Review

JOURNAL OF ENDOVASCULAR THERAPY
A SAGE Publication
An official publication of the ISEVS

Journal of Endovascular Therapy
1–10

DOI: 10.1177/15266028221075242
www.jevt.org
SAGE

Systematic Review of the Current In Vitro Experience of the Endovascular Treatment of Juxtarenal Abdominal Aortic Aneurysms by Fenestrated and Parallel Endografting

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Abstract

Objective: To identify and analyze the published in vitro benchtop experiments for the assessment of endovascular techniques used for the treatment of juxtarenal abdominal aortic aneurysms (jAAAs).

Data sources: Scopus, PubMed, and Web of Science.

Review methods: A systematic literature search was carried out throughout March 2021 following PRISMA guidelines. Two investigators independently performed title and abstract screening to reveal all benchtop testing evaluating the endovascular treatment of jAAA.

Results: A total of 19 studies were included, 8 evaluating fenestrated (FEVAR) and 11 parallel grafts (PGs). FEVAR studies used different custom testing apparatus (n=7) or 3D-printed models (n=1) to analyze dislodgement and migration resistance, misalignment consequences and causation, and bridging stents' radial force, flareability, fatigue, and fracture resistance. All PG studies used silicone-based models to analyze optimal oversizing, sealing length, gutter behavior, and possible reduction. Test evaluation in FEVAR in vitro testing was based on pullout force analysis (N=5), photo evaluation (n=1), fluoroscopy (n=1), X-rays (n=4), CT analysis (n=3), macro- and microscopic evaluation (n=4), water permeability (n=1), and fatigue simulator testing (n=1), while it was based on CT analysis in all PG studies adding ECG-gate in one study. The most frequently tested devices were Zenit (Cook) (n=7), Endurant (Medtronic) (n=5), and Excluder (Gore) (n=5) as main grafts, and Advanta V12 (n=14) as the bridging device.

Conclusions: This systematic review presents a broad analysis of the current in vitro methods evaluating the endovascular treatment of jAAA. Fundamental issues have been benchtop tested in both FEVAR and PGs. The analysis of the included studies allowed to recommend an optimal testing design. In vitro testing is a potential tool to further elucidate points of attention hard to investigate in vivo to finally enhance the endovascular treatment outcomes. Future in vitro studies are needed to evaluate the in vitro performance of all indistinctively used devices in the clinical practice.

Keywords

chimney graft/technique, fenestrated stent graft, juxtarenal aneurysm, in vitro model, parallel graft, benchtop model, flow model, endovascular aneurysm repair, fatigue testing, systematic review

Introduction

The endovascular treatment of juxtarenal abdominal aortic aneurysms (jAAAs) is challenging precluding the application of standard endovascular aneurysm repair (EVAR) in many cases, due to the lack of adequate proximal sealing zone.[1] Thus, alternative techniques are being employed prolonging and ensuring the proximal sealing zone, while preserving the correct perfusion of the renal and visceral arteries. These alternatives include fenestrated endograft technology (FEVAR, fenestrated endovascular aortic repair) and the use of parallel grafts (PGs). The FEVAR technique

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traditionally employs a custom-made patient-specific endograft with fenestrations for the visceral vessels, which need to be canulated and stented.[2] As an alternative, the use of PGs, either as aortic repair (CHEVAR, chimney endovascular aortic repair) or aneurysm sealing (CHEVAS, chimney endovascular aortic sealing), employs off-the-shelf available endografts allowing prompt treatment which can be essential in urgent cases. Different retrospective and even multicentric studies have been published evaluating the safety, mid-term, and even long-term results in terms of patency, reintervention rates, and mortality of these techniques.[1,3–5]

Although FEVAR and PG techniques have been used for decades, none of the available and employed bridging stent grafts (SGs) today are dedicated devices. Many different combinations of main grafts (MGs) and branch grafts have been applied; however, a head-to-head evaluation based on the best anatomical fit is difficult within cohort studies. The deployment of FEVAR and PG configurations in a close proximity to the human body in an in vitro environment provides a valuable tool keeping the test conditions such as jAAA anatomy and vessel wall characteristics. In vitro evaluation of the employed SGs before their in vivo application should be paramount to analyze and apprehend their possible behavior in the patient.[6] However, wide-ranging in vitro evidence on the endovascular treatment of jAAA is lacking.

