmed: 5/31 (16.1%) patients in the PTFE group had died vs. 28/56 (50%) patients in the TCC group. In the PTFE group, 3 patients died from cardiovascular diseases and 2 from sepsis. In the TCC group, 8 patients died from cardiovascular diseases, 7 from sepsis, 4 from cachexia, 3 from gastrointestinal disease, 2 from malignant neoplasm, and in 4 cases, the cause of death was not known. The Cox regression analysis revealed that TCC patients had a 3.2 times higher risk of death than the patients with PTFE graft.[1]

Peripheral arterial disease: One retrospective comparative study, published in 2014, reported systemic effects of precuffed ePTFE grafts compared with autologous saphenous vein (ASV) grafts used in patients with peripheral arterial disease through 5 years of follow-up. The following systemic responses were noted by study authors for PTFE vs. ASV: myocardial infarction 4 (2%) vs. 8 (3%); cord compression 6 (4%) vs. 5 (2%); arrhythmia 2 (1%) vs. 4 (1%); hypovolemic shock 0 vs. 1 (0%); pneumonia 5 (3%) vs. 4 (1%); respiratory insufficiency 5 (3%) vs. 2 (1%); cerebrovascular accident 1 (1%) vs. 2 (1%); neurologic 2 (1%) vs. 3 (1%); acute renal failure 2 (1%) vs. 5 (2%); diarrhea 3 (2%) vs. 2 (1%); ileus 0 vs. 1 (0%); and Delirium 5 (3%) vs. 4 (1%). None of these differences were statistically significant.[23]

Abdominal aortic aneurysm: One 2013 non-randomized prospective comparative study on treating AAA observed that fever was more intense in the group of patients receiving the Anaconda stent graft, mainly 24 hours postoperatively. The authors note that the maximum values of body temperature were positively correlated with the postoperative values of white blood cells (WBCs), IL-6, and IL-10, indicating a systemic inflammatory response. They recorded a more intense inflammatory response after Anaconda stent graft implantation compared with the other 3 endografts studied. Serum levels of IL-6 and IL-10 were significantly higher 24 hours and 48 hours postoperatively compared with preoperative levels in all groups. Patients in the Excluder group showed the smallest increase in levels of serum IL-6 and IL-10 at 24 hours and 48 hours postoperatively. Mean difference in cytokine levels after aneurysm exclusion was greater for Anaconda vs. Excluder compared with group Anaconda vs. Zenith.[24]

Anterior sector reconstruction: Finally, a 2018 retrospective comparative trial comparing nonringed ePTFE grafts to venous extension grafts for anterior segment reconstruction was unable to find a statistically significant difference in rates of sepsis between the two groups.[16]

Overall Quality of Evidence

The evidence base was large. While the bulk of the studies had control groups, the same intervention and comparator combination rarely occurred in more than one study. Therefore, the quality of evidence for local and systemic responses is low.

Stents

Nine human studies. (1 systematic review,[28] 3 RCTs,[29-31] and 5 non-randomized controlled studies[32-36]). For further information see Table 5 in Appendix D.

Local Host Responses (human studies)

The studies evaluated local responses of use of PTFE-covered stents for coronary procedures in 4 studies,[28,30,35,37] liver procedures in 3 studies,[29,32,36] and urethral procedures in 1 study.[34]

Coronary procedures: One systematic review[28] examined PTFE-covered stents and bare-metal stents for patients with focal infrarenal aortic occlusive disease, aortoiliac complex occlusive disease, or iliac artery occlusive disease in 49 studies, including RCTs and cohort studies/case series. Few included studies directly compared the 2 types of stents. The range of 1-year primary and secondary patency rates was similar in studies of covered stents and of bare stents. For recurrent stenosis and complications, the ranges of rates extended to greater frequencies in the studies of bare stents than in those of covered stents. One RCT[30] compared PTFE-covered stents and bare stents for patients with coarctation of aorta. Neither recoarctation nor pseudoaneurysm were significantly different between groups. There were no occurrences of obstruction, dissection, or post-coarctation of aorta syndrome in either group. One non-randomized controlled study[37] compared PTFE-covered stents and polyurethane-covered stents for patients with coronary artery perforation. Pericardial effusion was higher in the PTFE group (72% vs. 41%), but stent thrombosis and restenosis were not significantly different between the groups. One non-randomized controlled study[35] compared PTFE-covered stents with bare stents for patients with iliac artery occlusions. Overall primary patency was not statistically significant between the groups. Patency for Trans-Atlantic Intersociety Consensus (TASC) II D classified lesions significantly worse for the bare stent group (54% vs. 89%). No significant differences were found for TASC B and C classifications.

Liver procedures: One RCT[29] compared PTFE-covered stents with bare stents in patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) procedures. The risk of shunt dysfunction was significantly reduced in the covered stent group compared to the bare stent group (HR 0.60),. Early complications of the procedure (including death, thrombosis, and fever up to the first month of follow-up) and the risk of hepatic encephalopathy were not significantly different between the groups. One non-randomized comparative study[36] compared PTFE-covered stents with bare stents in patients undergoing TIPS. The occurrence of shunt dysfunction and reinterventions for stenosis were lower in patients with covered stents than in those with bare stents (22% vs 57% and 19% vs 33%, respectively),. Hepatic function deterioration was similar in both groups. One non-randomized comparative study[32] compared PTFE-covered stents with endoscopic therapy plus non-selective beta-blocker drugs in patients with liver cirrhosis and endoscopically confirmed gastroesophageal variceal bleeding. Variceal rebleeding occurred significantly less frequently for the PTFE-stent group (7.8% vs. 39.2%), but hepatic encephalopathy and overall adverse events were not significantly different between groups.

Urethral: One non-randomized controlled study[34] compared PTFE-covered external stents, PTFE-covered internal stents, and polyurethane-covered stents in patients with recurrent benign urethral strictures. Overall complications were significantly higher for external PTFE stents than the other 2 groups. Tissue ingrowth or membrane separation and stent migration were significantly higher for the internal PTFE stent group than the others. Patency was improved for external PTFE stents compared to internal PTFE stents (but not polyurethane stents) for up to 6 months after the procedure, but there were no significant differences in maintained patency beyond 6 months and up to 18 years. Granulation tissue formation was not significantly different between any of the groups.

Systemic Responses (human studies)

The studies evaluated systemic responses of use of PTFE-covered stents for coronary procedures in 5 studies[28,30,31,35,37] and liver procedures in 3 studies.[29,32,36]

Coronary procedures: One systematic review[28] examined PTFE-covered stents and bare-metal stents for patients with focal infrarenal aortic occlusive disease, aortoiliac complex occlusive disease, or iliac artery occlusive disease in 49 studies, including RCTs and cohort studies/case series. Few included studies directly compared the two types of stents. The range of distal embolism rates extended to greater frequencies in the studies of bare stents than in those of covered stents. One RCT[30] compared PTFE-covered stents and bare stents for patients with coarctation of aorta. There were no significant differences between groups in terms of mortality, duration of hospitalization, or number of normotensive patients. One RCT[31] compared Symbiot-covered stents, bare stents plus FilterWire, and bare-metal stents alone in patients with degenerative saphenous vein graft lesions. There were no significant differences between the groups for 6-month mortality, 6-month myocardial infarction (MI), or long-term MI. One non-randomized controlled study[37] compared PTFE-covered stents and polyurethane-covered stents for patients with coronary artery perforation. All-cause mortality, major adverse cardiovascular events, cardiac death, and MI were all not significantly different between the groups. One non-randomized controlled study[35] compared PTFE-covered stents with bare stents for patients with iliac artery occlusions. There were no significant differences between the groups in terms of overall complications, major cardiac events, respiratory failure, dialysis, and mortality.

Liver procedures: One RCT[29] compared PTFE-covered stents with bare stents in patients undergoing TIPS. There were fewer hospitalizations and number of hospital days in the covered group than in the bare group. Mortality was not significantly different between the groups. One non-randomized controlled study[36] compared PTFE-covered stents with bare stents in

patients undergoing TIPS. Median survival time was not significantly different between the groups. One non-randomized controlled study[32] compared PTFE-covered stents with endoscopic therapy plus non-selective beta-blocker drugs in patients with liver cirrhosis and endoscopically confirmed gastroesophageal variceal bleeding. Survival and overall adverse events were not significantly different between the groups.

Overall Quality of Evidence

The evidence base was moderately sized. Current evidence consistently suggests that occurrence of adverse events is lower or not significantly worse with PTFE stents than in control groups, suggesting that PTFE stents cause no unique harms (neither local toxicity, nor device events, nor systemic responses). The majority of the evidence comes from study designs with greater limitations. The single identified systematic review primarily included studies without control groups. Among the non-randomized comparative studies identified, most did not identify or control for potential confounding variables. Therefore, the quality of the evidence that PTFE in stents causes no harm is low.

Stent Grafts

Fifteen human studies (2 SRs,[38,39] 6 RCTs,[40-45] and 7 non-randomized comparative studies[46-52]). For further information, see Table 6 in Appendix D.

Local host responses (human studies):

Primary patency. Two SRs reviewed Viabahn and Hemobahn stent-grafts, one for the treatment of long de novo lesions of the superficial femoral artery and one for the treatment of popliteal aneurysms, and reported that the primary patency rate at 1 year varied between 44% and 86%.[38,39] Four RCTs compared the primary patency of PTFE stent-grafts (Flair, Fluency Plus, Viabahn with Proptan surface) to percutaneous transluminal angioplasty (PTA) for the treatment of in-stent restenosis in the superficial femoral artery or failing hemodialysis access.[40,42,44,45] All studies reported primary patency was significantly higher for the stent-graft groups at 12 (ranging 47.6 to 74.8%) and 24 months (ranging 26.9 to 58.4%).[40,42,44,45] One controlled cohort study found that for patients with portal hypertension undergoing the TIPS procedure, the Josent PTFE-covered stent-graft showed significantly better primary patency after 14 days (100%), 6 months (95%), and 2 years (82.9%) compared to the bare metal stent.[46]

However, an RCT and a controlled cohort study comparing the PTFE-covered stent-grafts to a bare metal stent found that primary patency rates did not significantly differ between the stent-graft groups and the bare metal stent groups at 3 and 4 years.[43,49] Patency rates diminish most rapidly in the first year after device implantation.[43]

Two studies reported that stent-graft failure was primarily due to occlusion and stenosis.[39,46] Portal venous thrombosis was identified also as a major risk factor for technical failure.[46] One controlled cohort study found that renal dysfunction was significantly associated with renal stent occlusion or stenosis.[49] One SR found significantly better patency with devices with a diameter of 6 mm or larger.[38] One RCT identified greater residual stenosis after initial PTA as a risk factor for loss of patency, and smaller diameter of the reference segment adjacent to the stenosis and the use of a deep vein as the outflow as predictors of primary patency, when treating failing dialysis vascular access due to restenosis.[45]

Restenosis. Two SRs,[38,39] 3 RCTs,[40-42] and one controlled cohort study[49] reported the occurrence of restenosis. In one SR reviewing Viabahn and Hemobahn stent-grafts for the treatment of long de novo lesions of the superficial femoral artery (SFA), in-stent restenosis occurred in only 5 cases out of 747 at 5 years, less than 1%.[38] Two RCTs reported the rate of restenosis was significantly lower for PTFE-covered stent-grafts (ranging 19.7 to 63.0%) compared to PTA (ranging 73.4 to 82.6%).[40,42] One study, in patients undergoing endovascular aneurysm repair (EVAR), found freedom from stenosis in renal artery stents was 92.9% at 1 year and 86.7% at 4 years for stent-grafts, significantly higher than bare-metal stents (84.5% and 58.9%, respectively).[49]

Occlusion. One SR,[39] 1 CC,[51] and 2 RCTs[41,42] reported the occurrence of occlusion. The SR reviewing Viabahn and Hemobahn stent-grafts reported occlusion leading to endograft failure in 19.8% of cases (n=42).[39] One RCT reported that the 12-month device-related/procedure-related AE rate was 2.3% for the Flair stent-graft, significantly lower than the rate for PTA (8.7%), and the most common adverse event was thrombotic occlusion (n=60).[42] Another RCT reported that target vessel occlusion for the Jostent stent-graft (14%) was comparable to bare metal stent at 5 years.[41] While another comparative cohort study,

comparing PTFE stent-graft to transcatheter embolization for the treatment of visceral artery aneurysm and pseudoaneurysm, reported occlusion as a complication in 2 out of 30 stent-grafts (6.7%) at 6 months.[51]

Thrombosis. One SR[38] and 3 RCTs[41,45,47] reported the occurrence of thrombosis. One RCT reported that stent thrombosis (10.9%) for the Jostent stent-graft was comparable to bare metal stent (5.6%) at 5 years.[41] In another RCT, new-onset thrombus occurred in 21% of Excluder ePTFE stent-grafts used in EVAR, compared to 14% in the bare metal stent group.[47] One RCT reported a single case of thrombosis (5%).[45] One SR noted that graft failure was related to acute thrombosis because of local disease progression, causing edge-stenosis and stent kinking.[38] One comparative cohort study postulated that the lack of pores in PTFE may prevent the formation of a thrombus and improve tissue repair by preventing platelets and inflammatory cells from crossing the graft.[52]

Embolism. One SR[38] and 1 RCT[42] reported a low occurrence of embolism. A SR reported a distal embolism rate of 3% among 747 patients across 14 studies.[38] One RCT reported a single case of embolism among 128 patients undergoing repair of hemodialysis access using the Flair stent-graft.[42]

Hematoma. One SR[39] and 1 RCT[42] reported a low occurrence of hematoma postimplantation. One SR reported 3 cases of access site hematoma requiring surgical revision in Viabahn and Hemobahn stent-grafts.[39] One RCT reported 5 cases hematoma after implant (4%).[42]

Stent fracture. One SR,[39] one RCT,[43] and 1 controlled cohort study[49] reported stent fractures. One SR reported 14 cases of endograft fracture (5.6%), which resulted in occlusion and type III and IV endoleaks.[39] The RCT found that stent fractures (2.6%) were significantly less common with the stent-graft, compared to bare metal stent (50%).[43] Similarly, 1 comparative cohort study reported stent fractures in 2 covered stents (1.2%), significantly fewer than in the bare metal stent group (n=8).[49] Another RCT reported no stent fractures observed in the 39 stent-grafts through 12 months.[44] PTFE-covered stent-grafts may be less prone to fracture due to greater flexibility provided by a strong fixation of the PTFE layers to the arteries.[49] Repetitive motility of the knee joint may predispose the endograft to kinking, fracture, and occlusion.[39]

Endoleak. One SR[39] and 1 controlled cohort study[52] reported endoleak as a postoperative complication. One SR reported 15 cases of endoleak (6%).[39] In 1 controlled cohort study, postoperative endoleak occurred in 13 cases (35.1%) after EVAR with the Excluder ePTFE stent-graft, comparable to 11 endoleaks in the Zenith group (21.6%). A change in fibrinogen degradation product (FDP) of ≤3.1 µg/mL at day 7 was predictive of an endoleak.[52]

Migration. One SR reported that postoperative endograft migration occurred in 13 cases (5.2%).[39] One RCT stated that there were no instances of device migration or kinking among 128 patients receiving a PTFE stent-graft.[42]

TVF, TVR, TLV. One RCT reported the significantly higher incidence of target vessel failure (TVF) (68.3%), target vessel revascularization (TVR) (48.2%), and target lesion revascularization (TLR) (43.9%) after percutaneous coronary intervention (PCI) in the stent-graft group than in the bare metal stent group after 2 years and annually up to 5 years.[41] TVF and TVR occurred more frequently after 2 years.[41]

Hemorrhage. One RCT reported 10 cases of postoperative hemorrhage (7.8%) in the PTFE stent-graft group.[42] One controlled cohort study reported a single case of hemorrhage requiring stent-graft removal out of 30 patients (3.3%).

Pseudoaneurysm and vessel rupture. One RCT also reported 9 cases of pseudoaneurysm (7%) and 2 cases of vessel rupture (1.6%) among 128 patients in the stent-graft group.[42]

Systemic Responses (human studies):

PIS. Two comparative cohort studies reported the occurrence of postimplantation syndrome after EVAR, defined as the composite of a body temperature of >38°C coinciding with C-reactive protein (CRP) >10 mg/L. In 1 study, the incidence of postimplantation syndrome (PIS) was 17.9%, significantly lower than the polyester stent-graft group (56.1%).[48] In this study, PIS occurred almost exclusively in the first 2 days after ePTFE implantation, and the amount of graft material implanted and new-onset thrombus were not associated with PIS.[48] In the other study, PIS occurred in 46.6% of the ePTFE stent-graft group within 72 hours post-EVAR procedure, not significantly different than the chromium-cobalt endoskeleton group (33.29%).[47] In this study, the development of PIS was found in part to be due to new-onset mural thrombus releasing pro-inflammatory

cytokines.[47] Although postoperative hospital stay was longer for patients with PIS, adverse outcomes at 24 months did not differ between those with and without PIS.[47]

Inflammatory markers. Two comparative cohort studies reported an increase in inflammatory markers after stent-graft implantation.[50,52] In 1 study, pulse wave velocity (PWV), and serum levels of IL-8 and IL-10 significantly increased at 12 months from baseline in both groups.[50] However, the effect on PWV and interleukins were was significantly less pronounced for PTFE compared to polyester. Additionally, WBC, highly sensitive CRP (hsCRP), and OPG, and decreased significantly from baseline for the PTFE group. Mean blood pressure, osteoprotegerin (OPG), and AAA diameter were independently associated with PWV, a marker of arterial stiffness.[50] In another study, WBC and CRP increased on day 1 after EVAR, peaked at day 3, and returned to pre-treatment level by day 7 in both groups, but the magnitude of change was significantly less in the ePTFE group.[52]

Hepatic encephalopathy. In 1 comparative cohort study, the Viatorr stent-graft was compared to bare metal stent for patients with portal hypertension undergoing TIPS. Hepatic encephalopathy (HE) occurred in 19.3% of cases in the Viatorr group (n=16), and required at least 1 revision within the first year after implantation in 4.8% of cases (n=4).[46]

Death. One SR,[39] 4 RCTs,[40-43] and 2 comparative cohort studies[46,51] reported deaths. In 3 RCTs[40,42,43] and 1 of the controlled cohort studies,[51] death was determined to be unrelated to the device. In the other studies, it was not stated whether death was attributable to the device. One SR reported that 1 patient died within 30 days from acute endograft thrombosis leading to acute myocardial infarction (AMI).[39] An RCT reported that all-cause deaths (29.8%) and MI (26.2%) were comparable to bare metal stent at 5 years.[41] The controlled cohort study reported 8.4% of patients in the PTFE stent-graft group died during the first year, which was also comparable to the incidence of death in the bare metal stent group.[46]

Overall quality of evidence:

The evidence base was large and included randomized and non-randomized comparative studies with more than 50 patients. The quality of evidence for patency and restenosis in PTFE stent-grafts is moderate, as this was reported in almost all human studies. Other local responses/events were reported in fewer studies, so the quality of evidence is low. The quality of evidence for systemic responses was low, because these outcomes rarely occurred (affecting few patients in the studies that reported them) and it is often unclear whether the response was due to the material.

Sutures

One human systematic review.[53] For further information see Table 7 in Appendix D.

Local Host Responses (human studies)

One systematic review reported PTFE has a significantly lower overall incidence of complications (5%, 95% CI 0.6–13) compared to fascia lata (25%, CI 14%–39%). However, PTFE had a higher rate of infections (1.9%, CI 0.2–5.4 vs. 1%, CI 0.5–1.6).

Local Host Responses (animal studies)

We did not identify any animal studies reporting local host responses.

Systemic Responses

We did not identify any studies reporting systemic responses.

Overall Quality of Evidence

This summary was based on a systematic review of 53 studies of a single procedure type using 4 materials. The rate of complications was lower with PTFE sutures, suggesting that they cause no harm. A moderate to large sample size was included for each material, but the study excluded RCTs, so the quality of evidence supporting the statement that PTFE sutures do not cause harm is low.

ECRI Surveillance Data

ECRI surveillance database searches were guided by the terms listed in Appendix F. The accident investigation and PRN data on PTFE devices generally involved a component breaking or migrating, resulting in a foreign body. The PSO data included 4 reports of complication with associated harm scores indicating error, but no harm to the patient. The healthcare technology alerts database returned the most results (32 alerts). These consisted of IFU and labeling recalls, but also more serious hazards such as graft and stent component separation and graft tears.

Patient Safety Organization

Search Results:

ECRI PSO identified 39 reports that involved PTFE materials. These incidents occurred between May 2017 and November 2020. Four reports involved complications, of which 3 reported no harm to the patient and 1 did not report a harm score.

All individual PSO event reports are redacted and included in Appendix F.

Table 3: Complications in PTFE-related PSO Event Reports

Complication	Suture	Graft	Total
Retained foreign object	1		1
Device malfunction	1		1
Hematoma/Hemorrhage	1		1
Occlusion		1	1
Total	**3**	**1**	**4**

Table 4: Harm score associated with PTFE-related event reports.

Harm Scores (NCC-MERP)		Suture	Graft	Total
A	No Error			
B1	Error, No Harm			
B2				
C				
D		3		3
E	Error, Harm			
F				
G				

Harm Scores (NCC-MERP)		Suture	Graft	Total
H				
I	Error, Death			
NULL*			1	1
Total		**3**	**1**	**4**

**Harm score was not reported*

Accident Investigations

Investigation files from 2005-2020 were searched to recover cases pertaining to the PTFE device categories listed above.

Search Results: 21 investigations were recovered but only 2 were considered relevant due to the following:

- Involved a device believed to be made of PTFE
- Used for longer than a temporary basis

These are summarized in **Error! Reference source not found.**.

A redacted description of these investigations are included in Appendix F.

Table 5: Accident Investigations of Patient Incidents Involving PTFE-related Devices

Device Type	# Investigations	Reported Problem and Findings
Intra-aortic Balloon	1	Systemic thrombosis reported
Sling	1	Foreign material migrated to abdomen

ECRI Problem Reports

Search Results: The search returned 10 reports submitted by ECRI members.

Key Issues: The reports detail includes device- tips breaking off and lodging in organs. Some reports specified patient injury.

Safety Concerns: The reports specified device failures and broken off tips migrating and lodging in organs.

All problem reports are redacted and included in Appendix F

Table 6: ECRI Problem Report Summary

Device Type	# Problem Reports	Reported Problem (number problem reports)
System, Endovascular Graft, Arteriovenous (Av)	1	Device tip broke off and migrated to the lung

Device Type	# Problem Reports	Reported Problem (number problem reports)
Dialysis Access Circuit Stenosis Treatment (PFV)		
System, Endovascular Graft, Aortic Aneurysm Treatment (MIH)	1	Wire tip broke off and lodged in aortic bifurcation
Prosthesis, Vascular Graft, Of 6mm And Greater Diameter (DSY)	1	Wire pulled out of graft during implanting
Catheter, Intravascular Occluding, Temporary (MJN)	7	Pre-use test failures, one failure during use

Healthcare Technology Alerts

Search Results: The search returned 33 manufacturer or regulatory agency-issued alerts describing problems with labeling, IFU updates, no FDA clearance, suspended manufacturing, failure to meet specifications, inclusion of incorrect components, broken component, component detachment, graft tears, leakage, and deployment and withdrawal difficulty, summarized in **Error! Reference source not found.**.

Table 7: Summary of Regulatory and Manufacturer Alerts

Device Type	# Alerts	Reported Problem
DQY (Percutaneous Catheter)	2 Manufacturer-issued	• Mislabeling
DSY (Prosthesis, Vascular Graft, of 6mm and Greater)	8 Manufacturer-issued	• Suspended manufacturing • Packaging issue • Mislabeling • IFU update
DSY (Prosthesis, Vascular Graft, of 6mm and Greater); DYF (Prosthesis, Vascular Graft, of less than 6mm)	2 Manufacturer-issued	• Graft tears • Mislabeling
MIH (System, Endovascular Graft, Aortic Aneurysm Treatment)	1 FDA-issued 16 Manufacturer-issued	• Component separation • Continued surveillance required • Deployment and/or withdrawal complications • Mislabeling • Wrong silicone lubricant used • Out of spec part leads to tip detachment • Leakage • Broken components • Rapidly emptying fill polymer syringe • IFU update
PFV (System, Endovascular Graft, AV Dialysis Access Circuit Stenosis Treatment)	16 Manufacturer-issued	• Deployment and/or withdrawal complications
PNF (Aortic Stent)	1 Manufacturer-issued	• No FDA clearance
PRL (Iliac covered Stent, Arterial)	1 Manufacturer-issued	• IFU update
NIP (Stent, Superficial Femoral Artery)	1 Manufacturer-issued	• Component separation

Potential Gaps

ECRI surveillance searches reflect mostly acute patient incidents that involved medical devices made of PTFE. Areas of particular concern involve incidents that result in direct tissue exposure to the material if there is moderate to high-quality evidence of acute or systemic reaction to this exposure, as determined by the systematic review. Topics with very low or low quality of evidence represent areas of potential gaps in the literature. If the literature revealed areas of new concern (e.g., systemic response to long-duration contact) and there is little supporting evidence, these are considered gaps.