Different in vitro tests have previously been performed to investigate the stability of fenestrated grafts or their components[7,8] to assess the specific properties of bridging stents[9,10–13] or chimney grafts (CGs)[14,15] and to define the ideal graft position and configuration for the chimney technique[16–18] and the potential benefits of the use of gutter fillings[19] or EndoAnchors.[20] The cornerstone of every in vitro study is the used phantom. In general, phantoms are always a simplification of reality; however, the key characteristics should be incorporated to investigate specific questions. Phantom characteristics can be categorized into three main aspects: material specifications, geometry, and fabrication. A phantom material and its specifications introduce the first consideration in an in vitro study. Ideally, a material should be selected to mimic the physical properties (eg, viscoelastic properties and wall thickness) and satisfy experimental pre-requisites (eg, durability, and optical and geometrical properties). Second, the phantom design process plays an important role in mimicking in vivo anatomic conditions, and models can be fabricated from simple tubes, averaged anatomy, or patient-specific anatomy. The geometry and design of phantoms define the overall complexity and quality of an in vitro study. Thus, a good understanding of the currently used phantoms and their limitations is of considerable importance in evaluating the clinical relevance of those studies, apart from formulating more realistic and reliable in vitro studies in the future.

The aim of this review was to identify and analyze the published in vitro benchtop experiments for the assessment of endovascular techniques used in the treatment of jAAAs. The main focus was on the in vitro model designs, configurations, and fabrications.

Materials and Methods

This systematic review was written in accordance with the guidelines provided within the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement.[21] The interfaces used for searching were Scopus, PubMed, and Web of Science. Articles were included until March 2021.

Definitions

A jAAA was defined as pathological degenerative widening of the infrarenal abdominal aorta adjacent to or including the lower margin of the renal artery origins.[8] We defined an in vitro phantom study, an experimental study, in which the proposed research questions and hypotheses were investigated using benchtop experiments. A search query containing all keywords from both categories was applied to the paper title, abstract, and keyword categories (Supplementary file 1). No search was performed to retrieve unpublished data or abstracts.

Study Selection

Two authors (G.T.T. and H.M.) independently screened the titles and abstracts of all identified non-duplicated articles. All publications regarding in vitro phantom studies focusing on the endovascular treatment of jAAA, such as FEVAR and PG as for CHEVAR and CHEVAS, were included. Unrelated studies such as computational fluid dynamic (CFD) simulations, animal investigations, and retrospective clinical cohort studies were excluded. Studies focusing on in situ fenestration evaluation, EVAR, EVAS, endovascular reconstruction of the aortic bifurcation, endovascular repair of the thoracic aorta, aortic dissection, or aortic arch repair, case reports, and commentary articles were also excluded. Then, full-text analysis of all suitable articles was performed by G.T.T. and H.M. to decide inclusion and exclusion. Any disagreement was resolved by discussion to reach consensus. Reference lists of the finally included studies were screened for any missed eligible studies (Figure 1).

Data Extraction and Processing

Data extraction and analysis were performed by G.T.T. and H.M. individually. Then, merging was performed, and any discrepancies were resolved with a check in the full-text