PTFE as a Material

Only 1 animal study was included that reported local response, and there were no studies on systemic responses for PTFE as a material. While the quality of evidence was very low, the single study did report inflammatory response and indicated potential for associated oxidative damage and destruction of implanted devices. This indicates an area of further research considering the complications noted in the surveillance data of components breaking and separating.

Catheters

A single systematic review on PTFE PICs reported a higher phlebitis incidence vs. polyurethane (PUR) PICs. One RCT of PIC use in newborns found no inflammation or blockage with PTFE or PUR PICs. Additional research is indicated in each patient population (adult and neonatal).

Filters

One study reported thrombus in or near a PTFE mesh filter. A second study reported major adverse events including 2 deaths, 7 strokes, and 1 MI out of 250 patients. There were no comparative studies in these reports. Controlled trials are indicated considering the severity of these outcomes.

Grafts

Included studies suggest no difference in local or system outcomes with PTFE grafts compared to another graft material or technique. While the bulk of the studies had control groups, the same intervention and comparator combination rarely occurred in more than 1 study. Additional controlled studies containing these variables together in the same study is indicated for confirmation of this trend.

Stents

Current evidence consistently suggests that occurrence of adverse events is lower or not significantly worse with PTFE stents than in control groups, however the quality of evidence is low. RCTs are indicated to confirm this observed trend.

Stent Grafts

There is moderate quality of evidence supporting lower or similar rate of occlusion and restenosis in PTFE stent-grafts compared to other materials. Additional research is indicated to confirm this observation with other local outcomes, which were not observed as frequently as occlusion and restenosis.

Sutures

Only one human systematic review was included that reported local responses, which reported lower overall complication rate, but a higher rate of infection. There were no systemic responses reported. Additional research is indicated for PTFE sutures to determine if its material properties affect infection rate.

Appendix A. Inclusion/Exclusion Criteria and Quality of Evidence Criteria

Inclusion Criteria

1. English language publication
2. Published between January 2010 and August 2020
3. Human studies
4. Systematic reviews, randomized controlled trials, cohort studies, case-control studies, cross-sectional studies, case series
5. Studies that evaluate toxicity/biocompatibility of HA or priority devices that include this material

Exclusion Criteria

1. Foreign language publication
2. Published before January 2010
3. Not a study design of interest (e.g., in vitro lab study, case report, narrative review, letter, editorial)
4. Off-topic study
5. On-topic study that does not address a key question
6. No device or material of interest
7. No relevant outcomes (adverse events or biocompatibility not reported)
8. Study is superseded by more recent or more comprehensive systematic review

Quality of Evidence Criteria

1. **Quality of comparison** – is there evidence from systematic reviews including randomized and/or matched study data and/or randomized or matched individual studies?
2. **Quantity of data** – number of systematic reviews and individual studies providing relevant data, as well as the proportion of included studies that reported a specific outcome.
3. **Consistency of data** – are the findings consistent across studies that report relevant data?
4. Magnitude of effect – what is the likelihood of adverse effects compared to controls (with no device, lower dosage, shorter exposure time), and possibly number of patients likely to have harms.
5. **Directness of evidence** – do human studies isolate the effect of the device (i.e., can the adverse effects be attributed to the device)?
6. Is there evidence of a **dose response or time response** (e.g., adverse effects increase with longer exposure time)?

Appendix B. Search Summary

Strategies crafted by ECRI's medical librarians combine controlled vocabulary terms and free-text words in conceptual search statements that are joined with Boolean logic (AND, OR, NOT).

Most medical bibliographic databases such as Medline and Embase include detailed controlled vocabularies for medical concepts accessible through an online thesaurus. Controlled vocabularies are a means of categorizing and standardizing information. Many are rich ontologies and greatly facilitate information transmission and retrieval. Frequently seen examples of controlled vocabularies include ICD-10, SNOMED-CT, RxNorm, LOINC, and CPT/HCPCS.

Citations in PubMed are indexed with MeSH terms and those in Embase are indexed with terms from EMTREE. These terms are assigned either by a medical indexer or an automated algorithm. Several terms are selected to represent the major concept of the article – these are called "major" headings. This "major" concept can be included in search strategies to limit search retrieval. The syntax in Embase for this is /mj. We have used this convention in our strategies sparingly since indexing is subjective and we are using a sensitive search approach which errs in the direction of comprehensiveness.

Database providers build functionality into their search engines to maximize the usefulness of indexing. One of the most frequently used shortcuts is term explosion. "Exploding" in the context of hierarchical controlled vocabularies means typing in the broadest (root or parent) term and having all the related more specific terms included in the search strategy with a Boolean OR relationship. We use term explosions whenever feasible for efficiency. Feasibility depends on whether you wish to include all of the related specific terms in your strategy. For example, in one of our approaches we explode the Emtree concept mechanics. This explosion automatically added the all the following terms (n=174) and their associated entry terms (lexical variants and synonyms) to the strategy using an "OR" without the searcher having to type them in. That's one of the major advantages to searching using controlled vocabularies. We don't rely exclusively on controlled vocabulary terms since there are possible limitations such as inconsistent indexing and the presence of unindexed content. That's why we also include free text words in our strategies.

Literature Search for Polytetrafluoroethylene (PTFE)

Set Number	Concept	Search Statement
Material		
1.	**PTFE**	**'polytetrafluoroethylene'/exp OR polytetrafluoroethylen* OR polytetrafluorethylen* OR 'poly tetra fluoro ethylene*' OR 'poly tetra fluoroethylene*' OR 'polytetra fluoroethylene*' OR 'polytetrafluoro ethylene*' OR 'ptfe'/exp OR ptfe* OR epfte* OR 'e-ptfe*' OR cpfte* OR 'c-ptfe*' OR 'uptfe*' OR 'hd-ptfe*' OR 'hep-ptfe*'**
2.	PTFE Trade Names	'politef':ti,ab OR polytef:ti,ab OR teflon OR 'gore-tex*' OR goretex* OR 'gor-tex*' OR algoflo OR chemfluor OR dyneon OR fluon OR fluoroflex OR fluoroplast OR halon OR hostaflon OR novaflon OR polyfene OR softform OR tarflen OR tecnoflon OR technoflon OR tetron OR monotex OR cytoplast OR 'chord-x' OR sealptfe
3.	PTFE devices	'axs catalyst' OR 'scepter xc':ab OR 'scepter c' OR 'surefire spark' OR 'surefire precision' OR (('hero' OR 'haemodialysis reliable outflow' OR 'hemodialysis reliable outflow') NEXT/3 (graft* OR device)) OR 'fusion vascular graft' OR 'fusion bioline' OR (('spiral flow' OR 'spiral laminar flow' OR 'slf spiral') NEXT/3 (graft* OR prosthesis)) OR acuseal OR flixene OR exxcel* OR ((advanta OR venaflo OR carboflo OR distaflo OR impra OR dynaflo OR liefstream OR rebel) NEXT/4 (graft* OR stent*)) OR 'gore hybrid' OR propaten OR 'stretch vascular graft' OR 'ringed vascular graft' OR (gore*:ti,ab,kw,dn AND ('excluder*' OR tag OR 'carotid stent*' OR 'hybrid vascular graft*')) OR 'excluder'/dn OR 'aorfix*' OR 'ovation*' OR 'powerlink*' OR 'endograft power link'/dn OR covera OR 'fluency plus' OR 'cheatham platinum' OR 'cp stent*' OR 'afx'/dn OR 'viabahn*' OR 'via-bahn*' OR ('tigris' AND (gore* OR vascular OR stent*)) OR 'resolute microtrac' OR 'resolute integrity' OR graftmaster* OR jostent* OR 'advanta':dn OR 'afx'/dn OR 'aorfix'/dn

		OR 'cheatham platinum':dn OR 'cp stent*'/dn OR 'covered cp stent*':dn OR 'covered cheatham platinum stent*':dn OR 'excluder':dn OR 'fluency':dn OR 'fluency plus':dn OR 'gore excluder':dn OR 'gore tag'/dn OR 'graftmaster*':dn OR 'ovation':dn OR 'powerlink':dn OR 'propaten':dn OR 'tag'/dn OR 'acuseal':dn OR 'axs catalyst*':dn OR 'scepter xc':dn OR 'flixene':dn OR 'hero':dn OR 'jostent graftmaster':dn OR 'jostent selfx'/dn OR 'scepter c':dn OR 'sofia':dn OR 'sofia plus':dn OR 'viabahn*':dn
4.	Combine and Limit by language and publication date	(#1 OR #2 OR #3) AND [english]/lim AND [2011-2021]/py
5.	Limit by publication type	#4 NOT ('book'/it OR 'chapter'/it OR 'conference abstract'/it OR 'conference paper'/it OR 'conference review'/it OR 'editorial'/it OR 'erratum'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it OR 'tombstone'/it)

Material Response

6.		**'biocompatibility'/de OR biocompat* OR tribolog* OR 'bio compat*' OR 'biological* compat*' OR 'biological* evaluation'**
7.		'degradation'/exp OR degrad* OR biodegrad* OR bioabsorb* OR bioadsorb* OR absorbable OR adsorbable OR split OR splitting OR split* OR wear OR deteriorat* OR atroph* OR migrat* OR movement OR shift* OR transfer* OR 'delamination'/exp OR delamina* OR leach* OR filtrate OR filter* OR seep* OR evaginat* OR subsidence
8.		Leachable* OR extractable*
9.		(swell* OR shrink* OR contract* OR stretch* OR retract* OR extension OR extend* OR deform* OR creep OR plasticity OR degrad* OR disintegrat* OR fail*) NEAR/3 (graft? OR endograft? OR stentgraft? OR stent? OR suture OR catheter? OR microcatheter?)
10.		'mechanics'/exp
11.		'device material'/exp/mj
12.		'Biomedical and dental materials'/exp/mj
13.	Combine sets	#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
14.	**PTFE + Material Response**	**#5 AND #13**

Host Response

15.		**Host NEAR/2 (reaction* OR response*)**
16.		'toxicity'/exp OR toxic*:ti OR cytotox* OR teratogenic* OR genotox* 'carcinogenicity'/exp OR carcinogen*:ti
17.		'immune response'/exp OR 'immunity'/exp/mj OR 'hypersensitivity'/exp OR 'immunopathology'/exp/mj
18.		(immun*:ti OR autoimmun*:ti OR hypersens*:ti) NOT immunofluorescenc*:ti
19.		'inflammation'/exp OR inflamm*
20.		'foreign body' OR granuloma* OR 'foreign body'/exp OR (fibro*NEAR/2 capsule*)

21.		'adhesion'/exp OR 'tissue adhesion'/exp OR 'tissue response' OR 'bone response'
22.		(protrude* OR protrus*)
23.		'thrombosis'/exp OR 'stenosis, occlusion and obstruction'/exp OR 'stent complication'/exp OR restenosis OR thromb*
24.	Combine sets	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23
25.	**Combine sets** **PTFE + Material Response+ Host Response**	**#14 AND #24**
26.	**PTFE devices + Host response (excluding thrombosis)**	#3 AND #5 AND (#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22)
27.	**Final set**	**#25 OR #26**

Example Embase Explosion

Mechanics/exp

- Biomechanics
- Compliance (physical)
    - Bladder compliance
    - Blood vessel compliance
        - Artery compliance
        - Vein compliance
    - Heart muscle compliance
        - Heart left ventricle compliance
        - Heart ventricle compliance
    - Lung compliance
- Compressive strength
- Dynamics
    - Compression
    - Computational fluid dynamics
    - Decompression
        - Explosive decompression
        - Rapid decompression
        - Slow decompression
    - Gravity
        - Gravitational stress
        - Microgravity
        - Weight
            - Body weight
                - Birth weight
                    - High birth weight
                    - Low birth weight
                        - Small for date infant
                        - Very low birth weight

        - Extremely low birth weight
    - Body weight change
        - Body weight fluctuation
        - Body weight gain
            - Gestational weight gain
        - Body weight loss
            - Emaciation
        - Body weight control
        - Fetus weight
        - Ideal body weight
        - Lean body weight
        - Live weight gain
    - Dry weight
    - Fresh weight
    - Molecular weight
    - Organ weight
        - Brain weight
        - Ear weight
        - Heart weight
        - Liver weight
        - Lung weight
        - Placenta weight
        - Spleen weight
        - Testis weight
        - Thyroid weight
        - Uterus weight
    - Seed weight
    - Tablet weight
    - Thrombus weight
- Weightlessness
- Hydrodynamics
    - Hypertonic solution
    - Hypotonic solution
    - Isotonic solution
    - Osmolality
        - Hyperosmolality
        - Hypoosmolality
        - Plasma osmolality
        - Serum osmolality
        - Urine osmolality
    - Osmolarity
        - Blood osmolarity
        - Hyperosmolarity
        - Hypoosmolarity
        - Plasma osmolarity
        - Serum osmolarity
        - Tear osmolarity
        - Urine osmolarity
    - Osmosis
        - Electroosmotic
        - Osmotic stress
            - Hyperosmotic stress
            - Hypoosmotic stress
- Photodynamics

        - Photoactivation
            - Photoreactivation
        - Photodegradation
        - Photoreactivity
            - Photocytotoxicity
            - Photosensitivity
            - Photosensitization
            - Phototaxis
            - Phototoxicity
        - Photostimulation
    - Proton motive force
    - Shock wave
        - High-energy shock wave
    - Stress strain relationship
    - Thermodynamics
        - Adiabaticity
        - Enthalpy
        - Entropy
- Elasticity
    - Viscoelasticity
    - Young modulus
- Force
- Friction
    - Orthodontic friction
- Hardness
- Kinetics
    - Adsorption kinetics
    - Flow kinetics
        - Electroosmotic flow
        - Flow rate
        - Gas flow
        - Laminar airflow
        - Laminar flow
        - Powder flow
            - Angle of repose
            - Hausner ration
        - Pulsatile flow
        - Shear flow
        - Thixotropy
        - Tube flow
        - Turbulent flow
        - Vortex motion
        - Water flow
    - Motion
        - Coriolis phenomenon
        - Rotation
        - Vibration
            - Hand arm vibration
            - High frequency oscillation
            - Oscillation
            - Oscillatory potential
            - Whole body vibration
    - Velocity
        - Acceleration

            - Deceleration
            - Processing speed
            - Wind speed
- Mass
    - Biomass
        - Fungal biomass
        - Immobilized biomass
        - Microbial biomass
    - Body mass
    - Bone mass
    - Dry mass
    - Fat free mass
    - Fat mass
    - Heart left ventricle mass
    - Kidney mass
- Materials testing
- Mechanical stress
    - Contact stress
    - Contraction stress
    - Shear stress
    - Surface stress
    - Wall stress
- Mechanical torsion
- Molecular mechanics
- Plasticity
- Pliability
- Quantum mechanics
    - Quantum theory
- Rigidity
- Torque
- Viscosity
    - Blood viscosity
        - Plasma viscosity
    - Gelatinization
    - Shear rate
    - Shear strength
    - Shear mass
    - Sputum viscosity
- Viscoelasticity

Appendix C. Study Flow Diagram

I. 1,782 Citations identified by searches:

1. 1154 citations were not screened manually due to likely irrelevance (based on text mining, logistic regression, etc.)

2. 629 citations were screened for potential inclusion at title/abstract level (535 citations were selected by text mining in Distiller (30%); and 94 additional citations were selected - 89 citations by logistic regression (5%), 4 citations for including "random" or "systematic" in the title or abstract) 1 citation identified in the search for another material

a. 312 citations were excluded at the title/abstract level. Citations excluded at this level were off-topic, or not published in English, did not address a Key Question, or did not report a device of interest, or did not report an outcome of interest.

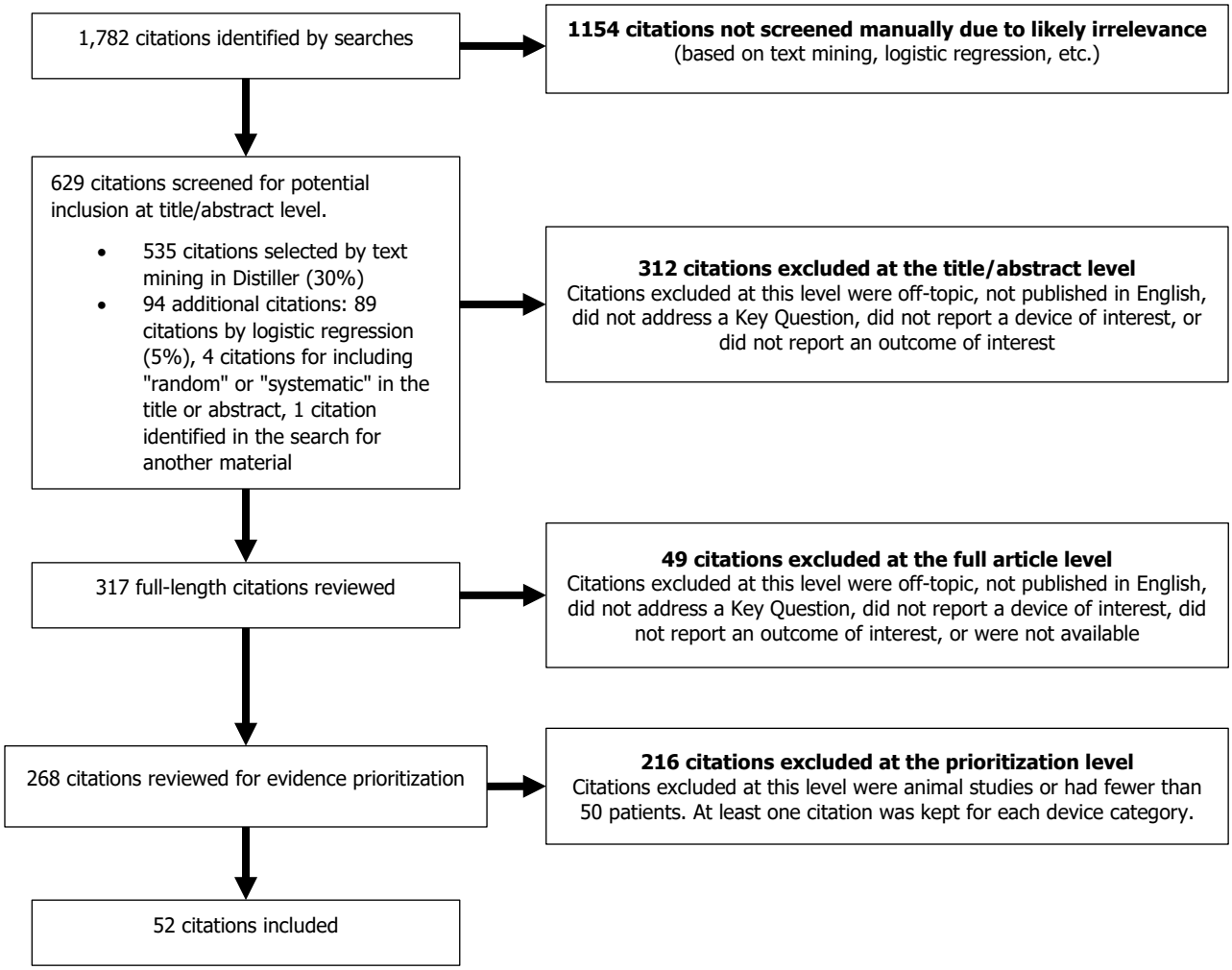
b. 317 full-length citations were reviewed:

i. 49 citations excluded at the full article level, Citations excluded at this level were off-topic, or not published in English, or did not address a Key Question, or did not report a device of interest, or did not report an outcome of interest, or were not available.

ii. 288 citations reviewed for evidence prioritization

1. 216 citations were excluded at the prioritization level. Citations excluded at this level were animal studies or had fewer than 50 patients. At least one citation was kept for each device category

2. 52 citations included.


1,782 citations identified by searches
1154 citations not screened manually due to likely irrelevance
(based on text mining, logistic regression, etc.)
629 citations screened for potential inclusion at title/abstract level.
535 citations selected by text mining in Distiller (30%)
94 additional citations: 89 citations by logistic regression (5%), 4 citations for including "random" or "systematic" in the title or abstract, 1 citation identified in the search for another material
312 citations excluded at the title/abstract level
Citations excluded at this level were off-topic, not published in English, did not address a Key Question, did not report a device of interest, or did not report an outcome of interest
317 full-length citations reviewed
49 citations excluded at the full article level
Citations excluded at this level were off-topic, not published in English, did not address a Key Question, did not report a device of interest, did not report an outcome of interest, or were not available
268 citations reviewed for evidence prioritization
216 citations excluded at the prioritization level
Citations excluded at this level were animal studies or had fewer than 50 patients. At least one citation was kept for each device category.
52 citations included

Appendix D. Evidence Tables

Table 8: PTFE as a Material - Health Effects (In Vivo) Animal Studies

Local Response/Toxicity

Source Citation: Ovcharenko 2020[2]

Study Design: Non-randomized comparative study

Device or Material: GORE-TEX vs. Hastalex [graphene oxide in poly(carbonate-urea)urethane] vs. glutaraldehyde

Route: Subcutaneous pouch on dorsum

Dose: 0.5 x 0.5 cm sample of each material

Frequency/Duration: 5 animals sacrificed at 14 days, 10 animals sacrificed at 60 days

Response: Dense connective tissues, FBGCs, Calcification

Species (strain): Wistar young rats

Gender: NR, NR.

Number per group: 15

Observed adverse effects: At 2 weeks, a loose 69 µm collagen-based fibrous capsule was observed around the sample, indicating the end of the inflammatory process. Implantation sites demonstrated no FBGCs or lymph nodes at 2 weeks. At 2 months, dense connective tissues 78 µm thick with evident collagen fibers were observed. FBGCs were present in the fibrous capsule. Such FBGCs can potentially contribute to oxidative damage and destruction of implanted devices. There were visible calcific deposits at the tissue/implant interaction.

Timing of adverse effects: 2 months

Factors that predict response: NR

FBGC = foreign body giant cell; NR = not reported

Table 9: Catheters - Health Effect (In Vivo) Human Studies

Local Response/Toxicity

Source Citation: Kale 2020[4]

Study Design: RCT

Device or Material: NEOCAN 24G PTFE PIC vs. Vasofix Certo 24G PUR PIC

Contact Duration: PTFE: 56±33 hours, PUR: 66±46 hours

Dose: 1 catheter

Frequency/Duration: Single administration

Response: Extravasation

Patient characteristics (gender, mean age): NR, PTFE: 34±4 weeks, PUR: 35±4 weeks.

Number per group: 32 PTFE, 32 PUR

Observed adverse effects: No inflammation or blockage was observed. 28 out of 32 PTFE catheters were removed due to extravasation, but this was not different than PUR catheters (25 out of 32).

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Lv 2020[3]

Study Design: Systematic review

Device or Material: Peripheral intravenous catheter

Contact Duration: NR

Dose: NR

Frequency/Duration: Single administration

Response: Phlebitis

Patient characteristics (gender, mean age): Overall 54% male, Overall mean: 57 yrs.

Number per group: 35 studies (9 RCT, 24 prospective, 2 retrospective) reporting on 20,697 PIVCs in 15,791 patients

Observed adverse effects: Anaysis concluded Teflon had a higher phlebitis incidence (33%, 95% CI 25–41) vs PUR Vialon (27%, 95% CI 21–32). 3 of the studies included in the review reported that Teflon catheter use was a risk factor for the development of phlebitis

Timing of adverse effects: NR

Factors that predict response: NR

CI= confidence interval; FBGC = foreign body giant cell; NR = not reported; PTFE = polytetrafluoroethylene; PUR = polyurethane; RCT = randomized controlled trial

Table 10: Filters - Health Effect (In Vivo) Human Studies

Local Response/Toxicity

Source Citation: Smouse 2013[6]

Study Design: Single-arm study

Device or Material: Crux Vena Cava Filter

Contact Duration: 180 days

Dose: 1 filter

Frequency/Duration: Single administration

Response: Thrombus in/near filter

Patient characteristics (gender, mean age): 58.4% male, 59.1±17.2 yrs.

Number per group: 125

Observed adverse effects: 9 cases of thrombus observed in or near the filter. No signs of filter migration or fracture were observed.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Gray 2018[5]

Study Design: Single-arm study

Device or Material: GORE Embolic Filter

Contact Duration: 30 days

Dose: 1 filter

Frequency/Duration: Single administration

Response: Death, Stroke, Myocardial infarction

Patient characteristics (gender, mean age): 61.2% male, mean 74.7 (51.3 - 92.6) years.

Number per group: 250

Observed adverse effects: The study reported 10 (4%) major adverse events (death, stroke, myocardial infarction). This was less than their goal of 12%. There were 2 deaths, 1 major stroke, 6 minor strokes, and 1 MI.

Timing of adverse effects: 1 death and the 6 minor strokes occurred within 2 days of carotid artery stenting (CAS). The MAEs occurred with 30 days of CAS.

Factors that predict response: NR

Source Citation: Smouse 2013[6]

Study Design: Single-arm study

Device or Material: Crux Vena Cava Filter

Contact Duration: 180 days

Dose: 1 filter

Frequency/Duration: Single administration

Response: Deep vein thrombosis, Pulmonary embolism

Patient characteristics (gender, mean age): 58.4% male, 59.1±17.2 yrs

Number per group: 125

Observed adverse effects: 13 cases of lower-limb DVT in 12 patients. 3 cases of definitive pulmonary embolism and 2 cases of suspected PE were reported.

Timing of adverse effects: The cases of PE occurred within 30 days of implantation.

Factors that predict response: NR

CAS= carotid artery stenting; DVT= deep vein thrombosis; MAE= major adverse event; MI= myocardial infarction; NR= not reported; PE= pulmonary embolism

Table 11: Vascular Grafts - Health Effect (In Vivo) Human Studies

Local Response/Toxicity

Source Citation: Drouven et al. 2019[14]

Study Design: Non-randomized comparative study

Device or Material: Basilic vein transposition vs. PTFE forearm loop graft as tertiary vascular access

Contact Duration: Mean follow-up 29 months

Dose: For the PTFE loop, a standard wall PTFE graft (Gore-Tex; W. L. Gore & Associates, Flagstaff, Ariz) with 6-mm diameter and 0.5-mm wall thickness was used.

Frequency/Duration: Single administration

Response: Aneurysm, Hematoma, Interventions required, Non-maturation, Occlusion, Primary assisted patency, Primary patency, Secondary patency, Stenosis, Thrombosis

Patient characteristics (gender, mean age): 69 males and 61 females; basilica vein 58.3 (SD 13.9) and PTFE 62.6 (SD 14.9) years

Number per group: Basilic vein 55 and PTFE 75

Observed adverse effects: A significantly higher 2-year primary assisted patency rate was found for the basilic vein group (72.7% (SE 6.5%) vs. 47.6% (SE 6.2%); p<.01). The 2-year primary patency rates and secondary patency rates were comparable between basilic vein and PTFE loop (25.1% (SE 6.6%) vs. 13.7% (SE 4.4%) [p=0.11] and 75.5% (SE 6.5%) vs. 73.9% (SE 5.3%) [p=0.17], respectively). Complications N and (PY^{-1}): Non-maturation: PTFE 0 (PY^{-1} 0.00) vs basilica vein 5 (PY^{-1} 0.04) p=0.008. Stenosis: PTFE 21 (PY^{-1} 0.11) vs. basilica vein 10 (PY^{-1} 0.07) p=0.073. Occlusion: PTFE 100 (PY^{-1} 0.54) v.s basilica vein 15 (PY^{-1} 0.11) p<0.001. Aneurysm: PTFE 3 (PY^{-1} 0.02) vs. basilica vein 1 (PY^{-1} 0.01) p=0.486. Hematoma: PTFE 0 (PY^{-1} 0.00) vs. basilica vein 2 (PY^{-1} 0.01) p=0.097

Timing of adverse effects: NR but mean follow-up was 29 months

Factors that predict response: Multivariate regression identified body mass index (HR 1.77; 95% CI 1.05–2.98; p=0.03) and age (HR 0.54; 95% CI 0.32–0.91; p=0.02) as predictors for failure regarding primary patency in PTFE loop patients. Previous catheter use (HR 0.29; 95% CI 0.12–0.70; p=0.006) and the presence of diabetes (HR 3.32; 95% CI 1.50-7.39; p=0.003) were independent predictors for failure regarding primary patency in basilic vein transposition patients. The incidence of total complications was significantly higher in the PTFE loop group with 0.70 PY^{-1} compared with 0.28 PY^{-1} in the basilic vein transposition group (p=0.001). In terms of intervention rate, a significantly higher percutaneous transluminal angioplasty rate and surgical revision rate were found in the PTFE loop group than in the basilic vein group (1.77 PY^{-1} vs. 1.05 PY^{-1} [p=0.022] and 0.20 PY^{-1} vs. 0.07 PY^{-1} [p=0.002], respectively).

Source Citation: Shakarchi et al. 2019[7]

Study Design: Systematic review

Device or Material: PTFE, Flixene, Acuseal, Polycarbonate, urethane, Avflo, Polyurethane

Vectra grafts

Contact Duration: 12 to 36 months

Dose: NR

Frequency/Duration: Single administration

Response: Access thrombosis, Cannulation time, Primary patency, Pseudoaneurysm, Secondary patency, Steal syndrome

Patient characteristics (gender, mean age): NR

Number per group: 19 studies total; number of patients for Flixene 230; Avflo 74; Acuseal 260; Vectra 762

Observed adverse effects: Flixene grafts (230 procedures in 5 studies): Primary patency rate at 12 months (95% CI): 43.3% (95% CI 31.6–55.4), Secondary patency rate at 12 months (95% CI): 73.4% (95% CI 63.0–82.7) Primary patency rate at 18 months range 21 to 34%, based on 2 studies. Secondary patency rate at 18 months range 51 to 57%, based on 2 studies Mean time to first cannulation (days) based on 3 studies: range 2 to 21 days. Avflo (4 studies and 74 procedures). Primary patency rate at 12 months (95% CI): 58.2% (95% CI 48.0–68.1). Secondary patency rate at 12 months (95% CI): 79.2% (95% CI 68.0–88.7). Primary patency rate at 24 months 56.3%, based on 1 study. Secondary patency rate at 24 months 81.8%, based on 1 study. Time to first cannulation was 7 days based on 1 study, and all patients cannulated within 48 hours: 2 studies. Acuseal (4 studies, 260 procedures). Primary patency rate at 12 months (95% CI): 43.6% (95% CI 30.7–56.9). Secondary patency rate at 12 months (95% CI): 70.5% (95% CI 49.7–87.8). Primary patency rate at 24 months was 0, based on 1 study. Secondary patency rate at 24 months was 35.1%, based on 1 study. Mean time to first cannulation (days) based on 3 studies: range 1.3 to 15 days. Vectra (based on 6 studies and 762 procedures). Primary patency rate at 12 months (95% CI): 63.7% (95% CI 53.4–73.4) based on 5 studies. Secondary patency rate at 12 months (95% CI): 85.8% (95% CI 82.9–88.4). Primary patency rate at 18 to 36 months range 15 to 63% based on 5 studies. Secondary patency rate at 18 to 36 months range 50 to 87%, based on 5 studies. Time to first cannulation range was 1 to 19 days based on 4 studies. Flixene, Access thrombosis: 11% to 29% based on 4 studies. Pseudoaneurysm: 0 to 6% based on 4 studies. Avflo, Access thrombosis: 16% to 42% based on 4 studies. Pseudoaneurysm: 0 based on 1 study. Acuseal, Access thrombosis: 17% to 41% based on 3 studies. Pseudoaneurysm: 0 to 15% based on 4 studies. Vectra, Access thrombosis: 23% to 37% based on 4 studies. Pseudoaneurysm: 0 to 17% based on 4 studies

Timing of adverse effects: Flixene ≤18 months; Avflo ≤24 months; Acuseal ≤24 months, Vectra ≤18 to 36 months follow-up

Factors that predict response: NR

Source Citation: Watanabe et al. 2019[8]

Study Design: Systematic review, Non-randomized comparative study conducted by study authors and a separate in-depth review of extrusions

Device or Material: Medialization laryngoplasty using **GORE-TEX** with or without arytenoid adduction

Contact Duration: NR

Dose: Case series: single 6 to 7 mm wide ribbon, SR: NR

Frequency/Duration: Single administration

Response: Displacement, Extrusion into the lumen, Inflammation requiring removal of the **GORE-TEX** implant

Patient characteristics (gender, mean age): Case series: 48 men and 20 women with a median age of 64 years (16 to 87 years).SR: 3/9 did not report gender; 176/310 patients were male; mean age NR. In-depth review of extrusions: 1 male, 6 female and 5 cases in which the gender was unknown.

Number per group: Case series conducted by authors: 68 cases. SR: 555 cases in 9 studies. In-depth review of extrusions: 12 cases

Observed adverse effects: Case series: One patient required emergent tracheostomy after developing cervical hematoma on postoperative day 1. After discharge, the patient repeatedly developed granulomas at the surgical site on his neck 3 months later. He developed laryngeal edema, and the GORE-TEX implant was

removed 6 months after surgery. One patient experienced unresolved edematous changes on the affected side of her larynx 1 month after the surgery. She then developed neck swelling. The GORE-TEX implant had extruded from the ventricle of the larynx 2 months after the surgery and required removal.

SR: The case series above is included in the 9 studies described here. 3/9 studies reported no complications associated with GORE-TEX. Of the 6/9 studies reporting complications associated with GORE-TEX, there were a total of 11 complications including 6 cases of extrusion into the lumen, 3 cases of persistent inflammation with granulation formation requiring removal of the GORE-TEX implant, and 2 cases of displacement. The 11 AEs were described in detail as follows: hyperthermia and granulation tissue (1 case), recalcitrant mucosal granulation and extrusion (1 case), rndolaryngeal extrusion (2 cases), persistent inflammation (1 case), extrusion (3 cases), implant displacement (2 cases), and inflammation and granulation (1 case)

Timing of adverse effects: Case series: median 19 months. Review of extrusions: 1 month to 10 years (median, 49 months)

Factors that predict response: Case series: The authors report "we found no specific factors, including age, sex, etiology, surgeon, operation time and intraoperative blood loss, associated with the occurrence of complications." SR: The authors report "Use of excessively large implants in women and occurrence of postoperative hematoma followed by infection are factors that may cause complications." "There was no significant difference in the incidence of GT extrusion between patients with a preserved perichondrium (2 in 286) and those without a preserved perichondrium (4 in 269), p = 0.44."

Source Citation: Cho et al. 2018[26]

Study Design: Single-arm study

Device or Material: Extra-cardiac Fontan procedure with 16 mm PTFE (**GORE-TEX** vascular graft; W.L. Gore & Associates, Inc., Flagstaff, AZ, USA) conduit vs. matched controls with conduit size of 19.2 ± 1.4mm (18 mm, n=34; 20 mm, n=23 and 22 mm, n=9)

Contact Duration: ≤16 years

Dose: 16 mm PTFE conduit vs. a larger conduit (mean 19.2±1.4 mm)

Frequency/Duration: Single administration

Response: Catheter intervention, Conduit-related events, Freedom from catheter-based intervention

Patient characteristics (gender, mean age): Mean age PTFE 16 mm 2.9±1.2 years and matched control group 3.1±1.2; gender NR

Number per group: PTFE 16 mm group 66 patients and 66 control patients matched for age and size

Observed adverse effects: There was a significant difference in conduit-related events between the groups (1 in 16-mm PTFE, 5 in matched controls; p=0.031). In a paired cohort from the 2 groups including patients who were followed up for more than 10 years (15 patients from each group), the body mass index was 51.0 ± 33.2% in 16 mm PTFE and 30.3 ± 34.2% in matched controls. The decreases in the conduit cross-sectional areas for the paired patients in 16 mm PTFE (n=20) and matched controls (n=20) were 14.9 ± 19.7% and 24.5 ± 15.5% (p=0.076), respectively. Final follow-up: There were no significant differences at the last follow-up catheterization between the 16 mm and matched control groups. There were also no differences in the inferior vena cava pressure or intraconduit pressure between the two groups.

Conduit change N: 16 mm group 1 (due to progressive valve regurgitation 16 years after the procedure) vs. matched controls 2 (due to conduit thrombosis and stenosis 2 months and 9 years after ECFP); Conduit thromboembolectomy N: 16 mm group 0 vs. matched controls 1; atrioventricular valve repair N: 16 mm group 1 vs. matched controls 2; atrioventricular valve replacement N: 16 mm group 1 vs. matched controls 0; aortic valve replacement N: 16 mm group 1 vs, matched controls 0; dub-aortic muscle resection N: 16 mm group 0 vs. matched controls 1; pulmonary artery angioplasty N: 16 mm group 0 vs. matched control 4;

pulmonary vein angioplasty N: 16 mm group 1 vs. matched control 1; Catheter intervention N: 16 mm group 11 vs. matched control 6, p=0.369; Collateral vessels closure N: 16 mm group 6 vs. matched control 6; Balloon pulmonary angioplasty N: 16 mm 5 vs. matched control 0; conduit-related events N: 16 mm group 1 vs. matched control 5, p=0.031;

Timing of adverse effects: Mean follow-up PTFE 7.8 ± 6.0 years and matched control 9.1 ± 4.9 years

Factors that predict response: NR

Source Citation: Goja et al.2018[16]

Study Design: Non-randomized comparative study

Device or Material: AS reconstruction using nonringed ePTFE grafts (GORE-TEX, W.L. Gore & Associates, Inc., Newark, DE, USA) vs. venous extension grafts

Contact Duration: ≤2 year

Dose: ≤5 mm

Frequency/Duration: Single administration

Response: Acute cellular rejection, Dysfunction (graft), Bile leak, Biliary stricture, Bleeding, Graft loss, Patency, Re-exploration, Small-for-size syndrome, Thrombosis, Vascular complications, allograft

Patient characteristics (gender, mean age): Mean age of patients was 48 ± 10.21 years; 366 male and 71 female.

Number per group: V graft 200 patients and ePTFE in 237 patients

Observed adverse effects: The MHV graft patency rate at 7 and 14 days was 100% in each group. Similarly, the patency rate for V vs. ePTFE at 1 month (99.5% vs. 97.5% p=0.09), 3 months (98.5% vs. 95.8% p=0.09), and 12 months (96% vs. 92.8% p=0.15) was comparable between the groups. No patient was re-explored for graft blockage. There was no complication attributable to ePTFE in this cohort. There was no difference in bile leak, biliary stricture, vascular complications, acute cellular rejection, re-exploration, small-for-size syndrome, or early allograft dysfunction.

Timing of adverse effects: 30-day, 90-day, and 1-year for survival; Graft patency was checked by Doppler ultrasonography intraoperatively, then once a day for the first week and weekly till hospital discharge. Follow-up USG Doppler was performed at 3, 6, and 12 months following transplantation. All the recipients were followed up twice a week for a month, then weekly for 3 months, fortnightly for 6 months, monthly for 24 months, and once in 2 months after 2 years.

Factors that predict response: There was no significant difference in graft patency rate at the different points of time in each type of RL graft harvested between V and ePTFE groups. Although 7- and 14-day patencies were similar between V and an ePTFE group among three types of RL graft, 12-month patency was low in non-MHV (V 90%, ePTFE 86.7%) as compared to MHV (V 97.4%, ePTFE 95.2%) grafts reflecting the increased tendency of blockage in multiple smaller tributaries.

Source Citation: Kaisar et al. 2018[17]

Study Design: Non-randomized comparative study

Device or Material: PROPATEN- heparin-bonded PTFE vascular graft with distal anastomotic patch versus autogenous saphenous vein graft in tibial artery bypass

Contact Duration: ≤4 years

Dose: 6 mm PROPATEN graft

Frequency/Duration: Single administration

Response: Hematoma, Interventions, Primary patency, Occlusion, Secondary patency

Patient characteristics (gender, mean age): Mean age PROPATEN 73 (SD 11.6) vs. vein group 75 (SD 13.4) years; 69 males and 39 females.

Number per group: 62 revascularizations in 59 patients in the PROPATEN group and 46 procedures in 44 patients in the vein group.

Observed adverse effects: Primary patency rates for 1-, 2-, 3-, and 4-year follow-up between the PROPATEN and vein groups (85%, 71%, 64%, and 57%, vs. 87%, 78%, 67%, and 61% respectively; p=0.97). Both groups had comparable secondary patency rates yearly over the same 4-year period (PROPATEN group: 84%, 76%, 74%, and 67%, respectively; the vein group: 88%, 79%, 76%, and 72%, respectively; p=0.94). There was no difference in the 30-day postoperative complication rates between the PROPATEN and vein group, which were 5% and 7%, respectively (NS). In the PROPATEN group, there were 2 wound complications and 1 groin hematoma that required surgical evacuation. In the vein group, 2 patients developed wound dehiscence from the saphenous vein harvest site while 1 patient developed postoperative bleeding that required surgical repair to achieve hemostasis. During the follow-up period, graft occlusion in the PROPATEN and the vein group occurred in 17 and 15 cases, respectively. In 13 of these PROPATEN graft occlusion cases, endovascular interventions with thrombolytic therapy were successful in restoring the graft flow that revealed stenosis in the distal anastomosis. Percutaneous balloon angioplasty was performed successfully in 7 of these cases to maintain the graft flow. A similar effort of endovascular interventions was performed in 6 vein graft occlusion cases of which it was successful only in 3 cases.

Timing of adverse effects: Postoperative ultrasound surveillance along with ankle-brachial index was performed at 1, 3, 6, 12 months, and every 6 months thereafter. Patency and limb salvage rates were reported yearly for up to 4 years. Postoperative complications were reported for 30-days postoperation.

Factors that predict response: Univariate analysis of primary patency for these bypass grafts showed that foot ulcers, active tobacco user, and poor run-off score of 0–1 were associated with this outcome.

Source Citation: Nguyen et al. 2018[15]

Study Design: Retrospective comparative study

Device or Material: PTFE grafts and femoral vein as conduits for femorofemoral crossover grafts

Contact Duration: Median follow-up was 9.8 months (range 0e107)

Dose: NR

Frequency/Duration: Single administration

Response: Blood transfusion, Primary assisted patency, Primary patency, Secondary patency, Wound complication

Patient characteristics (gender, mean age): 51 females and 68 males; mean age vein 65.5 (SD 8.5) and PTFE 66.5 (SD 10.8) years.

Number per group: 89 PTFE, 30 vein (18 were autogenous femoral veins, 12 were cryopreserved)

Observed adverse effects: The 30-day complication rate was 38.7% and was not different between groups (36% for PTFE, 44.4% for autologous vein grafts and 50% for cryovein, p=0.33) with wound complications being most frequent (18% PTFE, 27.8% autologous vein, 16.7% cryovein, p=0.25). Patients receiving vein grafts were more likely to receive blood transfusion (34.8% PTFE vs. 70% vein, p=0.001). 30-day complications: hematoma vein group 0% n=0 PTFE 4.5% n=4 p=0.57; seroma vein group 6.7% n=2 PTFE 5.6% n=5 p=1.00; renal insufficiency vein group 6.7% n=2 PTFE 9% n=8 p=1.00; hemodialysis vein group 0% n=0 PTFE 0% n=0 p=1.00; pseudoaneurysm vein group 3.3% n=1 PTFE 2.2% n=2 p=1.00; Primary patency rates at 1, 2, and 3 years were 83.7 %, 73.7% and 69.8%, respectively, for PTFE bypasses, and 100% for all time points for venous grafts, respectively (p=0.03). Primary-assisted and secondary patency rates were not significantly different between the 2 groups (p=0.16).

Timing of adverse effects: Intraoperative, 30 days and 1-, 2-, and 3-years; femorofemoral bypasses were evaluated with duplex ultrasound every 3 months for the first year and then every 6 months for the second year. If there were no complications or concerning ultrasound findings suggesting significant stenosis or impending graft failure, then patients were followed up annually with surveillance ultrasound.

Factors that predict response: A subgroup analysis of isolated femorofemoral bypasses was performed and showed no significant differences in primary patency at 1, 2, and 3 years (PTFE 86.8%, 74%, and 74% vs. vein 100% for all time points, respectively; p=0.40). Primary-assisted patencies at 1 and 2 years were significantly higher for bypasses created with femoral vein (100% for both time points) versus those created with PTFE graft (87% for both time points) (p=0.02). Secondary patency of isolated femorofemoral bypasses were not significantly different between veins and PTFE grafts (p=1.00). Survival at 1, 2, and 3 years (PTFE 79.2%, 64.5% and 54.8% vs. vein 86.7%, 86.7% and 65%, respectively; p=0.40) and amputation-free survival at 1, 2, and 3 years (PTFE 93% at all-time points vs. vein 87% at all-time points; p=0.86) between grafts created with prosthetic PTFE graft and those created with femoral vein were not statistically different. For axillobifemoral bypasses, a subgroup analysis was performed and showed no differences in patency rates (primary, p=0.12], primary-assisted [p=0.36], or secondary patencies [p=1.00] at 1, 2, or 3 years, p=1.00). However, survival was significantly higher in patients who received a PTFE conduit for the femorofemoral component of an axillobifemoral graft as compared with patients who received a femoral vein conduit for the femorofemoral component. Survival at 1, 2, and 3 years was 93.8%, 93.8%, and 93.8%, respectively, for patients with a PTFE femorofemoral component and 58%, 46%, and 46%, respectively, for patients with femoral vein (p=0.001). Amputation-free survival at 1, 2, and 3 years was not significantly different in patients who received vein grafts for the femorofemoral component as compared with those who received PTFE grafts for the femorofemoral component (p=0.21).

Source Citation: Veraldi et al. 2018[18]

Study Design: Non-randomized comparative study

Device or Material: Percutaneous transluminal angioplasty (PTA) ± bare metal stent (BMS) vs heparin-bonded ePTFE graft (PROPATEN-GORE) + Linton patch in patient affected by symptomatic femoropopliteal TASC II-D lesions

Contact Duration: Mean follow-up was 26.7 months

Dose: 6 or 7 mm PROPATEN-GORE graft was used as conduit

Frequency/Duration: Single administration

Response: Bleeding, Hematoma, Occlusion, Primary assisted patency, Primary Patency, Re-intervention, Restenosis, Secondary patency, technical success

Patient characteristics (gender, mean age): Mean age PTA/BMS 76 years and PTFE 72 years; sex reported by limb, 61 male and 19 female

Number per group: 68 patients total (80 limbs); PTA/BMS 40 limbs and PTFE 40 limbs

Observed adverse effects: Primary patency at 6, 12, and 24 months of PTA/BMS versus PTFE group was 76.9% vs. 97.5% (p=0.007), 65.7% vs. 89.1% (p=0.05), and 52.6% vs. 78.1% (p=0.005), respectively. Assisted primary patency was 76.9% vs. 97.5% (p=0.007), 68.5% vs. 91.8% (p=0.02), and 57.8% vs. 87.5% (p=0.001), respectively. Secondary patency was 94.8% vs. 97.5% (p=NS), 85.7% vs. 97.2% (p=NS), 73.6% vs. 93.7% (p=0.004), respectively. Rate of reintervention at 24 months was 45% in PTA/BMS vs. 20% in PTFE group (p=0.03). In PTA/BMS, technical success was obtained in 38 limbs (95%): it was impossible to cross the lesion in 2 cases, and a surgical revascularization with bypass was necessary. After the procedure, 3 limbs developed perioperative complications: 1 patient developed a retroperitoneal hematoma and 2 presented local bleeding at the site of femoral access. All complications were conservatively treated, and none of them required a reoperation before discharge.