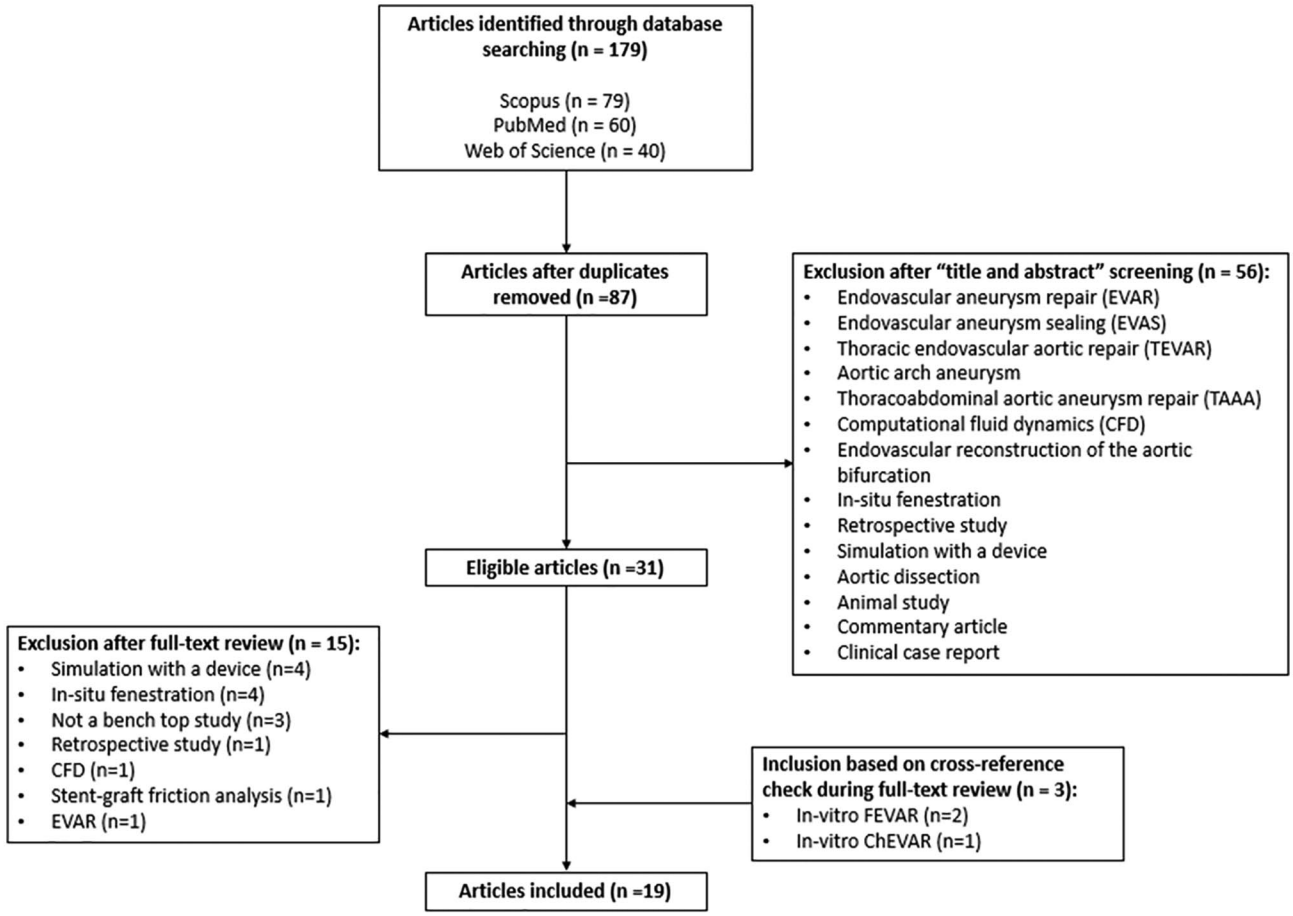

Figure 1. Flow chart illustrating study selection.

article. Due to the intrinsic differences between endovascular treatments and their clinical relevance, the extracted data were processed separately. After analysis, all included studies were classified according to phantom fabrication parameters and in vitro testing characteristics. The phantom material, its physical properties (specification), and the use of physiological condition simulation were extracted from the texts. The "anatomy" design of the phantom was divided into three types. The first design type was called "simplified," in which the investigated anatomy was designed based on few landmarking geometrical parameters. The second design type was labeled as "generalized," in which the average anatomical characteristics of the preoperative computed tomography angiography (CTA) of jAAA patient cohort were used in the design process. The third design type represents the "patient-specific" phantoms, in which the used geometry and its design were usually based on the preoperative CTA of one patient with jAAA. Finally, the phantom fabrication process was extracted and reported.

The studies were reported according to their investigational aims: (1) resistance to displacement and migration, positioning and misalignment, and bridging stents' radial force, fatigue, and fracture resistance evaluation in FEVAR studies; (2) stent-graft oversizing, CG compression, and gutter sizes in PGs. Differences between articles were reported, investigating based on the study design and parameters, the employed devices (ie, the main SG, CG), the number of SGs per testing, and the number of tests and evaluation techniques.

Results

Figure 1 depicts the flow chart for study selection. Nineteen papers were included in the study. In Tables 1 and 2, all the included studies are presented chronologically and classified according to the phantom fabrication parameter, in vitro testing characteristics, aim and results for a global overview of their content.

FEVAR Studies

A total of 8 in vitro studies evaluated the fenestrated technology for the endovascular treatment of jAAA[7–13] (Table 1).

Table 1. Benchtop Fenestrated Endovascular Aortic Repair (FEVAR) Testings Presented Chronologically and Classified According to the Phantom Fabrication Parameter, In Vitro Testing Characteristics, and Aim and Results for a Global Overview of Their Content.