In the PTFE group, technical success was 100%. Five limbs (12.5%) developed local complications: 2 cases of arterial bleeding requiring surgical hemostasis, 2 lymphatic fistulas (conservative treatment), and 1 skin necrosis requiring surgical debridement. In-hospital complications: PTA/BMS 3 (7.5%) vs PTFE 5 (12.5%) p=NS; Reintervention after discharge PTA/BMS 18 (45%) vs PTFE 8 (20%) p=0.03. During follow-up, 26 limbs (32.5%) required a reintervention for significant stenosis or symptomatic occlusion (18 patients, 45% in group PTA/BMS vs. 8 patients, 20% PTFE group, p=0.03).

In group PTA/BMS 14 limbs underwent to re-PTA, 2 of which required subsequent open revascularization for recurrence of occlusion. Four (10%) limbs developed symptomatic occlusion and were treated with a surgical revascularization without any other endovascular attempts. Two PTA procedures were planned following evidence of significant distal stenosis, and 1 target limb underwent to surgical correction of a proximal anastomotic aneurysm.

Timing of adverse effects: Patients were followed with a clinical assessment and duplex at 1, 6, and 12 months after procedure and then annually. A closer follow-up was performed in case of any complication.

Factors that predict response: Univariate analysis showed critical limb ischemia and poor runoff to be independent risk factors for significant restenosis/occlusion of target artery and reintervention.

Source Citation: Uhl et al. 2017[19]

Study Design: Non-randomized comparative study

Device or Material: Autologous vein vs. heparin bonded ePTFE for below knee femoropopliteal bypasses in patients with CLI in whom endovascular therapy was not possible or failed

Contact Duration: Mean follow-up was 34 months

Dose: HePTFE (6 mm ring enforced PROPATEN-GORE)

Frequency/Duration: Single administration

Response: Occlusion, Primary patency, Primary assisted, Patency, Restenosis, Revascularization Secondary patency

Patient characteristics (gender, mean age): Mean age: PTFE 73.0 (SD 10) and autologous vein 70.5 (SD 9), 90 male and 61 female

Number per group: Autologous vein 76 cases and heparin-bonded ePTFE 75 cases

Observed adverse effects: Early graft occlusion occurred in 9 cases (vein group 6.6% vs. HePTFE group 5.3%; p=0.508). No early occluded vein graft resulted in a major amputation within 30 days. Except for the 2 patients with the early occluded HePTFE grafts who underwent major amputation for the abovementioned reasons, all other early occluded grafts underwent thrombectomy within the first 24 hours. For 1-, 3-, and 5-years, primary patency in the vein group was 75.3%, 62.2%, and 55.5%; in the HePTFE group it was 73.6%, 51.7%, and 51.7% after the same time intervals. There was no significant difference after 5 years (p=0.897). After 1 year, primary assisted patency was 79.1% in the vein group and 75.0% in the HePTFE group, after 3 years it was 72.8% in the vein group and 54.9% in the HePTFE group, and after 5 years it was 66.8% in the vein group and 54.9% in the HePTFE group. Primary assisted patency rates in the 2 graft groups 5 years postoperatively again showed no significant difference (p=0.270). Comparing the 2 groups, vein and PTFE, the secondary patency was 91.1% vs. 82.7% after 1 year, 81.7% vs. 69.0% after 3 years, and 74.6% vs. 55.6% after 5 years, again without significant difference after 5 years (p=0.119) Restenosis: An intervention was performed in 15 cases to avoid a graft occlusion due to a stenosis (3 in the HePTFE group, 12 in the vein group).

Timing of adverse effects: ≤5 years for survival; Completion angiography was performed before leaving the operating room to exclude technical failure. Duplex scans and clinical examinations regarding wound healing and clinical symptoms were done before discharge from hospital and 6 months postoperatively. If the 6-month examination was satisfactory patients were checked at intervals of 12 months. For patency and limb salvage AEs were reported at 1-, 3-, and 5-years.

Factors that predict response: In subgroup analysis regarding 1-, 2-, and 3- vessel runoff, no significant difference was found in primary, primary assisted, or secondary patency; limb salvage; or survival between the 2 groups after 1 year. When comparing patients with previous endovascular treatment with patients without previous revascularization procedures, no significant difference was found regarding primary and secondary patency, limb salvage, and survival. In the multivariate analysis for secondary patency, smoking (p=0.01, 95% CI 1.2–5.5, HR 2.6) and prosthetic graft material (p=0.03, 95% CI 1.1–4.8, HR 2.3) were associated with a higher risk of graft failure, and prosthetic graft material was found to have an impact on limb salvage (p=0.04, 95% CI 1.1–8.8, HR 3.1).

Source Citation: Thorat et al. 2016[20]

Study Design: Non-randomized comparative study

Device or Material: Inferior right hepatic vein reconstruction using PTFE vs. direct IRHV-to-IVC anastomosis

Contact Duration: ≤2 months

Dose: PTFE graft: Liver allografts with MHV included requiring single ePTFE vascular graft for MHV reconstruction to form a common outflow channel (n=32). Bridging conduit plasty: Liver allografts without MHV requiring 2 ePTFE vascular grafts for backtable MHV reconstruction and IRHV reconstruction to facilitate second IRHV-to-IVC anastomosis (n=20

Frequency/Duration: Single administration

Response: Graft migration, Graft removal, Hepatic venous stenosis, Patency

Patient characteristics (gender, mean age): PTFE with MHV subgroup: 20 males and 12 females with a mean age of 54 years; PTFE bridging conduit plasty: 16 males and 4 females with an average age of 51±10 years; direct IRHV-IVC: males 30 and females 17 with a mean age 54±6

Number per group: ePTFE 52 patients total and direct IRHV-to-IVC anastomosis comparator 47 patients

Observed adverse effects: There were no thrombotic complications in either group of recipients; 4.2% of the recipients from direct IRHV-to-IVC anastomosis group developed hepatic venous stenosis but with no clinical deterioration 6 months postsurgery; and 1 patient from the PTFE group A developed ePTFE graft migration in the second portion of the duodenum that required surgical exploration and graft removal in the third postoperative month. No acute obstruction of ePTFE graft occurred in any of the recipients. All the recipients in the cohort recovered well in the postoperative period, with satisfactory liver functions. The patency rate of the ePTFE grafts used in studied recipients was 100% for the first 2 months.

Timing of adverse effects: Doppler ultrasonography was performed on first postoperative day, then every alternate day during the first week, and then once per week until the patient was discharged. CT scans were performed for patients with Doppler ultrasound showing abnormalities of outflow with high serum concentrations of liver enzymes (>300 to 400 IU/L) during the immediate posttransplant period. Patency was reported at the 2 month postoperative visit.

Factors that predict response: NR

Source Citation: AI Shakarchi et al. 2015[9]

Study Design: Systematic review

Device or Material: Reliable Outflow (HeRO) graft (Cryolife Inc company; Eden Prairie, MN, USA) in complex hemodialysis patients

Contact Duration: 7 to 18.5 months

Dose: NR

Frequency/Duration: Single administration

Response: Steal syndrome

Patient characteristics (gender, mean age): No difference in rate of male versus female; mean age NR

Number per group: 8 studies with 409 patients were included

Observed adverse effects: Primary and secondary pooled patency rates in this complex cohort of dialysis patients were 21.9% (9.6 to 37.2%) and 59.4% (39.4 to 78%).The rate of interventions required to maintain HeRO patency ranged between 1.5 and 3 procedures per year.

Timing of adverse effects: Through 7 to 18.5 months' follow-up period

Factors that predict response: NR

Source Citation: Anaya-Ayala et al. 2015[21]

Study Design: Non-randomized comparative study

Device or Material: Hybrid graft vs. standard PTFE graft for hemodialysis access

Contact Duration: Median follow-up was 21 months

Dose: NR

Frequency/Duration: Single administration

Response: Primary assisted patency, Primary patency, Reintervention, Secondary patency, technical success

Patient characteristics (gender, mean age): Mean age Hybrid graft group 65±14 years and PTFE 63±12 years; 33 males and 27 females

Number per group: Hybrid graft 25 patients and PTFE 35 patientsObserved adverse effects: Technical success was achieved in all cases, and all grafts were usable for hemodialysis. Estimated primary patency (24% vs. 18%, p>0.05), assisted primary patency (34% vs 28%; p>0.05), and secondary patency rates (40% vs 38%, p≥0.05) at 24 months were equivalent for Hybrid vs. PTFE grafts, respectively. Primary patency, assisted primary patency, and secondary patency rates at 12 months for the Hybrid graft patients vs. the standard PTFE patients were 66%±8% vs. 45%±8% (p=0.04), 69%±7% vs. 50%±7% (p=0.02), and 69%±7% vs 66%±7% (p>0.05), respectively. Six of 25 patients had graft occlusions and required open thrombectomy with a fistulogram of the Hybrid graft at a median of 2 months (range 1–8). Three did not require additional interventions, as no cause was determined. One patient required dilation of the innominate vein, and 1 patient required both dilation and stenting of the axillary and innominate veins. The final patient required surgical revision of the arterial anastomosis. None of these patients required a central venous line. For PTFE, 11/35 patients required open thrombectomy of the graft at a median of 2 months (range 1–8), with 5 needing additional endovascular interventions. Three patients required dilation of the innominate vein, and 2 patients had both dilation and stenting of the axillary and innominate veins.

Timing of adverse effects: 24 months for patient survival, thrombectomy needed at a median of 2 months post operation.

Factors that predict response: NR

Source Citation: Donati et al. 2015[1]

Study Design: Non-randomized comparative study

Device or Material: AVG made of PTFE GORE-TEX, W. L. Gore & Associates, Flagstaff, AZ, USA) Grafts vs Tunneled Cuffed Catheters for Hemodialysis

Contact Duration: ≤24-month follow-up

Dose: 19 PTFE grafts had an internal diameter of 6 mm, and 3 PTFE grafts had an internal diameter of 7 mm. 9 grafts had a conic feature, 5 of them had 6 mm diameter in the venous side and 4 mm diameter in the arterial side, 4 had a 7 mm diameter on the venous side and 4 mm diameter in the arterial side. In 19 cases out of 31 (61.3%), the PTFE grafts were placed in the arm

Frequency/Duration: Single administration

Response: Graft survival, Thrombosis

Patient characteristics (gender, mean age): 48 males and 39 females; PTFE mean age 63.8 ± 14.6 years and TCC mean age 73.5 ± 11.3 years

Number per group: TCC 56 patients and PTFE 31 patients

Observed adverse effects: Seventeen out of 31 patients (54.8%) with PTFE graft and 25/56 patients with TCC (44.6%) experienced a loss of the vascular access during a 1-year follow-up (p=NS). During a 24-month follow-up, loss of the vascular access was observed in 22/31 cases (71%) in the PTFE graft group and in 33/56 cases (58.9%) in the TCC group. Median survival of PTFE grafts at 24 months was 8.7±3.4 months, whereas TCC survival was 14.1±3.1 months (p=ns).

Vascular access lasted a median of 5.4 months longer in the TCC group than in the PTFE group, but the difference did not reach statistical significance (log-rank 1.34, p=0.25). Vascular access thrombosis caused vascular access loss in 20/31 cases (64.5%) in patients with a PTFE graft and in 4/56 cases (7.1%) in patients with TCC (P <0.001). Vascular access loss was due to infection in 4/31 cases (12.9%) in the PTFE group and in 9/56 cases (16.1%) in the TCC group (p=NS). The mean time interval between vascular access placement and the onset of these major complications was 7.5±7.9 months in the PTFE group and 13.0±14.9 months in the TCC group (p=NS). Vascular access infection occurred after a mean time of 9.4±7.2 months after vascular access placement in the PTFE group and after 16.4±15.6 months in the TCC group (p=NS). The time between vascular access placement and the diagnosis of thrombosis was 7.1±8.1 months in the PTFE group and after 1.8 ± 1.2 months in the TCC group (p=NS). The overall infectious and thrombotic complications of vascular access during the follow-up (any complication) were more frequent in the PTFE graft group compared with the TCC group: 13/31 (41.9%) in the PTFE group versus 7/56 (12.5%) in the TCC group (p<0.001).

Timing of adverse effects: Patients were monitored 3 times a week for adverse events during their hemodialysis sessions. Final follow-up was at 24 months.

Factors that predict response: Cox regression analysis adjusted for age, gender, type of vascular access, number of previously created arterial venous fistulae, diabetes, atrial fibrillation, and cigarette smoking confirmed that the survival of the vascular assess was similar between the TCC and the PTFE group at 12 months follow-up. However, in this analysis, diabetes (p=0.02) and all thrombotic and infectious complications of vascular access (p=0.01) proved to be significant independent predictors of access survival. In particular after 12 months, nondiabetic patients experienced vascular access survival 2.2 times higher than diabetic patients. Vascular access survived in 62.1% of nondiabetic patients, whereas it survived in 44.4% of diabetic patients during a 12-month follow-up. Moreover, patients experiencing any infectious or thrombotic complications had a 2.7 times higher risk of vascular access failure than those not experiencing complications. At the 24-month follow-up, only diabetes remained as a risk factor for vascular access survival. The absence of diabetes was significantly associated with an improvement in vascular access survival (p=0.02). Patients without diabetes had a 1.9 times higher probability of vascular access survival than that of diabetic patients independent of the type of vascular access. Vascular access survival was 27.8% in diabetic patients and 43.1% in nondiabetic patients.

Source Citation: Shemesh et al. 2015[27]

Study Design: Single-arm study

Device or Material: Standard ePTFE graft or a heparin-bonded ePTFE (PROPATEN) graft for hemodialysis access

Contact Duration: NR

Dose: Tapered 4- to 7-mm stretch ePTFE (W. L. Gore & Associates)

Frequency/Duration: Single administration

Response: Assisted primary patency, Bleeding complications, Cannulation time, Occlusion, Primary patency, Secondary patency, Thrombosis, Thrombolytic treatment

Patient characteristics (gender, mean age): 77 men and 83 women; mean age PROPATEN 69.9±10.2, standard 67.8±12 years

Number per group: 80 patients per group

Observed adverse effects: Primary patency was 35% and 14% for heparin-bonded grafts and 29% and 12% for standard ePTFE grafts at 6 and 12 months, respectively (p=0.48). Assisted primary patency was 54%, 41%, and 27% for heparin-bonded grafts and 41%, 30%, and 23% for standard grafts at 12, 24, and 36 months, respectively (p=0.12) by log-rank, p=0.04 by Gehan-Breslow-Wilcoxon. Secondary patency was 83%, 83%, and 81% for heparin-bonded grafts and 81%, 73%, and 68% for standard grafts at 12, 24, and 36 months, respectively (p=0.33).

All grafts were ready for cannulation between 2 and 4 weeks postoperatively with no difference between the groups. Of 80 standard grafts, 24 were eventually abandoned vs. 17 heparin-bonded grafts (p=0.188). Bleeding complications and intervention rates were similar in both groups. Mean time to first thrombosis was 9.7±10 months in the heparin-bonded group and 7.8±10.6 months in the standard group (p=0.17). An anatomic cause for occlusion in the first month could be found in 5 (83%) of the 6 heparin-bonded grafts compared with only 8 (50%) of the 16 standard grafts (p=0.18). There were no differences between upper and lower arm access and between the 2 graft types in the upper arm and the 2 graft types in the lower arm. Although the number of thrombolytic treatments was lower by 18% and the time to first thrombosis was longer by 24% in the heparin-bonded group, these differences did not reach statistical significance. 50/80 heparin-bonded grafts thrombosed during the follow-up period and required 119 thrombolytic treatments (range 0-8) compared with 57/80 standard grafts, which required 145 thrombolytic treatments (range 0-8) (p=0.16). 17 grafts were abandoned in the heparin-bonded group vs. 24 in the standard group (p=0.188).

Timing of adverse effects: Through median study follow-up period 23.5 months

Factors that predict response: There were significantly fewer thromboses in heparin-bonded grafts during the first month (8% vs. 20%, p=0.025) and first 5 months (p=0.02).

Source Citation: Attia et al. 2014[22]

Study Design: Non-randomized comparative study

Device or Material: Femoropopiteal bypass surgery for lower limb ischemia with PTFE vs. saphenous vein graft

Contact Duration: Mean and median follow-up period was 12 and 18 months, respectively

Dose: NR

Frequency/Duration: Single administration

Response: Patency

Patient characteristics (gender, mean age): 35 males and 15 females; median age 62 years (range 44 to 70)

Number per group: PTFE 18 patients and saphenous vein graft 32 patients

Observed adverse effects: Use of a prosthetic graft and construction of an intragenicular anastomosis (12 cases) was associated with lower graft patency rates, but statistical significance was not reached. According to study authors "The reversed saphenous vein is the preferred conduit in the present study. However, when the different surgical subgroup are examined separated femoro-distal bypass with vein graft is associated with increased patency rate than femoro distal bypass with synthetic graft."

Timing of adverse effects: Patients were assessed 6 weeks postoperation and at 3, 6, 9, 12, and 18 months.

Factors that predict response: NR for the PTFE patients. The authors looked at risk factors across all 50 patients combined, regardless of graft material.

Source Citation: Rychlik et al. 2014[10]

Study Design: Systematic review

Device or Material: Dacron versus PTFE grafts for above-knee femoropopliteal artery bypass

Contact Duration: ≤10 years

Dose: 5 to 8 mm grafts

Frequency/Duration: Single administration

Response: Antiplatelet/anticoagulation use, Primary patency, Secondary patency

Patient characteristics (gender, mean age): Mean age 66 years, gender NR

Number per group: 8 publications reporting on 6 RCTs with 601 Dacron and 591 PTFE

Observed adverse effects: Although primary and secondary patency rates at 12 months were not significantly different (RR 0.78; p=.08, and RR 0.84; p=0.52), 24-, 36-, and 60-month primary patency rates were significantly better with Dacron compared with PTFE grafts (RR 0.79; p=0.003; RR 0.80; p=0.03; RR 0.85; p=0.02). Statistical analysis also supported higher secondary patency rates for Dacron at 24 months (RR 0.75; p=0.02) and 60 months (RR 0.76-0.77; p=0.03-0.27). Although primary patency was similar between grafts (28% vs. 28%; p=0.12), secondary patencies were better with Dacron at 10 years (49% vs. 35%; p=0.01).

Timing of adverse effects: ≤10 years

Factors that predict response: There was no meta-analysis of this although individual RCTs identified some factors. One study that favored Dracon found that "in patients with only 1 patent crural vessel, the authors noticed decreased patency of both grafts and favored the use of PTFE graft". A second study that favored Dracon found "that the number of outflow vessels had a significant impact on the graft patency; 67% of patients with more than one crural vessel had patent graft (p=0.01). Another study that found no difference between PTFE and Dracon reported "a small graft size (5-6 mm) was a significant predictor of graft failure (p=0.0006). In another study that did not find a difference between Dracon and PTFE authors reported that "multivariate analysis revealed that below-knee anastomosis was the independent predicting factor of primary graft failure (RR 1.7; CI 1.05–2.8). Impaired secondary patency was associated with a below-knee bypass RR of 3.3 (CI 1.8–6.3) and distal gangrene RR of 2.0 (CI 1.01–3.8; p=0.048). Major amputation was predicted by infragenicular bypass, tissue necrosis, and poor runoff."

Source Citation: Van der Slegt 2014[23]

Study Design: Non-randomized comparative study

Device or Material: Precuffed ePTFE grafts compared with autologous saphenous vein (ASV) grafts used in patients with peripheral arterial disease

Contact Duration: ≤5 years

Dose: NR

Frequency/Duration: Single administration

Response: Bladder retention, Compartment syndrome , Decubitus ulcer, Hemorrhage, Primary patency, Primary assisted patency, Secondary patency, Seroma, Wound necrosis

Patient characteristics (gender, mean age): Mean age (range) PTFE 73.0 (41.0-92.7) and ASV 70.1 (36.8-96.5) years; 150 female and 317 male

Number per group: 169 precuffed ePTFE grafts and 298 ASV grafts

Observed adverse effects: **Primary patency rates** at 1, 2, and 5 years were supragenicular ePTFE 56%, 42%, 25% and for ASV 68%, 60%, and 60%, respectively ($p<0.05$); infragenicular PTFE 34%, 18% and 8% vs. ASV 65%, 60%, and 54%, respectively ($p<0.05$); femoro-crural PTFE 24%, 24%, 9% vs. ASV 39%, 39%, and 18%, respectively ($p\geq0.05$).

Primary assisted patency rates at 1, 2, and 5 years were supragenicular ePTFE 59%, 45%, 27% and for ASV 87%, 82%, and 82%, respectively ($p<0.05$); infragenicular PTFE 36%, 22%, and 11% vs. ASV 79%, 77%, and 74%, respectively ($p<0.05$); femoro-crural PTFE 24%, 24%, 9% vs. ASV 45%, 43%, and 30%, respectively ($p<0.05$).

Secondary patency rates of ePTFE vs. ASV at 1 and 5 years, respectively, were as follows: for 134 supragenicular femoropopliteal bypasses, 60% and 27% vs 89% and 85% ($p<.05$); for 190 infragenicular femoropopliteal bypasses, 40% and 25% vs. 86% and 79% ($p<.05$); and for 84 femoro-crural bypasses, 30% and 14% vs. 50% and 50% ($p<.05$).

Minor events PTFE vs. ASV: bladder retention 2 (1%) vs. 2 (1%) p=.62, decubitus 0 vs. 4 (1%) (p=0.30) Surgical events PTFE vs. ASV: wound necrosis 3 (2%) vs. 2 (1%) (p=0.36), seroma 4 (2%) vs. 3 (1%) (p=0.26); hemorrhage 11 (7%) vs. 15 (5%) (p=0.53), compartment syndrome 2 (1%) vs. 0 (p=0.13)

Timing of adverse effects: Mean follow-up PTFE 28.8 months and ASV 36.1 months; adverse events per procedure were recorded until 1 month after discharge of the primary procedure. Follow-up after ASV bypass surgery included routine duplex ultrasound and ABI at 3 months, 6 months, 1 year, and 2 years after the initial procedure, followed by ABI every subsequent 2 years. Follow-up after ePTFE bypass surgery was restricted to duplex ultrasound and ABI examination at 3 months, 1 year, and 2 years after the initial procedure. ABI was measured every subsequent 2 years. All other interim duplex ultrasound examinations were performed after suspicion of graft-related problems.

Factors that predict response: NR

Source Citation: Moulakakis et al. 2013[24]

Study Design: Non-randomized comparative study

Device or Material: Anaconda (Sulzer Vascutek, Bad Soden, Germany); Zenith (Cook Inc, Bloomington, Ind); Excluder (W. L. Gore and Assoc, Flagstaff, Ariz); and Endurant (Medtronic, Minneapolis, Minn)

Contact Duration: ≤30 day follow-up

Dose: NR

Frequency/Duration: Single administration

Response: Endoleaks, Hematoma

Patient characteristics (gender, mean age): Mean (SE) age years: Anaconda 73.11 (0.86), Zenith 73.08 (1.06), Excluder 70.87 (1.34), Endurant 74.17 (1.55); 81 males and 6 females

Number per group: Anaconda 28 patients, Zenith 26 patients, Excluder 23 patients, and Endurant 10 patients

Observed adverse effects: Endografts were successfully implanted in all patients. There were no open conversions, no deaths, and no major perioperative complications. There was no postoperative increase in troponin levels. Minor complications included local hematomas in femoral incisions in 3 patients (1 each in Anaconda, Zenith, and Excluder), who were treated conservatively. At 1-month follow-up, endoleaks were recorded in 12 (13.8%) patients (Anaconda n=5, 17.9%; Zenith n=3, 11.5%; Excluder n=3 patients, 13.0%; Enduran, 1 patient, 10%). No statistically significant differences were recorded for the presence of endoleak with regard to the endograft type. IL-10: the Anaconda group showed the highest mean value at 24 hours and differed significantly from the Excluder (p<.001) and Endurant (p=0.04) groups. The Zenith group also showed higher mean values than the Excluder (p=0.01). Comparisons among the groups of endograft types at 48 hours showed that mean values in patients treated with Anaconda endografts were higher compared with Endurant (p<0.001) and Excluder (p<0.001) endografts, whereas mean values in patients treated with Zenith endografts were significantly higher compared with Endurant (p<0.001) and Excluder (p<0.001) endografts. Patients treated with Anaconda endografts showed the highest IL-6 mean values at 24 hours postoperatively. Statistically significant differences were observed among patients treated with the Anaconda vs. the Excluder (p<0.001), Anaconda vs. Endurant (p=0.04), and Zenith vs. Excluder (p=0.01). Comparisons at 48 hours showed significant differences for Anaconda vs. Excluder (p<0.001), Anaconda vs. Endurant (p<0.001), Zenith vs. Excluder (p<0.001), and Zenith vs. Endurant (p<0.001). With regard to IL-8, although patients treated with Anaconda endografts showed the highest mean values at 24 hours and 48 hours postoperatively, no statistical differences were observed among the patients treated with different types of endografts. Patients in the Excluder group showed statistically lower mean values at 24 hours and 48 hours postoperatively.

For white blood cells (WBC), higher mean values were recorded after 24 hours in patients treated with the Anaconda endograft compared with the Excluder (p<0.001) and Zenith (p<0.001) endografts and the Endurant endograft compared with the Excluder (p=0.001) and Zenith (p=0.01) endografts. After 48 hours, statistically significant differences were observed among Anaconda vs. Excluder (p<0.001), Anaconda vs. Zenith (p<0.001), Anaconda vs. Endurant (p<.001), Endurant vs. Excluder (p=0.004), and Zenith vs.Excluder (p=0.02) groups.

Timing of adverse effects: Operative outcomes were recorded. Temperature, WBC count, platelet count, and serum concentrations of cytokines (IL-6, IL-8, and IL-10) were measured preoperatively, 24 hours postoperatively, and 48 hours postoperatively. Final follow-up was 30 days.

Factors that predict response: NR

Source Citation: Dorigo et al. 2012[25]

Study Design: Registry data

Device or Material: Heparin-bonded ePTFE graft (PROPATEN Gore- Tex, W.L. Gore & Associates Inc, Flagstaff, AZ, USA) and autologous saphenous vein in below-knee femoropopliteal bypasses

Contact Duration: 28.5±22.1 months

Dose: NR

Frequency/Duration: Single administration

Response: Adjunctive procedures, Antiplatelet/anticoagulation therapy, Primary patency, Secondary patency, Thrombosis

Patient characteristics (gender, mean age): 224 women and 726 male; median age PROPATEN 72.7 years and ASV 72.4 years

Number per group: PROPATEN 556 patients, and ASV group 394 patients

Observed adverse effects: Patients in HePTFE group more frequently had adjunctive procedures performed at distal anastomotic sites in order to improve run-off status. Postoperative and long-term medical treatment

consisted of single antiplatelet therapy in 40% of HePTFE group and in 39% (p=NS) in ASV group, double antiplatelet therapy in 17% of HePTFE group and 21% (p=NS) in ASV group and of oral anticoagulants in 43% of the HePTFE group and 40% (p=NS) in ASV group, the regimen for anti-coagulation or anti-platelet being determined on the basis of surgeon's preference. Primary patency rate at 48 months was significantly better in ASV group (61%) than in HePTFE group (44.5%; p=0.004). In below-knee bypasses, the corresponding figures were 45.2% in HePTFE group (SE 0.03) and 69% in ASV group (SE 0.04; p<0.001); in tibial bypasses, they were 39% (SE 0.07) and 53% (SE 0.04; p=0.04).

The rates of secondary patency at 48 months were 57% in HePTFE group (SE 0.03) and 67.5% in ASV group (SE 0.03), without significant differences between the two groups (p=0.1).

Early postoperative results: early graft thrombosis occurred in 55 patients (35 in HePTFE group and 20 in ASV group), with cumulative 30-day graft patency rates of 94 % and 95%, respectively (p=0.3).

Long-term follow-up: during follow-up, 263 new graft thromboses (173 in HePTFE group and 90 in ASV group) occurred. In 33 cases (8 in HePTFE group and 25 in ASV group) significant stenoses at anastomotic sites or at saphenous valves without graft thrombosis were detected; in 16 cases percutaneous transluminal angioplasty of the distal anastomosis or of the residual valves was performed, while in 13 patients endarterectomy of the common femoral artery with patching of the proximal anastomosis was required. Four patients were medically managed without developing graft occlusion.

Timing of adverse effects: Mean duration of follow-up was 28.5±22.1 months, Follow-up was performed within the third postoperative month, at 12 months and then yearly.

Factors that predict response: At univariate analysis, female gender, secondary intervention, distal tibial anastomosis, adjunctive distal procedures, poor run-off score, and kind of graft were found to significantly affect long-term primary patency; at multivariate analysis female gender, secondary intervention and kind of graft maintained their significance. For secondary patency, female gender, secondary intervention, distal tibial anastomosis, critical limb ischemia, adjunctive distal procedures, and poor run-off score were found to significantly affect it at univariate analysis, while at multivariate analysis only secondary interventions-maintained significance.

Source Citation: Kakkos et al. 2011[13]

Study Design: Non-randomized comparative study

Device or Material: Polyurethane Vectra vascular access grafts (C R Bard, Inc.) and PTFE carbon-impregnated IMPRA Carboflo vascular grafts (C R Bard, Inc.)

Contact Duration: ≤3 years

Dose: NR

Frequency/Duration: Single administration

Response: Assisted primary patency Functional secondary patency, Graft ligation/removal, Primary patency Pseudoaneurysm, Secondary patency, Thrombosis, Steal syndrome, Venous hypertension

Patient characteristics (gender, mean age): 167 women and 157 men; median (interquartile range) age was 63 (53–75) years

Number per group: 239 polyurethane and 125 carbon-impregnated PTFE vascular access grafts were placed in 324 consecutive patients.

Observed adverse effects: Twenty-nine grafts developed early postoperative complications including non-salvageable perioperative thrombosis in 19 (5.2%) patients and venous hypertension, steal syndrome, or infection in the remaining 10 (2.7%) patients, necessitating graft ligation or removal.

During follow-up, 36 patients (9.9%) developed a pseudoaneurysm, either anastomotic (1.6%: infected n=4, noninfected n=2) or at the needle-stick site (7.1%: infected n=4, non-infected n=26). Nineteen

additional patients (5.2%) developed graft infection requiring excision. Infected graft salvage was possible only in 2 patients (7%). Cumulative graft pseudoaneurysm formation (at needlestick site) rates at 3 years were not significantly different between Vectra and PTFE Carboflo grafts (17% vs. 23%; p=0.72). Both noninfected anastomotic aneurysms were surgically managed; 1 of them required graft ligation following unsuccessful management with a stent graft, while the second one was salvaged. Non-infected pseudoaneurysms at the needle-stick site (n=26) were mostly managed conservatively. In 5 cases (3 Vectra and 2 PTFE Carboflo grafts), a stent graft (Fluency, C R Bard, Inc.) was placed.

One of them was complicated by endoleak treated with placement of an additional stent graft, both removed later because of infection. Another was complicated by early occlusion. One pseudoaneurysm was seen in association with occlusion of the graft that was abandoned. The remaining 20 pseudoaneurysms were managed expectantly. There was a significant trend for better primary patency of Vectra compared with PTFE Carboflo grafts (15% vs. 11%, respectively, at 3 years; p=0.004). This difference in patency was 12% for primary assisted patency (39% vs. 27%, respectively, at 3 years; p<0.001) and secondary patency (69% vs. 57%, respectively, at 3 years; p=0.012) and 15% for functional secondary patency (61% vs. 46%, respectively, at 3 years; p=0.002).

Timing of adverse effects: ≤3 years

Factors that predict response: Straight upper arm Vectra grafts had the best secondary patency compared with their PTFE counterparts and loop (Vectra and PTFE) grafts (p=0.001); however, loop configuration was the single predictor of worse secondary patency on multivariate analysis (p=0.009; RR 1.7).

Source Citation: Kennealey et al. 2011[11]

Study Design: RCT

Device or Material: Standard cuffed ePTFE graft (Venaflo, Bard Peripheral Vascular, Tempe, Ariz) vs. the bovine carotid artery (BCA) graft (Artegraft, North Brunswick, NJ) for permanent hemodialysis access

Contact Duration: Mean 33 months

Dose: NR

Frequency/Duration: Single administration

Response: Angioplasty, assisted primary patency, Interventions needed, Primary patency, Pseudoaneurysm, Secondary patency, Steal syndrome, Survival of the graft, Thrombosis

Patient characteristics (gender, mean age): 27 male and 26 female, mean age BCA 63±13 years and ePTFE 59±16 years

Number per group: 26 patients in the BCA group and 27 patients in the ePTFE group

Observed adverse effects: Although there was no significant difference in secondary patency rates, primary and assisted primary patency rates were significantly higher in BCA than in the ePTFE grafts (60.5% vs.10.1% and 60.5% vs.20.8% at 1 year, respectively). The BCA graft survival advantage was most profound in the upper arm grafts with significantly higher primary and assisted patency rates (p<0.0001 and p<0.0005, respectively). The total number of interventions (upper arm grafts) and total number of angioplasties (overall and upper arm) required to maintain patency were significantly fewer in the BCA group. Graft thrombosis occurred 0.34±0.09 times per patient year in the BCA group compared to 0.77±0.16 times per patient year in the ePTFE group (p=0.01). In the BCA group, 4 patients underwent 7 interventions before the first episode of thrombosis, which was not significantly different from the ePTFE group (5 patients underwent 6 interventions). Total number of interventions per patient year needed to prolong patency was 1.45±0.19 in the BCA group and 1.99±0.25 in the ePTFE group (p=0.09). The most common intervention used to achieve this secondary patency was percutaneous angioplasty. There were 1.19±0.18 angioplasties per patient year compared to 1.86±0.24 (p=0.02) in the BCA and ePTFE groups, respectively.

The most common complication was graft thrombosis, which occurred 0.77±0.16 times per patient year in the ePTFE group compared to 0.34± 0.09 times per patient year in the BCA group (p=0.01). Thrombosis BCA 0.34±0.09 ePTFE 0.77±0.16 (p=0.01); pseudoaneurysm BCA 0 ePTFE 0.06±0.05 (p=0.07); steal syndrome BCA 0.03±0.03 ePTFE 0.03±0.03 (p=0.88)

Timing of adverse effects: Mean follow-up was 33 months, assessments were conducted every 4 months through month 40 and at year 1 and year 2.

Factors that predict response: The BCA graft survival advantage was most profound in the upper arm grafts with significantly higher primary and assisted patency rates (p<0.0001 and p<00005, respectively). There was no statistically significant difference in the rate of thrombosis, pseudoaneurysm formation, or arterial steal syndrome between the BCA and ePTFE groups within either graft location subset

Source Citation: Mousavi et al. 2011[12]

Study Design: RCT

Device or Material: Frozen saphenous vein vs. synthetic **GORE-TEX** vascular graft for A–V fistula

Contact Duration: ≤12 months

Dose: NR

Frequency/Duration: Single administration

Response: Auscultatable murmurs, Death, Renal insufficiency, Graft survival, Thrill sensation, Thrombosis

Patient characteristics (gender, mean age): 32 male, 28 female; Patients were 30 to 74 years old in the saphenous vein group (51.53±12.46) and 31 to 75 years old in the GORE-TEX group (51.6±11.68)

Number per group: 30 per group

Observed adverse effects: At the end of the follow-up period, 70.50% of the saphenous vein group and 72% of the GORE-TEX group were still being dialyzed from their shunts, which showed no significant difference. Flowmetry showed that at the end of the year, 41.66% of the GORE-TEX group had good flow, 41.66% had moderate flow, and 16.66% had poor flow. In the saphenous vein group, 40% had good flow, 50% had moderate flow, and 10% had poor flow, which did not show significant differences. One patient died from complications of renal insufficiency. 75% of the saphenous vein group and 76.66% of the GORE-TEX group had auscultatable murmurs on their shunts which showed no significant difference. There was no significant difference in thrill sensation between the 2 groups in any of the follow-up visits, and 71.42% of the saphenous vein group and 73.33% of the GORE-TEX group had sensible thrill on their fistulas at the end of the year. The overall thrombosis rate of the fistulas at the end of the follow-up period was 25% in the saphenous vein group and 20% in the GORE-TEX group, which were not statistically meaningful.

Timing of adverse effects: ≤12 months

Factors that predict response: NR

Source Citation: Drouven et al. 2019[14]

Study Design: Non-randomized comparative study

Device or Material: Basilic vein transposition vs. PTFE forearm loop graft as tertiary vascular access

Contact Duration: Mean follow-up 29 months

Dose: For the PTFE loop, a standard wall PTFE graft (Gore-Tex; W. L. Gore & Associates, Flagstaff, Ariz) with 6 mm diameter and 0.5 mm wall thickness was used.

Frequency/Duration: Single administration

Response: Steal syndrome and distal ischemia, Venous hypertension

Patient characteristics (gender, mean age): 69 males and 61 females; basilica vein 58.3 (SD 13.9) and PTFE 62.6 (SD 14.9) years

Number per group: Basilic vein 55 and PTFE 75

Observed adverse effects: Venous hypertension: PTFE 0 (PY^{-1} 0.00) vs. basilica vein 4 (PY^{-1} 0.03; p=0.242) Steal syndrome and distal ischemia: PTFE 1 (PY^{-1} 0.01) vs. basilica vein 1 (PY^{-1} 0.01; p=0.831)

Timing of adverse effects: NR but mean follow-up was 29 months

Factors that predict response: Multivariate regression identified body mass index (HR 1.77; 95% CI 1.05–2.98; p=0.03) and age (HR 0.54; 95% CI 0.32–0.91; p=0.02) as predictors for failure regarding primary patency in PTFE loop patients. Previous catheter use (HR 0.29; 95% CI 0.12–0.70; p=0.006) and the presence of diabetes (HR 3.32; 95% CI 1.50–7.39; p=0.003) were independent predictors for failure regarding primary patency in basilic vein transposition patients. The incidence rate of total complications was significantly higher in the PTFE loop group with 0.70 PY^{-1} compared with 0.28 PY^{-1} in the basilic vein transposition group (p=0.001). In terms of intervention rate, a significantly higher percutaneous transluminal angioplasty rate and surgical revision rate were found in the PTFE loop group than in the basilic vein group (1.77 PY^{-1} vs. 1.05 PY^{-1}; p=0.022 and 0.20 PY^{-1} vs. 0.07 PY^{-1}; p=0.002, respectively).

Source Citation: Shakarchi et al. 2019[7]

Study Design: Systematic review

Device or Material: PTFE Flixene, Acuseal Polycarbonate urethane, Avflo Polyurethane Vectra grafts

Contact Duration: 12 to 36 months

Dose: NR

Frequency/Duration: Single administration

Response: Steal syndrome

Patient characteristics (gender, mean age): NR

Number per group: 19 studies total; number of patients for Flixene 230; Avflo 74; Acuseal 260; Vectra 762

Observed adverse effects: Flixene Steal syndrome: 0 to 8% based on 3 studies, Avflo Steal syndrome: NR, Acuseal

Steal syndrome: 0 to 11% based on 3 studies Vectra, Steal syndrome: 0 to 3.5% based on 4 studies

Timing of adverse effects: Flixene ≤18 months; Avflo ≤24 months; Acuseal ≤24 months, Vectra ≤18 to 36 months follow-up

Factors that predict response: NR

Source Citation: Cho et al. 2018[26]

Study Design: Single-arm study

Device or Material: Extra-cardiac Fontan procedure with 16 mm PTFE (**GORE-TEX** vascular graft; W.L. Gore & Associates, Inc., Flagstaff, AZ, USA) conduit vs. matched controls with conduit size of 19.2±1.4mm (18 mm, n=34; 20 mm, n=23 and 22 mm, n=9)

Contact Duration: ≤16 years

Dose: 16 mm PTFE conduit vs. a larger conduit (mean 19.2±1.4 mm)

Frequency/Duration: Single administration

Response: Cirrhosis, Coarse liver parenchyma, Mortality, Protein-losing enteropathy, Reoperation, Thromboembolism

Patient characteristics (gender, mean age): Mean age PTFE 16 mm 2.9±1.2 years and matched control group 3.1±1.2; gender NR

Number per group: PTFE 16-mm group 66 patients and 66 control patients matched for age and size Observed adverse effects: There was no significant difference in mortality between the groups (p=0.109). The freedom from reoperation was 94.0±3.4% in 16 mm PTFE and for matched controls 79.3±5.7% after 10 years (p=0.070). Late-occurring morbidities included protein-losing enteropathy (2 in 16 mm PTFE, 4 in matched controls; p=0.491) and thromboembolism (0 in 16 mm PTFE, 4 in matched controls; p=0.206). Protein-losing enteropathy N: 16 mm group 2 vs. matched controls 4 (p=0.491); thromboembolism N: 16-mm group 0 vs. matched controls 4, p=0.206; reoperation N: 16 mm group 4 vs. matched controls 11 (p=0.070); mortality N: 16 mm group 1 vs. matched control 6 (p=0.109); early mortality 16 mm 0 matched control 3 (due to heart failures after ECFP); late mortality 16 mm 1 (due to recurrent pulmonary vein stenosis and heart failure 1 year after the procedure) vs. matched control 3 (due to septic shock after mediastinitis). Freedom from catheter-based intervention was present for 89.3±4.8% (16 mm PTFE) and 93.3±3.8% (matched controls) over 10 years (p=0.369), respectively. Coarse liver parenchyma was detected in 9 of 23 (39.1%) patients from the 16 mm PTFE group and in 7 of 18 (38.8%) patients from the matched control group upon ultrasonography. Among patients with >10 years of follow-up, 6 patients with liver cirrhosis were detected (16 mm: 3 of 23, 13%, matched control: 3 of 18, 16.6%), and coarse parenchyma was detected in 9 (39.1%) and 7 (38.3%) patients in 16 mm and matched control groups, respectively.

Timing of adverse effects: Mean follow-up PTFE 7.8±6.0 years and matched control 9.1±4.9 years

Factors that predict response: NR

Source Citation: Goja et al.2018[16]

Study Design: Non-randomized comparative study

Device or Material: AS reconstruction using nonringed ePTFE grafts (GORE-TEX, W.L. Gore & Associates, Inc., Newark, DE, USA) vs. venous extension grafts

Contact Duration: ≤2 year

Dose: ≤5 mm

Frequency/Duration: Single administration

Response: Hospital LOS, ICU LOS, Sepsis, Survival

Patient characteristics (gender, mean age): Mean age of patients was 48 ± 10.21 years; 366 male and 71 female

Number per group: Venous extension graft 200 patients, and ePTFE in 237 patients

Observed adverse effects: Sepsis: venous extension group 19 (9.5%) vs. PTFE 17 (7.1%) (p=0.4). There was no significant difference in ICU stay, hospital stay, 30-day (V 92%, ePTFE 94.5%; p=0.34), 90-day (V 90%, ePTFE 90.7%, p=0.87) and one-year (V 87.5%, ePTFE 89%; p=0.66) patient survival between the groups.

Timing of adverse effects: 30-day, 90-day and 1-year for survival: graft patency was checked by Doppler ultrasonography intraoperatively, then once a day for the first week and weekly till hospital discharge. Follow-up USG Doppler was performed at 3, 6, and 12 months following transplantation. All the recipients were followed up twice a week for a month, then weekly for 3 months, fortnightly for 6 months, monthly for 24 months, and once every 2 months after 2 years.

Factors that predict response: NR

Source Citation: Kaisar et al. 2018[17]

Study Design: Non-randomized comparative study

Device or Material: PROPATEN heparin-bonded PTFE vascular graft with distal anastomotic patch versus autogenous saphenous vein graft in tibial artery bypass

Contact Duration: ≤4 years

Dose: 6 mm PROPATEN graft

Frequency/Duration: Single administration

Response: Hospital LOS, Limb salvage

Patient characteristics (gender, mean age): Mean age PROPATEN 73 (SD 11.6) vs. vein group 75 (SD 13.4) years; 69 males and 39 females

Number per group: 62 revascularizations in 59 patients in the PROPATEN group and 46 procedures in 44 patients in the vein group

Observed adverse effects: The limb salvage rates were equivalent between the PROPATEN and vein group at 4 years (84% vs. 92%; p=0.89). Length of hospitalization, days (SD): PROPATEN 5.2 (SD 2.3) Vein group 7.5 (SD 3.6) (p=0.08).

Timing of adverse effects: Postoperative ultrasound surveillance along with ABI was performed at 1, 3, 6, 12 months, and every 6 months thereafter. Patency and limb salvage rates were reported yearly for up to 4 years. Postoperative complications were reported for 30-days postoperation.

Factors that predict response: Univariate analysis of primary patency for these bypass grafts showed that foot ulcers, active tobacco user, and poor run-off score of 0–1 were associated with this outcome. Multivariate analysis showed active tobacco usage and poor run-off score as predictors for graft occlusion.

Source Citation: Nguyen et al. 2018[15]

Study Design: Retrospective comparative study

Device or Material: PTFE grafts and femoral vein as conduits for femorofemoral crossover grafts

Contact Duration: Median follow-up was 9.8 months (range 0e107

Dose: NR

Frequency/Duration: Single administration

Response: Blood transfusion, Primary assisted patency, Primary patency, Secondary patency, Wound complication

Patient characteristics (gender, mean age): 51 females and 68 males; mean age vein 65.5 (SD 8.5) and PTFE 66.5 (SD 10.8) years

Number per group: 89 PTFE, 30 vein (18 were autogenous femoral veins, 12 were cryopreserved) Observed adverse effects: The 30-day complication rate was 38.7% and was not different between groups (36% for PTFE, 44.4% for autologous vein grafts and 50% for cryovein, p=0.33) with wound complications being most frequent (18% PTFE, 27.8% autologous vein, 16.7% cryovein, p=0.25). Patients receiving vein grafts were more likely to receive blood transfusion (34.8% PTFE vs. 70% vein, p=0.001). 30-day complications: hematoma vein group 0% n=0 PTFE 4.5% n=4 p=0.57; seroma vein group 6.7% n=2 PTFE 5.6% n=5 p=1.00; renal insufficiency vein group 6.7% n=2 PTFE 9% n=8 p=1.00; hemodialysis vein group 0% n=0 PTFE 0% n=0 p=1.00; pseudoaneurysm vein group 3.3% n=1 PTFE 2.2% n=2 p=1.00; Primary patency rates at 1, 2, and 3 years were 83.7 %, 73.7% and 69.8%, respectively, for PTFE bypasses, and 100% for all time points for venous grafts, respectively (p=0.03). Primary-assisted and secondary patency rates were not significantly different between the 2 groups (p=0.16).

Timing of adverse effects: Intraoperative, 30 days and 1-, 2-, and 3-years; femorofemoral bypasses were evaluated with duplex ultrasound every 3 months for the first year and then every 6 months for the second year. If there were no complications or concerning ultrasound findings suggesting significant stenosis or impending graft failure, then patients were followed up annually with surveillance ultrasound.

Factors that predict response: A subgroup analysis of isolated femorofemoral bypasses was performed and showed no significant differences in primary patency at 1, 2, and 3 years (PTFE 86.8%, 74%, and 74% vs. vein 100% for all time points, respectively; p=0.40). Primary-assisted patencies at 1 and 2 years were significantly higher for bypasses created with femoral vein (100% for both time points) versus those created with PTFE graft (87% for both time points) (p=0.02). Secondary patency of isolated femorofemoral bypasses were not significantly different between veins and PTFE grafts (p=1.00). Survival at 1, 2, and 3 years (PTFE 79.2%, 64.5% and 54.8% vs. vein 86.7%, 86.7% and 65%, respectively; p=0.40) and amputation-free survival at 1, 2, and 3 years (PTFE 93% at all-time points vs. vein 87% at all-time points; p=0.86) between grafts created with prosthetic PTFE graft and those created with femoral vein were not statistically different. For axillobifemoral bypasses, a subgroup analysis was performed and showed no differences in patency rates (primary, p=0.12], primary-assisted [p=0.36], or secondary patencies [p=1.00] at 1, 2, or 3 years, p=1.00). However, survival was significantly higher in patients who received a PTFE conduit for the femorofemoral component of an axillobifemoral graft as compared with patients who received a femoral vein conduit for the femorofemoral component. Survival at 1, 2, and 3 years was 93.8%, 93.8%, and 93.8%, respectively, for patients with a PTFE femorofemoral component and 58%, 46%, and 46%, respectively, for patients with femoral vein (p=0.001). Amputation-free survival at 1, 2, and 3 years was not significantly different in patients who received vein grafts for the femorofemoral component as compared with those who received PTFE grafts for the femorofemoral component (p=0.21).