				Phantom creation								
Author year, paper	Studied technique	Material/ specification	Geometry: type/anatomy	Design	Fabrication	Flow simulation (yes/no)	Aim	MG model	SG model	SG (n)	Tests (n)	Evaluation
Scurr 2008, JEVT	FEVAR	Acrylate	Simplified	Testing rig: 2 overlapping acrylic tubes with 2 sets of holes representing bilateral renal artery ostia and fenestrations.	M5; NENE Instruments Ltd (Wellingborough, UK)	No	Resistance to displacement/ migration	None	Jostent (Abbott), Advanta V12 (Getinge), Palmaz (Cordis)	2	18	Tenso-meter (M5, NENE Instruments Ltd, (Wellington, UK)
Scurr 2012, EJVES	FEVAR	—	Simplified	Testing rig: top end of the proximal body and bifurcated limbs attached to a tensile tester via plastic sealing plugs and pneumatic clamps.	M5; NENE Instruments Ltd (Wellingborough, UK)	No* Model soaked in saline solution and pressurized to 100 and 120 mmHg.*	Study the longitudinal migratory force to disconnect the bifurcated body from the fenestrated tube.	Zenit (Cook)	None	0	8	Tenso-meter (M5, NENE Instruments Ltd, (Wellington, UK)
Crawford 2016, Surgeon	FEVAR	Stainless steel	Simplified	Custom testing apparatus: ½" circular hose clamp adjusted to 90% of diameter of the MG. Steerable rods of different diameters passed through the fenestration simulating rigid stent.	McMaster-Carr (Elmhurst, IL, USA)	No	Evaluate impact of fenestrations misalignment to proximal neck apposition and luminal patency.	Anaconda (Vascutek), Zenit (Cook)	None	0	20	Photos taken at 10° increments clockwise and counter-clockwise
Crawford 2019, JEVT	FEVAR	PLA, PVA-c/ Young's modulus measured using uniaxial tensile tester Polymer	Generalized and patient-specific/ iliac artery, jAAA	- Idealized aortoiliac geometries through 3D printing (rigid) or through casting with PVA using 3D-printed molds (flexible). - Three flexible patient-specific models were created based on the preoperative CTA.	No* 3D printing and mold casting techniques.*	Yes Model pressurized to 100 mmHg with saline (37°C).*	Evaluate aortoiliac variables associated with SG rotation and assess common deployment techniques that contribute to rotation.	Zenit (Cook)	None	0	N/S	Fluoroscopy
Torsello 2019, JEVT	FEVAR	Polyester	Simplified	Test sheets with 2 rows of 5 fenestrations with 5 or 10 mm diameter.	Z005 material testing machine (Zwick-Roell, Ulm, Germany). HumanX (GmbH, Wildau, Germany)	Yes	Investigate VBX safety and integrity as bridging device in fenestrated MG.	Zenit (Cook)	VBX (Gore)	2	50	- Rx - CT - Microscopic and macroscopic - Water permeability testing - POF testing
Torsello 2019, JEVT	FEVAR	Polyester	Simplified	Test sheets with 2 rows of 5 fenestrations with 5 or 10 mm diameter.	Z005 material testing machine (Zwick-Roell, Ulm, Germany)	No	Investigate BeGraft and BeGraft+ as bridging devices in fenestrated MG	Zenit (Cook)	BeGraft and BeGraft+ (Bentley)	2	40	- Rx - CT - Microscopic and macroscopic - POF testing
Torsello 2020, JEVT	FEVAR	Polyester	Simplified	Test sheets with 2 rows of 5 fenestrations with 5 or 10 mm diameter.	Z005 material testing machine (Zwick-Roell, Ulm, Germany)	No* Model submerged in water (37°C).*	Compare VBX vs Advanta V12 as widely used FEVAR bridging device	Zenit (Cook)	Advanta V12 (Getinge), VBX (Gore)	2	40	- Rx - CT - Microscopic and macroscopic - POF testing
Torsello 2021, JEVT	FEVAR	Polyester	Simplified	Test sheets with 2 rows of 5 fenestrations with 5 or 10 mm diameter.	Z005 material testing machine (Zwick-Roell, Ulm, Germany)	No	Compare VBX fatigue resistance vs Advanta V12 as widely used FEVAR bridging device	Zenit (Cook)	Advanta V12 (Getinge), VBX (Gore)	2	10	- Rx - Microscopic and macroscopic - Fatigue test simulator of 75 months life span

Abbreviations: CT, computed tomography; CTA, computed tomography angiography; MG, main graft; SG, stent graft; jAAA, juxtarenal abdominal aortic aneurysm; N/S, non-specified; VBX, Viabahn balloon-expandable; PLA, polylactic acid; PVA-c, polyvinyl alcohol cryogel; POF, pullout forces.

Table 2. Benchtop Parallel Graft Testings Presented Chronologically and Classified According to Phantom Fabrication Parameter, In Vitro Testing Characteristics, Aim and Results for a Global Overview of Their Content.

				Phantom creation								
Author year, paper	Studied technique	Material/ specification	Geometry: type/ anatomy	Design	Fabrication	Flow simulation (yes/ no)	Aim	MG model	SG model	SG (n)	Tests (n)	Evaluation
Mestres 2012, EJVES	CHEVAR	Silicone	Simplified/ jAAA neck	Straight intersecting tubes with different inner diameters and 1 side branch	N/S	No* Model submerged in saline bath a(37°C).*	Optimal MG oversizing	Endurant (Medtronic), Excluder (Gore) (15%, 30%, 40% oversizing)	Advanta V12 (Getinge), Viabahn (Gore)	1	36	CT
Niepoth 2013, JEVT	CHEVAR + EndoAnchors	Silicone	Simplified/ jAAA	- Straight tubes with 2 sizes of branch arteries and 2 sizes of aorta - diverging tube design	N/S	No* Model submerged in gelatin water (37°C) simulating blood viscosity.*	Gutter reduction with endo-anchors evaluation	Excluder (Gore) EndoAnchors (Medtronic)	Advanta V12 (Getinge)	1	12	64-slice CT
de Bruin 2013, JEVT	CHEVAR	Silicone	Simplified/ jAAA	- Straight tubes with 2 sizes of branch arteries and 2 sizes of aorta - diverging tube design	N/S	No* Model submerged in gelatin water (37°C) simulating blood viscosity.*	Gutter size and compression with BE or SE CG	Excluder (Gore)	Advanta V12 (Getinge), Viabahn (Gore)	1	16	64-slice CT
Niepoth 2013, de Bruin et al 2013, JEVT	CHEVAS	Silicone	Generalized/ jAAA	- Model mimicking the compliance of the human aorta with jAAA. - Two renal arteries, 2 lumbar arteries, and iliac axes with sealed internal iliac arteries.	N/S	Yes Gelatin water initiated after CG deployment.	Investigate the feasibility and efficacy of CHEVAS in a jAAA	Nellix (Endologix)	Advanta V12 (Getinge), Viabahn (Gore)	2 different CG	12	64-slice contrast-enhanced CT
Mestres 2017, JVS	CHEVAR	Silicone/external mesh to deflect silicone elasticity	Simplified/ jAAA neck	Straight intersecting tubes with different diameters and 2 or 3 side branches simulating SMA and renal arteries	N/S	No* Model submerged in saline bath (37°C).*	Optimal MG oversizing and CG combination for 2/3 CG	Endurant (Medtronic), Excluder (Gore) (15%, 30%, 40% oversizing)	Advanta V12 (Getinge), Viabahn (Gore)	2/3	36	CT
Boersen 2017, JVS	CHEVAR/ CHEVAS	Silicone	Generalized/ jAAA	Seven jAAA flow phantoms based on the average measurements from 25 preoperative CTAs.	Elastrat Inc (Geneva, Switzerland)	Yes - blood mimicking fluid. - Renal Flow study.	Geometry and renal artery flow comparison between CHEVAR and CHEVAS	Endurant (Medtronic), AFX (Endologix), Nellix (Endologix)	Advanta V12 (Getinge), Viabahn (Gore)	2	6	256-slice CT
Overeem 2018, JEVT	CHEVAR	Silicone	Generalized/ jAAA	Average measurements from 25 preoperative CTAs	Elastrat Inc (Geneva, Switzerland)	Yes Blood mimicking fluid.	Assess the dynamic behavior of CG during cardiac cycle.	Endurant (Medtronic)	Advanta V12 (Getinge), Viabahn (Gore), BeGraft (Bentley)	2	3	256-slice ECG-gated contrast-enhanced CT
Shukuzawa 2019, IJAO	CHEVAR	Silicone/arterial stiffness parameter was adjusted	Generalized/ jAAA	General anatomical human data referencing from suprarenal till common iliac arteries.	N/S	No	Evaluate the influence of the sealing length on gutter formation and incidence of flow channels.	Excluder (Gore) (20%, 30% oversizing)	Advanta V12 (Getinge)	2	36	Micro- CT
Taneva 2019, JEVT	CHEVAR	Silicone/ultraviolet-cured silicone stiffer than the aortic wall	Patient-specific/ jAAA	Anatomical characteristics based on the preoperative CTA of a patient with 7 cm jAAA successfully treated with CHEVAR.	Medizinische Modellbau Manufak-tur GmbH (Wildau, Germany)	Yes - blood mimicking fluid. - adjustable parameters: pressure, temperature, volume, frequency.	Compare other BECS to the Advanta V12 as standard of care.	Endurant (Medtronic)	Advanta V12 (Getinge), VBX (Gore), BeGraft+ (Bentley)	1	9	128-slice contrast-enhanced CT
Van Schaik 2019, JEVT	CHEVAS	Silicone	Generalized/ jAAA	Two sizes models of jAAA mimicking human aorta. Same-level renal arteries, distal bifurcation representing iliac arteries.	DBC Laboratories (Wheat Ridge, CO, USA)	No* Model submerged in gelatin water (37°C) simulating blood viscosity.*	Investigate possible gutter reduction with secondary endobags filling	Nellix (Endologix)	Advanta V12 (Getinge), Viabahn (Gore)	2 same CG	4	64-slice CT
Meekel 2020, JEVT	CHEVAR	Silicone	Simplified/ jAAA	Straight tubes with 2 sizes of branch arteries and 2 sizes of aorta; a diverging tube design	N/S	No* Model submerged in gelatin water solution with blood viscosity (37°C).*	Assess the gutter characteristics and compression of different types of CG configurations .	Excluder C3 or Conformable (Gore)	Advanta V12 (Getinge), VBX (Gore), Viabahn (Gore)	1	57	64-slice CT