Source Citation: Veraldi et al. 2018[18]

Study Design: Non-randomized comparative study

Device or Material: Percutaneous transluminal angioplasty (PTA) ± bare metal stent (BMS) vs heparin-bonded ePTFE graft (PROPATEN-GORE) + Linton patch in patient affected by symptomatic femoropopliteal TASC II-D lesions

Contact Duration: Mean follow-up was 26.7 months

Dose: 6 or 7 mm PROPATEN-GORE graft was used as conduit

Frequency/Duration: Single administration

Response: Bleeding, Hematoma, Occlusion, Primary assisted patency, Primary Patency, Re-intervention, Restenosis, Secondary patency, technical success

Patient characteristics (gender, mean age): Mean age PTA/BMS 76 years and PTFE 72 years; sex reported by limb, 61 male and 19 female

Number per group: 68 patients total (80 limbs); PTA/BMS 40 limbs and PTFE 40 limbs

Observed adverse effects: Primary patency at 6, 12, and 24 months of PTA/BMS versus PTFE group was 76.9% vs. 97.5% (p=0.007), 65.7% vs. 89.1% (p=0.05), and 52.6% vs. 78.1% (p=0.005), respectively. Assisted primary patency was 76.9% vs. 97.5% (p=0.007), 68.5% vs. 91.8% (p=0.02), and 57.8% vs. 87.5% (p=0.001), respectively. Secondary patency was 94.8% vs. 97.5% (p=NS), 85.7% vs. 97.2% (p=NS), 73.6% vs. 93.7% (p=0.004), respectively. Rate of reintervention at 24 months was 45% in PTA/BMS vs. 20% in PTFE group (p=0.03). In PTA/BMS, technical success was obtained in 38 limbs (95%): it was impossible to cross the lesion in 2 cases, and a surgical revascularization with bypass was necessary. After the procedure, 3 limbs developed perioperative complications: 1 patient developed a retroperitoneal hematoma and 2 presented local bleeding at the site of femoral access. All complications were conservatively treated, and none of them required a reoperation before discharge.

In the PTFE group, technical success was 100%. Five limbs (12.5%) developed local complications: 2 cases of arterial bleeding requiring surgical hemostasis, 2 lymphatic fistulas (conservative treatment), and 1 skin necrosis requiring surgical debridement. In-hospital complications: PTA/BMS 3 (7.5%) vs PTFE 5 (12.5%) p=NS; Reintervention after discharge PTA/BMS 18 (45%) vs PTFE 8 (20%) p=0.03. During follow-up, 26 limbs (32.5%) required a reintervention for significant stenosis or symptomatic occlusion (18 patients, 45% in group PTA/BMS vs. 8 patients, 20% PTFE group, p=0.03).

In group PTA/BMS 14 limbs underwent to re-PTA, 2 of which required subsequent open revascularization for recurrence of occlusion. Four (10%) limbs developed symptomatic occlusion and were treated with a surgical revascularization without any other endovascular attempts. Two PTA procedures were planned following evidence of significant distal stenosis, and 1 target limb underwent to surgical correction of a proximal anastomotic aneurysm.

Timing of adverse effects: Patients were followed with a clinical assessment and duplex at 1, 6, and 12 months after procedure and then annually. A closer follow-up was performed in case of any complication.

Factors that predict response: Univariate analysis showed critical limb ischemia and poor runoff to be independent risk factors for significant restenosis/occlusion of target artery and reintervention.

Source Citation: Uhl et al. 2017[19]

Study Design: Non-randomized comparative study

Device or Material: Autologous vein vs. heparin bonded ePTFE for below knee femoropopliteal bypasses in patients with CLI in whom endovascular therapy was not possible or failed

Contact Duration: Mean follow-up was 34 months

Dose: HePTFE (6 mm ring enforced PROPATEN-GORE)

Frequency/Duration: Single administration

Response: Occlusion, Primary patency, Primary assisted, Patency, Restenosis, Revascularization Secondary patency

Patient characteristics (gender, mean age): Mean age: PTFE 73.0 (SD 10) and autologous vein 70.5 (SD 9), 90 male and 61 female

Number per group: Autologous vein 76 cases and heparin-bonded ePTFE 75 cases

Observed adverse effects: Early graft occlusion occurred in 9 cases (vein group 6.6% vs. HePTFE group 5.3%; p=0.508). No early occluded vein graft resulted in a major amputation within 30 days. Except for the 2 patients with the early occluded HePTFE grafts who underwent major amputation for the abovementioned reasons, all other early occluded grafts underwent thrombectomy within the first 24 hours. For 1-, 3-, and 5-years, primary patency in the vein group was 75.3%, 62.2%, and 55.5%; in the HePTFE group it was 73.6%, 51.7%, and 51.7% after the same time intervals. There was no significant difference after 5 years (p=0.897). After 1 year, primary assisted patency was 79.1% in the vein group and 75.0% in the HePTFE group, after 3 years it was 72.8% in the vein group and 54.9% in the HePTFE group, and after 5 years it was 66.8% in the vein group and 54.9% in the HePTFE group. Primary assisted patency rates in the 2 graft groups 5 years postoperatively again showed no significant difference (p=0.270). Comparing the 2 groups, vein and PTFE, the secondary patency was 91.1% vs. 82.7% after 1 year, 81.7% vs. 69.0% after 3 years, and 74.6% vs. 55.6% after 5 years, again without significant difference after 5 years (p=0.119) Restenosis: An intervention was performed in 15 cases to avoid a graft occlusion due to a stenosis (3 in the HePTFE group, 12 in the vein group).

Timing of adverse effects: ≤5 years for survival; Completion angiography was performed before leaving the operating room to exclude technical failure. Duplex scans and clinical examinations regarding wound healing and clinical symptoms were done before discharge from hospital and 6 months postoperatively. If the 6-month examination was satisfactory patients were checked at intervals of 12 months. For patency and limb salvage AEs were reported at 1-, 3-, and 5-years.

Factors that predict response: In subgroup analysis regarding 1-, 2-, and 3- vessel runoff, no significant difference was found in primary, primary assisted, or secondary patency; limb salvage; or survival between the 2 groups after 1 year. When comparing patients with previous endovascular treatment with patients without previous revascularization procedures, no significant difference was found regarding primary and secondary patency, limb salvage, and survival. In the multivariate analysis for secondary patency, smoking (p=0.01, 95% CI 1.2–5.5, HR 2.6) and prosthetic graft material (p=0.03, 95% CI 1.1–4.8, HR 2.3) were associated with a higher risk of graft failure, and prosthetic graft material was found to have an impact on limb salvage (p=0.04, 95% CI 1.1–8.8, HR 3.1).

Source Citation: Thorat et al. 2016[20]

Study Design: Non-randomized comparative study

Device or Material: Inferior right hepatic vein reconstruction using PTFE vs. direct IRHV-to-IVC anastomosis

Contact Duration: ≤2 months

Dose: PTFE graft: Liver allografts with MHV included requiring single ePTFE vascular graft for MHV reconstruction to form a common outflow channel (n=32). Bridging conduit plasty: Liver allografts without MHV requiring 2 ePTFE vascular grafts for backtable MHV reconstruction and IRHV reconstruction to facilitate second IRHV-to-IVC anastomosis (n=20)

Frequency/Duration: Single administration

Response: Graft migration, Graft removal, Hepatic venous stenosis, Patency

Patient characteristics (gender, mean age): PTFE with MHV subgroup: 20 males and 12 females with a mean age of 54 years; PTFE bridging conduit plasty: 16 males and 4 females with an average age of 51±10 years; direct IRHV-IVC: males 30 and females 17 with a mean age 54±6

Number per group: ePTFE 52 patients total and direct IRHV-to-IVC anastomosis comparator 47 patients

Observed adverse effects: There were no thrombotic complications in either group of recipients; 4.2% of the recipients from direct IRHV-to-IVC anastomosis group developed hepatic venous stenosis but with no clinical deterioration 6 months post-surgery; and 1 patient from the PTFE group A developed ePTFE graft migration in the second portion of the duodenum that required surgical exploration and graft removal in the third postoperative month. No acute obstruction of ePTFE graft occurred in any of the recipients. All the recipients in the cohort recovered well in the postoperative period, with satisfactory liver functions. The patency rate of the ePTFE grafts used in studied recipients was 100% for the first 2 months.

Timing of adverse effects: Doppler ultrasonography was performed on first postoperative day, then every alternate day during the first week, and then once per week until the patient was discharged. CT scans were performed for patients with Doppler ultrasound showing abnormalities of outflow with high serum concentrations of liver enzymes (>300 to 400 IU/L) during the immediate posttransplant period. Patency was reported at the 2-month postoperative visit.

Factors that predict response: NR

Source Citation: AI Shakarchi et al. 2015[9]

Study Design: Systematic review

Device or Material: Hemodialysis Reliable Outflow (HeRO) graft (Cryolife Inc company; Eden Prairie, MN, USA) in complex hemodialysis patients

Contact Duration: 7 to 18.5 months

Dose: NR

Frequency/Duration: Single administration

Response: Steal syndrome

Patient characteristics (gender, mean age): No difference in rate of male versus female; mean age NR

Number per group: 8 studies with 409 patients were included

Observed adverse effects: Primary and secondary pooled patency rates in this complex cohort of dialysis patients were 21.9% (9.6 to 37.2%) and 59.4% (39.4 to 78%). The rate of interventions required to maintain HeRO patency ranged between 1.5 and 3 procedures per year.

Timing of adverse effects: Through 7 to 18.5 months' follow-up period

Factors that predict response: NR

Source Citation: Anaya-Ayala et al. 2015[21]

Study Design: Non-randomized comparative study

Device or Material: Hybrid graft vs. standard PTFE graft for hemodialysis access

Contact Duration: Median follow-up was 21 months

Dose: NR

Frequency/Duration: Single administration

Response: Primary assisted patency, Primary patency, Reintervention, Secondary patency, Technical success

Patient characteristics (gender, mean age):

Number per group: Mean age Hybrid graft group 65±14 years and PTFE 63±12 years; 33 males and 27 females

Observed adverse effects: Hybrid graft 25 patients and PTFE 35 patients

Timing of adverse effects: Technical success was achieved in all cases, and all grafts were usable for hemodialysis. Estimated primary patency (24% vs. 18%, p>0.05), assisted primary patency (34% vs 28%; p>0.05), and secondary patency rates (40% vs 38%, p≥0.05) at 24 months were equivalent for Hybrid vs. PTFE grafts, respectively. Primary patency, assisted primary patency, and secondary patency rates at 12 months for the Hybrid graft patients vs. the standard PTFE patients were 66%±8% vs. 45%±8% (p=0.04), 69%±7% vs. 50%±7% (p=0.02), and 69%±7% vs 66%±7% (p>0.05), respectively. Six of 25 patients had graft occlusions and required open thrombectomy with a fistulogram of the Hybrid graft at a median of 2 months (range 1–8). Three did not require additional interventions, as no cause was determined. One patient required dilation of the innominate vein, and 1 patient required both dilation and stenting of the axillary and innominate veins. The final patient required surgical revision of the arterial anastomosis. None of these patients required a central venous line. For PTFE, 11/35 patients required open thrombectomy of the graft at a median of 2 months (range 1–8), with 5 needing additional endovascular interventions. Three patients required dilation of the innominate vein, and 2 patients had both dilation and stenting of the axillary and innominate veins.

Factors that predict response: 24 months for patient survival, thrombectomy needed at a median of 2 months postoperation.

Source Citation: Donati et al. 2015[1]

Study Design: Non-randomized comparative study

Device or Material: AVG made of PTFE GORE-TEX, W. L. Gore & Associates, Flagstaff, AZ, USA) Grafts vs Tunneled Cuffed Catheters for Hemodialysis

Contact Duration: ≤24 month follow-up

Dose: 19 PTFE grafts had an internal diameter of 6 mm, and 3 PTFE grafts had an internal diameter of 7 mm. 9 grafts had a conic feature, 5 of them had 6 mm diameter in the venous side and 4 mm diameter in the arterial side, 4 had a 7 mm diameter on the venous side and 4 mm diameter in the arterial side. In 19 cases out of 31 (61.3%), the PTFE grafts were placed in the arm

Frequency/Duration: Single administration

Response: Graft survival, Thrombosis

Patient characteristics (gender, mean age): 48 males and 39 females; PTFE mean age 63.8 ± 14.6 years and TCC mean age 73.5 ± 11.3 years

Number per group: TCC 56 patients and PTFE 31 patients

Observed adverse effects: Seventeen out of 31 patients (54.8%) with PTFE graft and 25/56 patients with TCC (44.6%) experienced a loss of the vascular access during a 1-year follow-up (p=NS). During a 24-month follow-up, loss of the vascular access was observed in 22/31 cases (71%) in the PTFE graft group and in 33/56 cases (58.9%) in the TCC group. Median survival of PTFE grafts at 24 months was 8.7±3.4 months, whereas TCC survival was 14.1±3.1 months (p=ns).

Vascular access lasted a median of 5.4 months longer in the TCC group than in the PTFE group, but the difference did not reach statistical significance (log-rank 1.34, p=0.25). Vascular access thrombosis caused vascular access loss in 20/31 cases (64.5%) in patients with a PTFE graft and in 4/56 cases (7.1%) in patients with TCC (P <0.001). Vascular access loss was due to infection in 4/31 cases (12.9%) in the PTFE group and in 9/56 cases (16.1%) in the TCC group (p=NS). The mean time interval between vascular access placement and the onset of these major complications was 7.5±7.9 months in the PTFE group and 13.0±14.9 months in the TCC group (p=NS). Vascular access infection occurred after a mean time of 9.4±7.2 months after vascular access placement in the PTFE group and after 16.4±15.6 months in the TCC group (p=NS). The time between vascular access placement and the diagnosis of thrombosis was 7.1±8.1 months in the PTFE group and after 1.8 ± 1.2 months in the TCC group (p=NS). The overall infectious and thrombotic complications of vascular access during the follow-up (any complication) were more frequent in the PTFE graft group compared with the TCC group: 13/31 (41.9%) in the PTFE group versus 7/56 (12.5%) in the TCC group (p<0.001).

Timing of adverse effects: Patients were monitored 3 times a week for adverse events during their hemodialysis sessions. Final follow-up was at 24 months.

Factors that predict response: Cox regression analysis adjusted for age, gender, type of vascular access, number of previously created arterial venous fistulae, diabetes, atrial fibrillation, and cigarette smoking confirmed that the survival of the vascular assess was similar between the TCC and the PTFE group at 12 months follow-up. However, in this analysis, diabetes (p=0.02) and all thrombotic and infectious complications of vascular access (p=0.01) proved to be significant independent predictors of access survival. In particular after 12 months, nondiabetic patients experienced vascular access survival 2.2 times higher than diabetic patients. Vascular access survived in 62.1% of nondiabetic patients, whereas it survived in 44.4% of diabetic patients during a 12-month follow-up. Moreover, patients experiencing any infectious or thrombotic complications had a 2.7 times higher risk of vascular access failure than those not experiencing complications. At the 24-month follow-up, only diabetes remained as a risk factor for vascular access survival. The absence of diabetes was significantly associated with an improvement in vascular access survival (p=0.02). Patients without diabetes had a 1.9 times higher probability of vascular access survival than that of diabetic patients independent of the type of vascular access. Vascular access survival was 27.8% in diabetic patients and 43.1% in nondiabetic patients.

Source Citation: Shemesh et al. 2015[27]

Study Design: Single-arm study

Device or Material: Standard ePTFE graft or a heparin-bonded ePTFE (PROPATEN) graft for hemodialysis access

Contact Duration: NR

Dose: Tapered 4- to 7-mm stretch ePTFE (W. L. Gore & Associates)

Frequency/Duration: Single administration

Response: Assisted primary patency, Bleeding complications, Cannulation time, Occlusion, Primary patency, Secondary patency, Thrombosis, Thrombolytic treatment

Patient characteristics (gender, mean age): 77 men and 83 women; mean age PROPATEN 69.9±10.2, standard 67.8±12 years

Number per group: 80 patients per group

Observed adverse effects: Primary patency was 35% and 14% for heparin-bonded grafts and 29% and 12% for standard ePTFE grafts at 6 and 12 months, respectively (p=0.48). Assisted primary patency was 54%, 41%, and 27% for heparin-bonded grafts and 41%, 30%, and 23% for standard grafts at 12, 24, and 36 months, respectively (p=0.12) by log-rank, p=0.04 by Gehan-Breslow-Wilcoxon. Secondary patency was 83%, 83%, and 81% for heparin-bonded grafts and 81%, 73%, and 68% for standard grafts at 12, 24, and 36 months, respectively (p=0.33). All grafts were ready for cannulation between 2 and 4 weeks postoperatively with no difference between the groups. Of 80 standard grafts, 24 were eventually abandoned vs. 17 heparin-bonded grafts (p=0.188). Bleeding complications and intervention rates were similar in both groups. Mean time to first thrombosis was 9.7±10 months in the heparin-bonded group and 7.8±10.6 months in the standard group (p=0.17). An anatomic cause for occlusion in the first month could be found in 5 (83%) of the 6 heparin-bonded grafts compared with only 8 (50%) of the 16 standard grafts (p=0.18). There were no differences between upper and lower arm access and between the 2 graft types in the upper arm and the 2 graft types in the lower arm. Although the number of thrombolytic treatments was lower by 18% and the time to first thrombosis was longer by 24% in the heparin-bonded group, these differences did not reach statistical significance. 50/80 heparin-bonded grafts thrombosed during the follow-up period and required 119 thrombolytic treatments (range 0-8) compared with 57/80 standard grafts, which required 145 thrombolytic treatments (range 0-8) (p=0.16). 17 grafts were abandoned in the heparin-bonded group vs. 24 in the standard group (p=0.188).

Timing of adverse effects: Through median study follow-up period 23.5 months

Factors that predict response: There were significantly fewer thromboses in heparin-bonded grafts during the first month (8% vs. 20%, p=0.025) and first 5 months (p=0.02).

Source Citation: Attia et al. 2014[22]

Study Design: Non-randomized comparative study

Device or Material: Femoropopiteal bypass surgery for lower limb ischemia with PTFE vs. saphenous vein graft

Contact Duration: Mean and median follow-up period was 12 and 18 months, respectively

Dose: NR

Frequency/Duration: Single administration

Response: Patency

Patient characteristics (gender, mean age): 35 males and 15 females; median age 62 years (range 44 to 70)

Number per group: PTFE 18 patients and saphenous vein graft 32 patients

Observed adverse effects: Use of a prosthetic graft and construction of an intragenicular anastomosis (12 cases) was associated with lower graft patency rates, but statistical significance was not reached. According to study authors "The reversed saphenous vein is the preferred conduit in the present study. However when the

different surgical subgroup are examined separated femoro-distal bypass with vein graft is associated with increased patency rate than femoro distal bypass with synthetic graft."

Timing of adverse effects: Patients were assessed 6 weeks postoperation and at 3, 6, 9, 12, and 18 months.

Factors that predict response: NR for the PTFE patients. The authors looked at risk factors across all 50 patients combined, regardless of graft material.

Source Citation: Rychlik et al. 2014[10]

Study Design: Systematic review

Device or Material: Dacron versus PTFE grafts for above-knee femoropopliteal artery bypass

Contact Duration: ≤10 years

Dose: 5 to 8 mm grafts

Frequency/Duration: Single administration

Response: Antiplatelet/anticoagulation use, Primary patency, Secondary patency

Patient characteristics (gender, mean age): Mean age 66 years, gender NR

Number per group: 8 publications reporting on 6 RCTs with 601 Dacron and 591 PTFE

Observed adverse effects: Although primary and secondary patency rates at 12 months were not significantly different (RR 0.78; p=.08, and RR 0.84; p=0.52), 24-, 36-, and 60-month primary patency rates were significantly better with Dacron compared with PTFE grafts (RR 0.79; p=0.003; RR 0.80; p=0.03; RR 0.85; p=0.02). Statistical analysis also supported higher secondary patency rates for Dacron at 24 months (RR 0.75; p=0.02) and 60 months (RR 0.76-0.77; p=0.03-0.27). Although primary patency was similar between grafts (28% vs. 28%; p=0.12), secondary patencies were better with Dacron at 10 years (49% vs. 35%; p=0.01).

Timing of adverse effects: ≤10 years

Factors that predict response: There was no meta-analysis of this although individual RCTs identified some factors. One study that favored Dracon found that "in patients with only 1 patent crural vessel, the authors noticed decreased patency of both grafts and favored the use of PTFE graft". A second study that favored Dracon found "that the number of outflow vessels had a significant impact on the graft patency; 67% of patients with more than one crural vessel had patent graft (p=0.01). Another study that found no difference between PTFE and Dracon reported "a small graft size (5-6 mm) was a significant predictor of graft failure (p=0.0006). In another study that did not find a difference between Dracon and PTFE authors reported that "multivariate analysis revealed that below-knee anastomosis was the independent predicting factor of primary graft failure (RR 1.7; CI 1.05–2.8). Impaired secondary patency was associated with a below-knee bypass RR of 3.3 (CI 1.8–6.3) and distal gangrene RR of 2.0 (CI 1.01–3.8; p=0.048). Major amputation was predicted by infragenicular bypass, tissue necrosis, and poor runoff."

Source Citation: Van der Slegt 2014[23]

Study Design: Non-randomized comparative study

Device or Material: Precuffed ePTFE grafts compared with autologous saphenous vein (ASV) grafts used in patients with peripheral arterial disease

Contact Duration: ≤5 years

Dose: NR

Frequency/Duration: Single administration

Response: Bladder retention, Compartment syndrome, Decubitus ulcer, Hemorrhage, Primary patency, Primary assisted patency, Secondary patency, Seroma, Wound necrosis

Patient characteristics (gender, mean age): Mean age (range) PTFE 73.0 (41.0-92.7) and ASV 70.1 (36.8-96.5) years; 150 female and 317 male

Number per group: 169 precuffed ePTFE grafts and 298 ASV grafts

Observed adverse effects: **Primary patency rates** at 1, 2, and 5 years were supragenicular ePTFE 56%, 42%, 25% and for ASV 68%, 60%, and 60%, respectively ($p<0.05$); infragenicular PTFE 34%, 18% and 8% vs. ASV 65%, 60%, and 54%, respectively ($p<0.05$); femoro-crural PTFE 24%, 24%, 9% vs. ASV 39%, 39%, and 18%, respectively ($p\geq0.05$).

Primary assisted patency rates at 1, 2, and 5 years were supragenicular ePTFE 59%, 45%, 27% and for ASV 87%, 82%, and 82%, respectively ($p<0.05$); infragenicular PTFE 36%, 22%, and 11% vs. ASV 79%, 77%, and 74%, respectively ($p<0.05$); femoro-crural PTFE 24%, 24%, 9% vs. ASV 45%, 43%, and 30%, respectively ($p<0.05$).

Secondary patency rates of ePTFE vs. ASV at 1 and 5 years, respectively, were as follows: for 134 supragenicular femoropopliteal bypasses, 60% and 27% vs 89% and 85% ($p<.05$); for 190 infragenicular femoropopliteal bypasses, 40% and 25% vs. 86% and 79% ($p<.05$); and for 84 femoro-crural bypasses, 30% and 14% vs. 50% and 50% ($p<.05$).

Minor events PTFE vs. ASV: bladder retention 2 (1%) vs. 2 (1%) p=.62, decubitus 0 vs. 4 (1%) (p=0.30) Surgical events PTFE vs. ASV: wound necrosis 3 (2%) vs. 2 (1%) (p=0.36), seroma 4 (2%) vs. 3 (1%) (p=0.26); hemorrhage 11 (7%) vs. 15 (5%) (p=0.53), compartment syndrome 2 (1%) vs. 0 (p=0.13)

Timing of adverse effects: Mean follow-up PTFE 28.8 months and ASV 36.1 months; adverse events per procedure were recorded until 1 month after discharge of the primary procedure. Follow-up after ASV bypass surgery included routine duplex ultrasound and ABI at 3 months, 6 months, 1 year, and 2 years after the initial procedure, followed by ABI every subsequent 2 years. Follow-up after ePTFE bypass surgery was restricted to duplex ultrasound and ABI examination at 3 months, 1 year, and 2 years after the initial procedure. ABI was measured every subsequent 2 years. All other interim duplex ultrasound examinations were performed after suspicion of graft-related problems.