Abbreviations: CT, computed tomography; CTA, computed tomography angiography; CHEVAR, chimney endovascular aortic repair; CHEVAS, chimney endovascular aortic sealing; jAAA, juxtarenal abdominal aortic aneurysm; MG, main graft; SG, stent graft; N/S, non-specified; VBX, Viabahn balloon-expandable ; JVS, Journal of Vascular Surgery; SMA, superior mesenteric artery; BECS, balloon-expandable chimney graft.

The resistance to displacement and migration in FEVAR was studied by Scurr et al using a testing rig with two overlapping acrylic tubes with two sets of holes representing bilateral renal artery in their first study in 2008[9] and a tensile tester via plastic sealing plugs and pneumatic clamps in their second study in 2012.[7] FEVAR misalignment consequences and causation were studied by Crawford et al in 2016[8] employing a testing apparatus made of a circular hose clamp adjusted to 90% of the diameter of the FEVAR device and steerable rods of different diameters passed through the fenestration simulating rigid stents, and in 2019 using an idealized aortoiliac phantom with helical iliac artery geometry fabricated through 3D printing (rigid) or through casting with polyvinyl alcohol using 3D-printed molds (flexible) connected to a recirculating pump filled with saline pressurized to 100 mmHg and at 37°C.[22] Additionally, three flexible patient-specific models were created based on the patients preoperative CTA.[22] Bridging stents' radial force, flareability, fatigue, and fracture resistance were studied in the four studies conducted by Torsello et al. They used test sheets with two rows of 5 fenestrations with 5 or 10 mm diameter in all their studies.[10–13] They used water permeability test for the bridging stent when evaluating the GORE VIABAHN VBX Balloon Expandable Endoprosthesis (W.L. Gore and Associates, Flagstaff, AZ, USA) due to the increased translucency in the microscopic pretests.[11]

Seven out of 8 studies gave information on the phantom material of fabrication. Seven studies employed a simplified model, while the testing by Crawford et al[22] was based on generalized and patient-specific phantoms. Physiological condition simulation was performed in 5 of the 8 studies by submerging the model in a water bath at 37° or in a saline solution and pressurizing the SG. The Zenit fenestrated device was analyzed in 7 out of 8 studies while the Anaconda fenestrated device (Vascutek, Terumo, Inchinnan, Scotland) was employed in one study.[8] Advanta V12 and VBX SG were employed in three in vitro experiments each, while BeGraft and BeGraft+, Jostent (Abbott Vascular, Santa Clara, CA, USA), and Palmaz stent (Cordis Corporation, Miami Lakes, FL, USA) were employed in one study each. Test evaluation in the selected studies was based on different parameters as for pullout force (POF) analysis, photo evaluation, fluoroscopy, X-rays and CTs, macro- and microscopic evaluation, water permeability test, and fatigue simulator test were applied (Table 1).

CHEVAR/CHEVAS Studies

A total of 11 studies evaluated the endovascular treatment of jAAA using PG, of which 8 focused on CHEVAR,[14–18,20,23,24] 2 on CHEVAS,[19,25] and 1 study compared CHEVAR and CHEVAS techniques in terms of CG geometry and renal artery flow.[26] The degree of MG oversizing was investigated in both papers by Mestres et al when using a single chimney[23] or double/triple chimneys.[18] PG compression and gutters were studied by de Bruin et al,[24] Meekel et al,[15] and Taneva et al[14] depending on the use of different types of CGs: balloon-expandable covered stents (BECS) such as Advanta V12,[14,15,24] VBX,[14,15] and BeGraft+,[14] or self-expandable covered stents (SECS) such as Viabahn (Gore).[15,24] Three articles investigated possible gutter reduction either employing EndoAnchors,[20] evaluating the sealing length of the EVAR device,[16] or employing secondary filling of the endobags.[19] CG behavior during the cardiac cycle was studied by Overeem et al.[17] In vitro comparison between CHEVAR and CHEVAS renal artery flow was performed by Boersen et al.[26]

All in vitro studies employing the chimney technique used silicone-based models (Table 2). Three studies added material specifications for the use of stiffer silicone than the aortic wall,[14] adjustment of the material to the arterial stiffness,[16] or the use of an external mesh to limit the silicone elasticity.[18] A total of 5 studies employed simplified phantom designs. Mestres et al[18,23] designed phantoms representing jAAA necks using straight tubes with different inner diameters. Niepoth et al, de Bruin et al, and Meekel et al created phantoms considering different straight tube diameters and diverging tube designs, mimicking the aorta and the renal arteries.[15,20,24] The other 5 studies employed generalized phantoms.[16,17,19,20,26] Taneva et al employed a patient-specific model based on the preoperative CTA of a patient treated succesfully with the chimney technique.[14] Four studies gave information on the external fabrication of the phantoms outsourcing the production to a company.[14,17,19,26] Four studies connected the phantom to a fluid circulation loop to include physiological hemodynamics.[14,17,20,26] Six studies submerged the phantom in gelatine water or saline bath at 37°C in order to simulate physiological conditions. Shukuzawa et al did not report on the use of any physiological conditions.[16]

The Endurant and Excluder were the most in vitro analyzed EVAR devices for the chimney technique employed in 5 studies each, followed by the Nellix technology (Endologix, Irvine, CA, USA) employed in 3 studies and AFX (Endologix) used in 1 study (Table 2). Advanta BECS was investigated as CG in all the 11 included studies. Viabahn was employed in 8 studies, VBX in 2 studies, and BeGraft and BeGraft+ in 1 study each (Table 2). Testing evaluation was mainly based on CT analysis in all the studies.

Discussion

We here present the first systematic review of literature evaluating the in vitro methods for the endovascular repair of jAAA with FEVAR or PG techniques. Despite

the evolution of the endovascular treatment of jAAA, the available in vitro benchtop evidence is limited presenting only 7 FEVAR and 11 PG studies. Seemingly, different SGs perform differently in consequence to their distinctive characteristics. The assessed articles described a wide variety of models and methods precluding an uniform comparison between studies, while underlying the need for standardized in vitro evaluation manifesting the relevance of our paper.

Essential issues have been addressed by in vitro testing in fenestrated grafts. The MG proximal seal (type I endoleak), stability and resistance to dislodgment (type III endoleak), MG torsion and misalignment cause and consequences, as well as bridging devices resistance and flareability have been benchtop studied. However, other specific questions like MG resistance to cardiac cycle or breathing movements have not been investigated. Six out of 7 studies evaluated the Zenith fenestrated endograft highlighting the lack of in vitro evidence on other employed fenestrated endografts. Also, although Advanta V12 has been cited as the standard of care,[11,13] many other off-the-shelf SGs are employed in the everyday practice without any in vitro differentiation and characterization for their use as bridging stents, underlying the necessity of a dedicated SG.