Factors that predict response: NR

Source Citation: Moulakakis et al. 2013[24]

Study Design: Non-randomized comparative study

Device or Material: Anaconda (Sulzer Vascutek, Bad Soden, Germany); Zenith (Cook Inc, Bloomington, Ind); Excluder (W. L. Gore and Assoc, Flagstaff, Ariz); and Endurant (Medtronic, Minneapolis, Minn)

Contact Duration: ≤30 day follow-up

Dose: NR

Frequency/Duration: Single administration

Response: Endoleaks, Hematoma

Patient characteristics (gender, mean age): Mean (SE) age years: Anaconda 73.11 (0.86), Zenith 73.08 (1.06), Excluder 70.87 (1.34), Endurant 74.17 (1.55); 81 males and 6 females

Number per group: Anaconda 28 patients, Zenith 26 patients, Excluder 23 patients, and Endurant 10 patients

Observed adverse effects: Endografts were successfully implanted in all patients. There were no open conversions, no deaths, and no major perioperative complications. There was no postoperative increase in troponin

levels. Minor complications included local hematomas in femoral incisions in 3 patients (1 each in Anaconda, Zenith, and Excluder), who were treated conservatively. At 1-month follow-up, endoleaks were recorded in 12 (13.8%) patients (Anaconda n=5, 17.9%; Zenith n=3, 11.5%; Excluder n=3 patients, 13.0%; Enduran, 1 patient, 10%). No statistically significant differences were recorded for the presence of endoleak with regard to the endograft type.

IL-10: the Anaconda group showed the highest mean value at 24 hours and differed significantly from the Excluder (p<.001) and Endurant (p=0.04) groups. The Zenith group also showed higher mean values than the Excluder (p=0.01). Comparisons among the groups of endograft types at 48 hours showed that mean values in patients treated with Anaconda endografts were higher compared with Endurant (p<0.001) and Excluder (p<0.001) endografts, whereas mean values in patients treated with Zenith endografts were significantly higher compared with Endurant (p<0.001) and Excluder (p<0.001) endografts. Patients treated with Anaconda endografts showed the highest IL-6 mean values at 24 hours postoperatively. Statistically significant differences were observed among patients treated with the Anaconda vs. the Excluder (p<0.001), Anaconda vs. Endurant (p=0.04), and Zenith vs. Excluder (p=0.01). Comparisons at 48 hours showed significant differences for Anaconda vs. Excluder (p<0.001), Anaconda vs. Endurant (p<0.001), Zenith vs. Excluder (p<0.001), and Zenith vs. Endurant (p<0.001). With regard to IL-8, although patients treated with Anaconda endografts showed the highest mean values at 24 hours and 48 hours postoperatively, no statistical differences were observed among the patients treated with different types of endografts. Patients in the Excluder group showed statistically lower mean values at 24 hours and 48 hours postoperatively.

For white blood cells (WBC), higher mean values were recorded after 24 hours in patients treated with the Anaconda endograft compared with the Excluder (p<0.001) and Zenith (p<0.001) endografts and the Endurant endograft compared with the Excluder (p=0.001) and Zenith (p=0.01) endografts. After 48 hours, statistically significant differences were observed among Anaconda vs. Excluder (p<0.001), Anaconda vs. Zenith (p<0.001), Anaconda vs. Endurant (p<.001), Endurant vs. Excluder (p=0.004), and Zenith vs.Excluder (p=0.02) groups.

Timing of adverse effects: Operative outcomes were recorded. Temperature, WBC count, platelet count, and serum concentrations of cytokines (IL-6, IL-8, and IL-10) were measured preoperatively, 24 hours postoperatively, and 48 hours postoperatively. Final follow-up was 30 days.

Factors that predict response: NR

Source Citation: Dorigo et al. 2012[25]

Study Design: Registry data

Device or Material: Heparin-bonded ePTFE graft (PROPATEN Gore-Tex, W.L. Gore & Associates Inc, Flagstaff, AZ, USA) and autologous saphenous vein in below-knee femoropopliteal bypasses

Contact Duration: 28.5±22.1 months

Dose: NR

Frequency/Duration: Single administration

Response: Adjunctive procedures, Antiplatelet/anticoagulation therapy, Primary patency, Secondary patency, Thrombosis

Patient characteristics (gender, mean age): 224 women and 726 male; median age PROPATEN 72.7 years and ASV 72.4 years

Number per group: PROPATEN 556 patients, and ASV group 394 patients

Observed adverse effects: Patients in HePTFE group more frequently had adjunctive procedures performed at distal anastomotic sites in order to improve run-off status. Postoperative and long-term medical treatment consisted of single antiplatelet therapy in 40% of HePTFE group and in 39% (p=NS) in ASV group, double

antiplatelet therapy in 17% of HePTFE group and 21% (p=NS) in ASV group and of oral anticoagulants in 43% of the HePTFE group and 40% (p=NS) in ASV group, the regimen for anti-coagulation or anti-platelet being determined on the basis of surgeon's preference. Primary patency rate at 48 months was significantly better in ASV group (61%) than in HePTFE group (44.5%; p=0.004).

In below-knee bypasses, the corresponding figures were 45.2% in HePTFE group (SE 0.03) and 69% in ASV group (SE 0.04; p<0.001); in tibial bypasses, they were 39% (SE 0.07) and 53% (SE 0.04; p=0.04).

The rates of secondary patency at 48 months were 57% in HePTFE group (SE 0.03) and 67.5% in ASV group (SE 0.03), without significant differences between the two groups (p=0.1).

Early postoperative results: early graft thrombosis occurred in 55 patients (35 in HePTFE group and 20 in ASV group), with cumulative 30-day graft patency rates of 94 % and 95%, respectively (p=0.3).

Long-term follow-up: during follow-up, 263 new graft thromboses (173 in HePTFE group and 90 in ASV group) occurred. In 33 cases (8 in HePTFE group and 25 in ASV group) significant stenoses at anastomotic sites or at saphenous valves without graft thrombosis were detected; in 16 cases percutaneous transluminal angioplasty of the distal anastomosis or of the residual valves was performed, while in 13 patients endarterectomy of the common femoral artery with patching of the proximal anastomosis was required. Four patients were medically managed without developing graft occlusion.

Timing of adverse effects: Mean duration of follow-up was 28.5±22.1 months, Follow-up was performed within the third postoperative month, at 12 months and then yearly.

Factors that predict response: At univariate analysis, female gender, secondary intervention, distal tibial anastomosis, adjunctive distal procedures, poor run-off score, and kind of graft were found to significantly affect long-term primary patency; at multivariate analysis female gender, secondary intervention and kind of graft maintained their significance. For secondary patency, female gender, secondary intervention, distal tibial anastomosis, critical limb ischemia, adjunctive distal procedures, and poor run-off score were found to significantly affect it at univariate analysis, while at multivariate analysis only secondary interventions-maintained significance.

AAA = abdominal aortic aneurysm; ABI = ankle-brachial index; AE = adverse event; AS = anterior sector; ASV = autologous saphenous vein; CI = confidence interval; ECFP = Extra-cardiac Fontan procedure; HR = hazard ratio; IL = interleukin; IRHV to IVC = inferior right hepatic vein to inferior vena cava; LOS = length of stay; MAE = major adverse events; MHV = middle hepatic vein; NR = not reported; NS = not significant; OR = odds ratio; p = p value; PTFE = polytetrafluoroethylene; $PY^{-}1$ = incidence rate per patient year; RL = right lobe; RR = relative risk; SD = standard deviation; SE = standard error; TCC = tunneled cuffed catheter

Table 12: Stents - Health Effect (In Vivo) Human Studies

Local Response/Toxicity

Source Citation: Zhou et al. 2020[32]

Study Design: Non-randomized controlled study

Device or Material: PTFE-covered stent (Viatorr Endoprosthesis, GORE and Assoc., AZ, USA vs. ET with NSBB drugs

Contact Duration: Median 20 months

Dose: NR

Frequency/Duration: Single administration

Response: Variceal rebleeding, Hepatic encephalopathy, overall adverse events (includes local and systemic)

Patient characteristics (gender, mean age): Patients with liver cirrhosis and endoscopically confirmed gastroesophageal variceal bleeding; 56.4% male; 59.1 and 53.9 years, by group

Number per group: 179 total; 77 TIPS with PTFE-covered stents; 102 ET with NSBB

Observed adverse effects: **Variceal rebleeding** significantly less for PTFE-stent group (7.8% vs. 39.2% for ET group; p<0.001); **Hepatic encephalopathy** not significantly different between TIPS and ET groups (15.6% vs. 12.7%; p=0.73); **Overall adverse events** not significantly different between groups (56% for PTFE vs. 56% for ET; p=0.53). Shunt dysfunction (on placement) 7.8% for PTFE stent group.

Timing of adverse effects: Rebleeding rate over 2 years. Median follow-up time was 20 months.

Factors that predict response: Subgroup multivariate analysis showed patients with **HVPG, gastro-renal shunts, and ep-GVs** showed significantly different **2-year rebleeding free rate** when compared between treatment groups. Values higher for PTFE stent group than ET group for subjects with **HVPG ≥ 20 mmHg** (91% vs. 67%; p=0.02); for PTFE stent group with **gastro-renal shunts** (94% vs. 59%; p=0.03); and for PTFE-stent subjects with **ep-GVs** (90% vs. 58%; p=0.016). Variceal rebleeding influenced by treatment and etiology.

Source Citation: Hernandez-Enriquez et al. 2018[37]

Study Design: Non-randomized controlled study

Device or Material: **PTFE-covered** (Jostent-Graftmaster stent; Abbott Vascular, Santa Clara, CA) vs. **PUR-covered** stent (PK Papyrus stent; BIOTRONIK, Berlin)

Contact Duration: 1 year

Dose: NR

Frequency/Duration: Single administration

Response: In-stent restenosis, Thrombosis, Pericardial effusion

Patient characteristics (gender, mean age): Patients with coronary artery perforation (CAP); 75% male; mean 77 years

Number per group: 39 (65%) PTFE; 22 (36%) PUR

Observed adverse effects: **Stent thrombosis** not significantly different between groups (n=1/group; 3% PTFE vs. 6% PUR); **restenosis** not significantly different between groups (n=1, 3% PTFE vs. n=2, 12% PUR); **pericardial effusion** higher for PTFE group (72% vs. 41%; p=0.028)

Timing of adverse effects: Up to 1 year

Factors that predict response: NR

Source Citation: Kim et al. 2017[34]

Study Design: Non-randomized controlled study

Device or Material: PTFE (ext/int)- vs. PUR-covered REMs; Niti-S Urethral Stent, Taewoong, S. Korea

Contact Duration: Long-term follow-up of 18 years

Dose: NR

Frequency/Duration: Frequency/duration variable depending on results; 39.5% removed electively after mean 95 days; 60.5% removed at mean 48.6 days due to complications

Response: Overall complications, Tissue ingrowth, Granulation tissue, Patency, Stent migration

Patient characteristics (gender, mean age): Patients with recurrent benign urethral strictures; 100% male; 51 years (range 16 to 77)

Number per group: 54 patients: 21 (38.9%) internal PTFE; 20 (37%) external PTFE; 13 (24.1%) PUR; 114 REMs placed: 47 int-PTFE, 41 ext-PTFE, and 26 PUR REMs

Observed adverse effects: **Overall complications** significantly higher for ext-PTFE (78.7%) than other 2 groups (46.3% and 50% for ext-PTFE and PUR, respectively); **Tissue ingrowth/membrane separation** significantly higher for int-PTFE (17.0%) and PUR (23.1%) groups vs. ext-PTFE (0%); **Granulation tissue** formation not significantly different between groups (8.5% int-PTFE; 14.6% ext-PTFE; 11.5% PUR); **Stent migration** significantly higher for int-PTFE group (51.1%) vs. ext-PTFE (26.8%) and PUR (15.4%) groups; **patency** (up to 6 months) longer for ext-PTFE (significantly better than int-PTFE; not significantly different than PUR); **maintained patency** not significantly better for any group beyond 6 months and up to 18 years

Timing of adverse effects: Overall complications: mean 67.3 months; migration 29.7 months; tissue ingrowth 58 months; granulation tissue 89.9 months

Factors that predict response: **Stent indwelling time** only significant factor associated with maintained patency after temporary placement (OR 5.4; p=0.02)

Source Citation: Piazza et al. 2017[35]

Study Design: Non-randomized controlled study

Device or Material: PTFE-covered self-expanding stents vs. BMS (specific devices not reported)

Contact Duration: Mean 23±17 months; up to 36 months

Dose: N/A

Frequency/Duration: Single Administration

Response: Patency

Patient characteristics (gender, mean age): Patients with IAOs; 79% male; mean 68 years

Number per group: 128 patients total; 78 PTFE-covered; 50 BMS (n=47 per group for propensity matched cohort)

Observed adverse effects: **Overall primary patency** not significantly different (but borderline significant) but worse for BMS group (68.3 vs. 88.3 for unmatched cohort; p=0.07, and 66.1 vs. 87.1 for matched cohort; p=0.06). **Patency** for TASC II D-classified lesions significantly worse for BMS group (56.8 vs. 89.7 for unmatched cohort; p=0.01 and 54.3 vs. 88.6 for matched cohort; p=0.03). No significant difference found for TASC B and C classifications.

Timing of adverse effects: Mean 23±17 months; up to 36 months

Factors that predict response: Patency favored PTFE-covered stents for **IAO size** > 3.5 cm in length (p=0.04), **total lesion length** > 6 cm (p=0.04), and **IAO with calcification** > 75% of the arterial wall circumference (p=0.01).

Source Citation: Perarnau et al. 2014[29]

Study Design: RCT

Device or Material: PTFE-covered stent vs. BMS

Contact Duration: 2 years

Dose: NR

Frequency/Duration: Single administration

Response: Shunt dysfunction, Early complications, Hepatic encephalopathy

Patient characteristics (gender, mean age): 75% male, 58 years

Number per group: 137 (66 covered, 71 bare) patients undergoing TIPS

Observed adverse effects: The risk of shunt dysfunction was significantly reduced in the covered stent group compared to the bare stent group (HR 0.60, 95% CI 0.38–0.96; p=0.032). Early complications of the procedure (including death, thrombosis, and fever up to the first month of follow-up) were not significantly different between the groups (covered: 22.4%, bare: 34.9%; p=0.13). The risk of hepatic encephalopathy was not significantly different between the groups (HR 0.84, 95% CI 0.46–1.55; p=0.58).

Timing of adverse effects: 1 month to 2 years

Factors that predict response: NR

Source Citation: Sohrabi et al. 2014[30]

Study Design: RC

Device or Material: PTFE-covered stent vs. BMS (NuMed, Hopkinton, New York)

Contact Duration: Up to 60 months (Mean 31.1 months)

Dose: NR

Frequency/Duration: Single administration

Response: Recoarctation, Pseudoaneurysm, Left subclavian artery obstruction, Aortic dissection, Postcoarctation of aorta syndrome

Patient characteristics (gender, mean age): 67% male, 23.6 years

Number per group: 120 (60 per group) coarctation of aorta patients

Observed adverse effects: Recoarctation was not significantly different between groups (covered: 0%, bare: 6.7%). Pseudoaneurysm was not significantly different between groups (covered 3.3%, bare: 0%). There were no occurrences of obstruction, dissection, or postcoarctation of aorta syndrome.

Timing of adverse effects: 1 month to 60 months

Factors that predict response: NR

Source Citation: Grimme et al. 2012[28]

Study Design: Systematic review (including RCTs and cohort studies/case series)

Device or Material: PTFE-covered stent vs. BMS

Contact Duration: Range of mean of 8 to 21 months across included studies

Dose: NR

Frequency/Duration: Single administration

Response: Recurrent stenosis, Patency, Complications

Patient characteristics (gender, mean age): Range of 24% to 100% male, 46 to 71 years

Number per group: 4,188 (262 covered, 3,926 bare) with focal infrarenal aortic occlusive disease, aortoiliac complex occlusive disease, or iliac artery occlusive disease across 49 studies

Observed adverse effects: Recurrent stenosis rate ranged from 0% to 8% in studies with patients receiving covered stents and 0% to 75% in studies with patients receiving bare stents. 1-year primary patency rates ranged from 70% to 100% in studies of patients with either covered or bare stents. 1-year secondary patency rates ranged from 88% to 100% in studies of patients with covered stents and from 84% to 100% in those of patients with bare stents. No studies of patients with covered stents reported on 4-year primary or secondary patency. Complication rates ranged from 0% to 17% in studies of patients with covered stents and 0% to 29% in those of patients with bare stents.

Timing of adverse effects: 1 to 4 years

Factors that predict response: NR

Source Citation: Clark et al. 2011[36]

Study Design: Non-randomized controlled study

Device or Material: PTFE-covered stent vs. BMS

Contact Duration: Median of 19 months

Dose: NR

Frequency/Duration: Single administration

Response: Shunt dysfunction, Reinterventions for stenosis, Hepatic function deterioration

Patient characteristics (gender, mean age): 61% male, median 56 years

Number per group: 246 (176 covered, 70 bare) patients undergoing TIPS

Observed adverse effects: Shunt dysfunction occurred in 22% of patients with covered stents and 57% of patients with bare stents (p=0.05). Reinterventions for stenosis occurred in 19% of patients with covered stents and 33% of patients with bare stents (p=0.01). Hepatic function deterioration occurred in 30% of patients with covered stents and 31% of patients with bare stents (p=0.32).

Timing of adverse effects: Up to 167 months

Factors that predict response: NR

Systemic Response/Toxicity

Source Citation: Zhou et al. 2020[32]

Study Design: Non-randomized controlled study

Device or Material: PTFE-covered stent (Viatorr Endoprosthesis, GORE and Assoc., AZ, USA vs. ET with NSBB drugs

Contact Duration: Median 20 months

Dose: NR

Frequency/Duration: Single administration

Response: Survival, overall adverse events (includes local and systemic)

Patient characteristics (gender, mean age): Patients with liver cirrhosis and endoscopically confirmed GEVB; 56.4% male; 59.1 and 53.9 years, by group

Number per group: 179 total; 77 TIPS with PTFE-covered stents; 102 ET with NSBB

Observed adverse effects: **Survival** not significantly different between groups (6.5% and 8.8% died in stent and ET groups after 36 months; p=0.53) **Overall adverse events** not significantly different between groups (56% for PTFE vs. 56% for ET; p=0.53).

Timing of adverse effects: Median follow-up time was 20 months. Median times of individual adverse events NR.

Factors that predict response: Hepatic encephalopathy influenced by **albumin**; survival influenced by **total bilirubin**, **albumin**, and **model for end-stage liver disease score**.

Source Citation: Hernandez-Enriquez et al. 2018[37]

Study Design: Non-randomized controlled study

Device or Material: PTFE-covered stent vs. PUR-covered stent

Contact Duration: 1 year

Dose: NR

Frequency/Duration: Single administration

Response: All-cause mortality, MACE, Cardiac death, MI

Patient characteristics (gender, mean age): Patients with CAP; 75% male, 77 years

Number per group: 39 (65%) PTFE; 22 (36%) PUR

Observed adverse effects: **All-cause mortality** not significantly different between groups (n=16, 41% PTFE vs. n=5, 26% PUR); **MACE** not significantly different (n=22, 56% PTFE vs. n=11, 58% PUR); **Cardiac death** not significantly different (n=14, 36% PTFE vs. n=5, 26% PUR); **MI** not significantly different (n=3, 8% PTFE vs. n=2, 11% PUR)

Timing of adverse effects: Up to 1 year

Factors that predict response: NR

Source Citation: Piazza et al. 2017[35]

Study Design: Non-randomized controlled study

Device or Material: PTFE-covered self-expanding stents vs. BMS (specific devices not reported)

Contact Duration: Mean 23±17 months; up to 36 months

Dose: N/A

Frequency/Duration: Single Administration

Response: Overall medical complications, Intra- or perioperative major cardiac events requiring intervention, Respiratory failure (embolism or respiratory distress), Dialysis, Death

Patient characteristics (gender, mean age): Patients with IAOs; 79% male; mean 68 years

Number per group: 128 patients total; 78 PTFE-covered; 50 BMS (n=47 per group for propensity matched cohort)

Observed adverse effects: No significant differences between groups: overall complications (p=0.45), major cardiac events (p=1.0), respiratory failure (p=0.53), dialysis (p=1.0), and death (p=1.0); propensity matched group also not significant.

Timing of adverse effects: Medical complications <30 days from treatment

Factors that predict response: NR

Source Citation: Perarnau et al. 2014[29]

Study Design: RCT

Device or Material: PTFE-covered stent vs. BMS

Contact Duration: 2 years

Dose: NR

Frequency/Duration: Single administration

Response: Mortality, Hospitalization

Patient characteristics (gender, mean age): 75% male, 58 years

Number per group: 137 (66 covered, 71 bare) patients undergoing TIPS

Observed adverse effects: Mortality was not significantly different between the groups. The average number of hospitalizations in the covered group was 6.4 vs. 7.9 in the bare group. The average number of hospital days was 32 in the covered group vs. 37.5 in the bare group.

Timing of adverse effects: 1 month to 2 years

Factors that predict response: NR

Source Citation: Sohrabi et al. 2014[30]

Study Design: RCT

Device or Material: PTFE-covered stent vs. BMS (NuMed, Hopkinton, New York)

Contact Duration: Up to 60 months (Mean 31.1 months)

Dose: NR

Frequency/Duration: Single administration

Response: Mortality, Hospitalization, Hypertension

Patient characteristics (gender, mean age): 67% male, 23.6 years

Number per group: 120 (60 per group) coarctation of aorta patients

Observed adverse effects: Mortality was not significantly different between the groups (covered: 0, bare: 1). Duration of hospitalization was not significantly different between groups (covered: 3.05 days, bare: 3.44

days). The numbers of normotensive patients after the procedure were not significantly different between the groups (covered: 78.3%, bare: 73.3%).

Timing of adverse effects: 1 month to up to 60 months

Factors that predict response: NR

Source Citation: Bennett et al. 2013[31]

Study Design: RCT

Device or Material: Symbiot covered stent (Boston Scientific, Natick, MA) vs. BMS + FilterWire EX (Boston Scientific, Natick, MA) vs. BMS alone

Contact Duration: 7.3 to 7.6 years by group

Dose: NR

Frequency/Duration: Single administration

Response: All-cause mortality, MI, Target vessel failure (composite for MACE: all-cause death, MI, and target lesion revasularization)

Patient characteristics (gender, mean age): Patients with degenerative SVG lesions; 88% male; mean 70 years

Number per group: 90 patients; 30 patients per device

Observed adverse effects: **All-cause mortality** not significantly different between groups at 6 months (10%, 7%, and 3% for Symbiot, FilterWire, and BMS groups) or long-term (20%, 43%, and 37%); **MI** not significantly different between groups at 6 months (7%, for all groups) or long-term (23%, 17%, and 23%, respectively, for Symbiot, FilterWire, and BMS groups); **target vessel failure** (composite end point of all-cause death, Q-wave or non-Q-wave MI, or target lesion revascularization) not significantly different between groups at 6 months (20%, 13%, and 10% for Symbiot, FilterWire, and BMS groups) or long-term (57%, 57%, and 60%)

Timing of adverse effects: Reported at 6 months and long-term

Factors that predict response: NR

Source Citation: Grimme et al. 2012[28]

Study Design: Systematic review (including RCTs and cohort studies/case series)

Device or Material: PTFE-covered stent vs. BMS

Contact Duration: Range of mean of 8 to 21 months across included studies

Dose: NR

Frequency/Duration: Single administration

Response: Distal embolization

Patient characteristics (gender, mean age): Range of 24% to 100% male, Range of 46 to 71 years

Number per group: 4188 (262 covered, 3926 bare) with focal infrarenal aortic occlusive disease, aortoiliac complex occlusive disease, or iliac artery occlusive disease across 49 studies

Observed adverse effects: Distal embolization rates were all 0% in studies reporting this outcome for patients with covered stents and ranged from 0% to 89% in studies on patients with bare stents.

Timing of adverse effects: 1 to 4 years

Factors that predict response: NR

Source Citation: Clark et al. 2011[36]

Study Design: Non-randomized controlled study

Device or Material: PTFE-covered stent vs. BMS

Contact Duration: Median of 19 months

Dose: NR

Frequency/Duration: Single administration

Response: Mortality

Patient characteristics (gender, mean age): 61% male, Median 56 years

Number per group: 246 (176 covered, 70 bare) patients undergoing TIPS

Observed adverse effects: Median survival time was 33 months for patients receiving covered stents and 31 months for those receiving bare stents (p = 0.5).

Timing of adverse effects: Up to 167 months

Factors that predict response: NR

BMS= bare metal stent; CAP= coronary artery perforation; CI= confidence interval; Ep-GV= extraluminal para-gastric vein; ET= endoscopic therapy; GEVB= gastroesophageal variceal bleeding; HR= hazard ratio; HVPG= hepatic vein pressure gradient; IAO= iliac artery occlusion; MACE= major adverse cardiac event; MI= myocardial infarction; NR= not reported; NSBB= non-selective β-blockers; OR= odds ratio; PTFE= polytetrafluoroethylene; PUR= polyurethane; REMS= retrievable self-expandable metallic stent; SVG= saphenous vein graft; TASC II= Trans-Atlantic InterSociety Consensus; TIPS= transjugular intrahepatic portosystemic shunt

Table 13: Stent-Grafts - Health Effect (In Vivo) Human Studies

Local Response/Toxicity

Source Citation: Bosiers et al 2020[44]

Study Design: RCT RELINE trial (NCT01108861)

Device or Material: Stent-graft (Viabahn with PROPATEN Bioactive Surface [W.L. Gore]) vs. PTA to treat restenotic or reoccluded lesions in the femoropopliteal arteries

Contact Duration: Follow-up 24 months

Dose: Lesion length 30 to 330 mm

Frequency/Duration: Single administration

Response: Primary Patency

Patient characteristics (gender, mean age): 74.4% male. 67.7 years

Number per group: 83 (39 stent-graft, 44 PTA)

Observed adverse effects: No patients were reported to have device-related serious adverse events within 30 days postprocedure. At 12 months, the primary patency rates were 74.8% for the stent-graft group and 28.0% for the PTA group ($p<0.001$), and at 24 months were 58.4% and 11.6%, respectively ($p<0.001$). No stent fractures were observed through 12 months.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Martinelli et al 2020[47]

Study Design: Non-randomized comparative cohort

Device or Material: Stent-graft (Excluder & C3 [W.L. Gore]) vs. chromium-cobalt endoskeleton (AFX Endologix) for EVAR

Contact Duration: Mean follow-up 24 months

Dose: NR

Frequency/Duration: Single administration

Response: New-onset thrombus

Patient characteristics (gender, mean age): 84.1% male, 74±10 years

Number per group: 110 (43 PTFE stent-graft, 56 AFX device)

Observed adverse effects: New-onset thrombus occurred in 21% of ePTFE stent-grafts.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Kavan et al 2019[45]

Study Design: RCT

Device or Material: Stent-graft [Fluency Plus [Bard Peripheral Vascular]) vs. self-expanding BMS (E-Luminexx [Bard Peripheral Vascular]) vs. PTA to treat failing hemodialysis access

Contact Duration: Median follow-up 22.4 months

Dose: Reference diameter 6.3 mm

Frequency/Duration: Single administration

Response: Occlusion, Restenosis, Thrombosis

Patient characteristics (gender, mean age): 71% female, 64 years

Number per group: 50 (20 stent-graft, 19 BMS, 20 PTA)

Observed adverse effects: Stent-graft required significantly fewer secondary interventions at 1 year (mean 1.7±2.1; p=0.015), and 2 years (mean 2.2±5.1, p=.037) compared to both PTA and BMS. Thrombosis occurred in 1 case. Patency was 65% at 12 months and 37% at 24 months, significantly better than for PTA or stent (p<0.0001). Secondary patency rates were 89% at 12 months and 79% at 24 months, and did not significantly differ.

Timing of adverse effects: NR

Factors that predict response: Greater residual stenosis after initial PTA (HR=1.048; p=0.007) is a risk factor for loss of patency. Smaller diameter of the reference segment adjacent to the stenosis (HR=0.498, p=0.005) and the use of a deep vein as the outflow (HR=0.457, p=0.022) are predictors of primary patency.

Source Citation: Venturini et al 2017[51]

Study Design: Non-randomized comparative cohort

Device or Material: Stent-graft (Viabahn [W.L. Gore]) vs. transcatheter embolization (TE) to treat VAAs and VAPAs

Contact Duration: Median follow-up 32.8 months

Dose: Diameter 5 to 9 mm, length 2.5 to 5 cm

Frequency/Duration: Single administration of 1 to 3 stent-grafts

Response: Hemorrhage, Occlusion, Patency

Patient characteristics (gender, mean age): 58% men, 59±14 years

Number per group: 100 (30 covered-stent, 70 TE)

Observed adverse effects: Complications included hemorrhage requiring stent removal (n=1) and occlusion (n=2). Two deaths occurred within 30 days in patients who were treated emergently and had septic complications; therefore, not device related. In covered-stent patients, aneurysm exclusion and stent patency were observed in 20/22 patients at 3 to 6 months and aneurysm exclusion in 19/19 patients and stent patency in 17/19 after >6 months.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Haskal et al 2016[42]

Study Design: RCT RENOVA trial (NCT00677235)

Device or Material: Stent-graft (FLAIR [BARD Peripheral Vascular]) vs. PTA to treat failing hemodialysis access

Contact Duration: Follow-up 24 months

Dose: Mean length 44.6 mm ±4.9

Frequency/Duration: Single administration of 1-2 stent-grafts

Response: Embolism, Hematoma, Hemorrhage, Occlusion, Patency, Pseudoaneurysm, Restenosis, Vessel rupture

Patient characteristics (gender, mean age): 64.1% female, 63.1 years

Number per group: 270 (142 stent-grafts in 128 patients [21 straight, 121 flared]; 132 PTA)

Observed adverse effects: The overall rate of stenosis requiring reintervention was significantly lower in the stent-graft group (63.0%) compared with the PTA group (82.6%; p<0.001). The 12-month device-related/procedure-related AE rate was 2.3% for the stent graft, compared to 8.7 for PTA (p=0.001). Adverse events included thrombotic occlusion (n=60), hemorrhage (n=10), pseudoaneurysm (n=9), hematoma (n=5), vessel rupture (n=2), embolism (n=1). There were no instances of device migration or kinking. Death was comparable in the stent-graft group (n=38) and PTA group (n=36); no deaths were reported as device-related. ACPP was significantly higher for the stent-graft group at 12 (24%; p=0.007) and 24 months (9.5%; p=0.011) compared to PTA. TAPP at 12 months was significantly better for the stent graft group (47.6%) compared with PTA group (24.8%; p<0.001), and remained significant at 24 months, 26.9% versus 13.5% (p<0.001).

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Falk et al 2016[40]

Study Design: RCT RESCUE trial (NCT01257438)

Device or Material: Stent-graft (Fluency Plus [Bard Peripheral Vascular]) vs. PTA to treat failing hemodialysis access

Contact Duration: Follow-up 24 months

Dose: Median diameter 8 and 9 mm, median length 40 and 60 mm

Frequency/Duration: Single administration

Response: Binary restenosis, Patency

Patient characteristics (gender, mean age): 51.3% male, 61.9 years

Number per group: 275 (132 stent-graft, 143 PTA)

Observed adverse effects: Binary restenosis occurred in 19.7% of patients in the stent-graft group compared to 73.4% in the PTA group. ACPP was significantly higher in the stent-graft group (18.6%) than in the PTA group (4.5%; p<0.001) at 6 months. TAPP was higher for the stent-graft group (15.6%) compared to PTA (2.2%) at 24 months. Major complications that resulted in death occurred in 4 stent-graft recipients (3%) but they were not classified as device-related.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Lauermann et al 2015[46]

Study Design: Non-randomized comparative cohort

Device or Material: Stent-graft (Viatorr [W.L. Gore]) vs. BMS (Wallstent [Boston Scientific]) for TIPS

Contact Duration: NR

Dose: Mean length 92.29 mm, mean diameter 9. 71 mm

Frequency/Duration: Single administration

Response: Occlusion, Patency, Restenosis

Patient characteristics (gender, mean age): 67.1% male, 56±12 years. Portal hypertension, primarily due to liver cirrhosis.

Number per group: 163 (83 stent graft, 80 BMS)

Observed adverse effects: The stent-graft showed significantly better primary patency after 14 days (100%; p=0.004), 6 months (95%; p=0.047) and 2 years (82.9%; p=0.037) compared to BMS. Revisions were required in 13.4% of cases, primarily due to stenosis, occlusion, and HE.

Timing of adverse effects: NR

Factors that predict response: Portal venous thrombosis was identified as a major risk factor for technical failure. Liver capsule perforation was associated with significantly lower probability of 1-year survival (38.1% vs. 86.4%; p<0.001).

Source Citation: Grimme et al 2014[49]

Study Design: Non-randomized comparative cohort

Device or Material: Stent-graft [Josent [Abbott Laboratories]; Advanta V12 [Atrium Medical]) vs. BMS (Genesis [Cordis Corporation]) for F-EVAR

Contact Duration: Follow-up 4 years, median follow-up 13 months

Dose: NR

Frequency/Duration: NR

Response: Occlusion, Patency, Restenosis, Stent fracture

Patient characteristics (gender, mean age): 89.1% male. 73 years.

Number per group: 138

Observed adverse effects: Renal artery patency was 97.3% at one year and 92.4% at 4 years for stents-grafts, not significantly higher than bare-metal stents. Freedom from stenosis in renal artery stents (occluded stents excluded) was 92.9% at 1 year and 86.7% at 4 years for stent-grafts, significantly higher than bare-metal stents (84.5% and 58.9%, respectively; p=0.04). Freedom from occlusion and stenosis was 91.4% at 1 year and 80.9% at 4 years for covered stents. Stent fractures were seen in 2 covered stents (1.2%).

Timing of adverse effects: NR

Factors that predict response: Material fracture significantly reduced stent patency. Stent-grafts fractured significantly less than uncovered stents (p=0.01). PTFE-covered stent-grafts may less prone to fracture due to greater flexibility provided by a strong fixation of the PTFE layers to the arteries. Renal dysfunction was significantly associated with renal stent occlusion or stenosis.

Source Citation: Geraghty et al 2013[43]

Study Design: RCT VIBRANT trial (NCT00228384)

Device or Material: Stent-graft (Viabahn [W.L. Gore]) vs. BMS for symptomatic superficial femoral artery disease

Contact Duration: Follow-up 36 months

Dose: Diameter 6 to 8 mm

Frequency/Duration: Single administration of a median of two stent-grafts

Response: Occlusion, Patency, Restenosis, Stent fracture

Patient characteristics (gender, mean age): 62.5% male, 69 years (patients receiving the Viabahn device were significantly older than those receiving bare nitinol stents.)

Number per group: 148 (72 Viabahn stent-graft, 76 bare nitinol stent)

Observed adverse effects: Stent fractures (2.6%) were significantly less common with the stent-graft, compared to bare nitinol stent (50%; $p<0.001$). At 3 years, primary patency rates did not significantly differ between the stent-graft group and the bare nitinol stent group (24.2% vs. 25.9%; $p=0.392$). Primary-assisted patency rate was significantly lower for stent-grafts (69.8%) compared to bare nitinol stents (88.8%; $p=0.04$). Secondary patency rates did not differ. There was no significant difference in overall re-intervention rates between the stent-graft (34.7%) and bare nitinol stent (34.2%). Death occurred in 9 patients (12%), compared to 3 (3.9%) in the bare stent group, none were determined to be device-related.

Timing of adverse effects: Patency rates diminish most rapidly in the first year after device implantation.

Factors that predict response: NR

Source Citation: Ikoma et al 2013[52]

Study Design: Non-randomized comparative cohort

Device or Material: ePTFE-covered stent-graft (Excluder [W.L. Gore]) vs. polyester stent-graft (Zenith [Cook Inc.]) for EVAR

Contact Duration: 10 days

Dose: NR

Frequency/Duration: Single administration

Response: Endoleak

Patient characteristics (gender, mean age): 76.4 years.

Number per group: 88 (37 PTFE, 51 polyester)

Observed adverse effects: Postoperative endoleak occurred in 13 cases (35.1%).

Timing of adverse effects: NR

Factors that predict response: A change in FDP of ≤3.1 μg/mL at day 7 was predictive of an endoleak after EVAR. The lack of pores in PTFE may improve tissue repair by preventing platelets and inflammatory cells from crossing the graft, preventing the formation of a thrombus.

Source Citation: Möllenhoff et al 2013[39]

Study Design: Systematic Review

Device or Material: Viabahn [W.L. Gore] and Hemobahn [W.L. Gore] stent-grafts to treat popliteal aneurysms

Contact Duration: Mean follow-up 36.9 months

Dose: Mean PPA diameter 29 mm

Frequency/Duration: Single administration of 1 to 4 stent-grafts

Response: Access site hematoma, Acute thrombosis, Endoleak, Stent fracture, Migration, Occlusion, Restenosis, Patency

Patient characteristics (gender, mean age): 92.3% male, 72.4 years.

Number per group: 8 studies included; 251 PPA in 222 patients

Observed adverse effects: Perioperative complications (1.6%) included access site hematomas (n=3) and acute endograft thrombosis (n=1). Postoperative complications included endoleak (6%, n=15) and endograft migration (5.2%; n=13). Endograft fracture (5.6%; n=14) resulted in occlusion (n=6) and type III and IV endoleaks (n=2). Endograft failure (n=46) was due to occlusion (n=42) and stenosis (n=4). Amputation was required in 2 patients due to endograft occlusion, one of these patients died within 30 days from acute endograft thrombosis leading to acute MI. Primary patency rate at 1 year was 85.6%, and 78.5% at 2 years. Secondary patency rate at 1 year was 93.5% and 90.4% at 2 years.

Timing of adverse effects: NR

Factors that predict response: Repetitive motility of the knee joint may predispose the endograft to kinking, fracture, and occlusion.

Source Citation: Doomernik et al 2012[38]

Study Design: Systematic review

Device or Material: Stent-grafts (Viabahn [W.L. Gore] and Hemobahn [W.L. Gore]) to treat long de novo lesions of the SFA

Contact Duration: Follow-up ranging 2 to 5 years

Dose: Mean length 2.5 to 47 cm; diameter 5 to 8 mm

Frequency/Duration: Single administration

Response: Hematoma, Acute thromboembolism, Edge-stenosis, Patency, Restenosis

Patient characteristics (gender, mean age): Gender NR. 58 to 73 years.

Number per group: 14 studies included; 789 stent-grafts in 747 patients

Observed adverse effects: Treatment-related complications seen in 17.9% (99/554), including groin hematoma, acute thromboembolism, and edge dissection. Distal embolism rate was low (3%). Graft failure was related to acute thrombosis due to disease progression, causing edge-stenosis and stent kinking. In-stent restenosis reported in 5 cases. One-year primary patency rate varied between 44 and 86%, and secondary patency rates between 58 to 93%.

Timing of adverse effects: NR

Factors that predict response: Significantly better patency with devices with a diameter of 6 mm or larger. No statistically significant difference in patency rates was observed with regard to age, smoking, comorbidities (hypertension, diabetes, CAD).

Source Citation: Stone et al 2011[41]

Study Design: RCT

Device or Material: PTFE-covered stent (JOSTENT/GraftMaster [Abbott]) vs. BMS for PCI post-CABG

Contact Duration: Follow-up 5 years; mean age of graft

Dose: Mean length 20.7 mm

Frequency/Duration: Single administration of 1-2 stent-grafts

Response: Binary restenosis, Occlusion, Thrombosis, TVF

Patient characteristics (gender, mean age): 81.5% male; 67.9 years.

Number per group: 243 (115 stent-graft; 128 BMS)

Observed adverse effects: There were no significant differences in adverse events at 30 days or 9 months. Occurring significantly more often in the stent-graft group than in the BMS group after 2 years and annually up to 5 years, were target vessel failure (68.3%; p=0.0007), target vessel revascularization (48.2%; p=0.04), and target lesion revascularization (43.9%; p=0.04). Stent thrombosis (10.9%) and target vessel occlusion (14%) were comparable to BMS at 5 years.

Timing of adverse effects: TVF and TVR occurred more frequently after 2 years

Factors that predict response: NR

Systemic Response/Toxicity

Source Citation: Martinelli et al 2020[47]

Study Design: Non-randomized comparative cohort

Device or Material: PTFE stent-graft (Excluder & C3 [W.L. Gore]) vs. chromium-cobalt endoskeleton (AFX Endologix) for EVAR

Contact Duration: Mean follow-up 24 months

Dose: NR

Frequency/Duration: Single administration

Response: PIS (fever coinciding with elevated serum CRP level)

Patient characteristics (gender, mean age): 84.1% male, 74±10 years

Number per group: 110 (43 PTFE stent-graft, 56 AFX device)

Observed adverse effects: PIS incidence between the ePTFE stent-graft group (46.6%) and the chromium-cobalt endoskeleton group (33.29%) was not significantly different (p=0.333) at 72 hours postprocedure.

Timing of adverse effects: NR

Factors that predict response: New-onset mural thrombus may release pro-inflammatory cytokines.

Source Citation: Lauermann et al 2015[46]

Study Design: Non-randomized comparative cohort

Device or Material: Stent-graft (Viatorr [W.L. Gore]) vs. BMS (Wallstent [Boston Scientific]) for TIPS

Contact Duration: NR

Dose: Mean length 92.29 mm, mean diameter 9.71 mm

Frequency/Duration: Single administration

Response: Hepatic encephalopathy, Death

Patient characteristics (gender, mean age): 67.1% male, 56±12 years; Portal hypertension, primarily due to liver cirrhosis

Number per group: 163 (83 stent graft, 80 BMS)

Observed adverse effects: Hepatic encephalopathy occurred in 19.3% of cases (n=16), requiring at least one revision in 4.8% of cases (n=4). Death during the first year was 8.4% (n=7), not significantly different than BMS.

Timing of adverse effects: NR

Factors that predict response: Revisions due to hepatic encephalopathy were within 1 year of initial implantation.

Source Citation: Kadoglou et al 2014[50]

Study Design: Non-randomized comparative cohort

Device or Material: PTFE-covered stent-graft (Excluder [W.L. Gore]) vs. polyester-covered stent-graft (Anaconda [Vascutek], Talent, Endurant [Medtronic], Zenith FB [Cook Inc.]) for EVAR

Contact Duration: Follow-up 12 months

Dose: Mean diameter 2.65±.24, mean length 12.75±1.63

Frequency/Duration: Single administration

Response: Increased PWV, an and index of arterial stiffening, Increased serum IL-8 and IL-10, Decreased WBC, Decreased hsCRP

Patient characteristics (gender, mean age): 100% male. 71±8 years.

Number per group: 118 (46 PTFE-covered stent-grafts, 72 polyester-covered stent-grafts)

Observed adverse effects: At 12 months, PWV (mean change +2.82±.25 m/s; p=0.003), and serum levels of IL-8 (17.97±8.1 pg/mL; p<0.05) and IL-10 (8.39±2.22 pg/mL; p<0.05) significantly increased from baseline in both groups. However, the effect on PWV and ILs was significantly less pronounced for PTFE compared to polyester. WBC (mean change -878±152; p<0.05), hsCRP (mean change -4.8±1.01; p<0.05), and OPG (10.51±4.46 pmol/L; p<0.05), and decreased significantly from baseline for the PTFE group.

Timing of adverse effects: NR

Factors that predict response: Mean blood pressure, OPG, and AAA diameter were independently associated with PWV (R^2=0.729, p=0.036).

Source Citation: Ikoma et al 2013[52]

Study Design: Non-randomized comparative cohort

Device or Material: ePTFE-covered stent-graft (Excluder [W.L. Gore]) vs. polyester stent-graft (Zenith [Cook Inc.]) for EVAR

Contact Duration: 10 days

Dose: NR

Frequency/Duration: Single administration

Response: Elevated WBC, Elevated CR

Patient characteristics (gender, mean age): 76.4 years.

Number per group: 88 (37 PTFE, 51 polyester)

Observed adverse effects: WBC count and CRP increased on day 1 after EVAR, peaked at day 3, and returned to pretreatment level by day 7 in both groups, but the magnitude of change was significantly less in the ePTFE group.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Voute et al 2012[48]

Study Design: Non-randomized comparative cohort

Device or Material: ePTFE stent-graft (Excluder [W.L. Gore]) vs. polyester stent-graft (Talent & Endurant [Medtronic]) for EVAR

Contact Duration: 4 days

Dose: Mean in-graft volume 37.7± 10.6 mL

Frequency/Duration: Single administration

Response: PIS (fever coinciding with elevated serum CRP level)

Patient characteristics (gender, mean age): 87.9% male. 72.6±7.5 years.

Number per group: 149 (67 ePTFE stent graft, 82 woven polyester stent-graft)

Observed adverse effects: Incid ence of PIS was 17.9%, significantly lower than the polyester stent-graft group (56.1%; $p<0.001$).

Timing of adverse effects: PIS occurred almost exclusively in the first 2 days after ePTFE implantation.

Factors that predict response: The amount of graft material implanted, and new-onset thrombus were not associated with PIS.

Source Citation: Stone et al 2011[41]

Study Design: RCT

Device or Material: PTFE-covered stent (JOSTENT/GraftMaster [Abbott]) vs. BMS for PCI post-CABG

Contact Duration: Follow-up 5 years; mean age of graft

Dose: Mean length 20.7 mm

Frequency/Duration: Single administration of 1 to 2 stent-grafts

Response: Death, MI

Patient characteristics (gender, mean age): 81.5% male, 67.9 years.

Number per group: 243 (115 stent-graft; 128 BMS)

Observed adverse effects: All-cause death (29.8%) and MI (26.2%) were comparable to BMS at 5 years.

Timing of adverse effects: NR

Factors that predict response: NR

AAA = abdominal aortic aneurysm; ACPP = access circuit primary patency; AE = adverse event; BMS = bare-metal stent; CABG = coronary artery bypass graft; CRP = C-reactive protein; EVAR = endovascular abdominal aortic aneurysm repair; F-EVAR = fenestrated endovascular abdominal aortic aneurysm repair; FDP = fibrinogen degradation product; HE = hepatic Encephalopathy; HR = hazard ratio; hsCRP = high sensitivity C-reactive protein; IL = interleukin; MI = myocardial infarction; NR = not reported; OPG = osteoprotegerin; PCI = percutaneous coronary intervention; PIS = post-implantation syndrome; PPA = popliteal artery aneurysm; PTA = percutaneous transluminal angioplasty; PWV = pulse wave velocity; RCT = randomized controlled study; SFA = superficial femoral artery; TAPP = treatment area primary patency; TIPS = transjugular intrahepatic portosystemic shunt; TVF = target vessel failure; TVR = target vessel revascularization; WBC = white blood cell

Table 14: Sutures - Health Effect (In Vivo) Human Studies

Local Response/Toxicity

Source Citation: Pacella 2016[53]

Study Design: Systematic review

Device or Material: Suture for frontalis suspension surgery

Contact Duration: NR

Dose: NR

Frequency/Duration: Single Administration

Response: Infection, Granuloma, Preseptal cellulitis, Abscess

Patient characteristics (gender, mean age): NR, NR.

Number per group: PTFE: 5 studies including 216 patients, total: 53 studies including 1,921 patients using fascia lata, Mersilene, PTFE, and silicone.

Observed adverse effects: PTFE has a significant lower overall incidence of complications (5%, 95% CI 0.6–13%) compared to fascia lata (25%, CI 14–39%). However, PTFE had a higher rate of infections (1.9%, CI 0.2–5.4% vs. 1%, CI 0.5–1.6%).

Timing of adverse effects: NR

Factors that predict response: NR

CI= confidence interval; NR= not reported; PTFE= polytetrafluoroethylene

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Appendix F. Surveillance Event Reports - PSO and Accident Investigation

Provided with this report as separate Excel spreadsheet.

Appendix G. Regulatory and Manufacturer Safety Alerts

Specific search terms are provided here. The associated alerts are provided with this report as a separate PDF.