Essential matters like MG oversizing, PG compression, and gutters have also been addressed by in vitro testing in PG studies. However, other issues like migration, friction between devices, and positioning have not been addressed. The in vitro evaluation of PG for the treatment of jAAA used a silicone-based phantom of different complexities in all the studies and focused mainly on gutter evaluation and different techniques to reduce them. Although CHEVAS presents several in vitro studies evaluating different crucial parameters, the Nellix device's CE-mark has been suspended after suboptimal performance in infrarenal AAA[27–30] and recall of the existing inventory was announced in 2019 only being available afterwards under clinical protocol. The Endurant and Excluder abdominal endografts showed broad in vitro testing background on the contrary to other off-the-shelf abdominal endografts lacking in vitro evaluation and characterization. Many nowadays available SGs were tested as CGs. Although the combination of Endurant and Advanta V12 as the standard of care received has CE-mark approval,[31] here, again a dedicated PG bridging device has not been established yet.

Several limitations of the analyzed studies have been detected. Due to the nature of in vitro testing, and even though mimicking physiological conditions are employed, the testing mechanisms do not represent exactly the biological human conditions. The silicon phantom material mimicking aortic wall elasticity does not match the properties of a vessel wall, lacking also the presence of calcium and thrombus we frequently find in patients with AAA. Even if simplified, generalized, or patient-specific phantoms are used, they may not approach the diversity of patients' anatomy, vessel and aortic angulations, possible ostium stenosis, and particularities, which may influence the performance. When the tested material and devices are submerged in gelatine water solution simulating blood viscosity at 37°C, this may only approach the biological conditions. Other biological factors such as respiratory movements and cardiac cycle also influence SG performance, being this last one evaluated in only one study.[32] Fluid simulation, which may seem essential to simulate biological conditions, was employed in only 1 of 7 FEVAR studies and 4 of 11 PG studies. Probably due to the different nature of both techniques, while different CFD simulation studies to investigate possible devices' behavior can be found regarding FEVAR,[33–37] none of the same nature was found analyzing the PG technique. Although excluded from the present analyses due to the lack of benchtop testing, CFD studies may represent a valuable tool to analyze SG behavior in diverse preselected patients' anatomy. However, the lack of validated boundary conditions may impact the reliability of CFD. Also, in vitro testing represents only an initial evaluation of the devices after their deployment, not evaluating the possible further complications derived during patients' follow-up.

After analyzing the here-presented cohort which sets the base of in vitro testing, an optimal testing phantom design may be suggested. Currently, silicone-based materials are mostly used in in vitro studies; however, one of the remaining challenges is to adjust the biomechanical properties of the developed phantom to the in vivo conditions. Silicone (polydimethylsiloxane) is widely used to develop arterial phantoms, for which the mechanical properties such as Young's, shear and bulk moduli have been reported based on different curing settings.[38,39] Ostensibly, a silicon-based model mimicking the thickness and compliance of aortic wall, following a generalized, but complex anatomy may be more adequate, although not representing patient-specific particularities. It should be noted that the generalized phantoms are usually developed to correspond to a specific patient cohort's mean anatomical features, which are extracted using morphometric clinical protocols. These protocols tend to simplify the anatomy by calculating diameters and angulations from a few landmarks, introducing limitations in an in vitro study. Therefore, it is advised to expand the horizon by investigating other techniques based on mathematical algorithms capable of producing more sophisticated anatomical mean geometry of the analyzed cohort. For instance, non-parametric statistical shape modeling (SSM) is a mathematical algorithm combining all anatomical shape information and produces an anatomical model that represents a realistic average geometry of the investigated cohort.[40] Outsourcing the fabrication of the phantom or apparatus to a specific specialized unit may be optimal for reproducibility of the results. The use of blood mimicking fluid seems useful to mimic blood viscosity and density.[41] Fluid simulation technology connecting the phantom to a pulsatile pumping system allowing pressure, temperature, and pulsatility settings is suggested as paramount to simulate

physiological deployment and analysis conditions. Each test shall be repeated at least 3 times for inter-reader reproducibility. Although the evaluation of the testing was based on POF analysis in the majority of FEVAR tests and CT imaging in all PG testing, other modalities like the biplanar digital radiography to detect possible changes of the stent structure or SG fracture, microscopic evaluation of possible fabric or stent changes,[10–13] and ECG-gated CT to evaluate device changes with cardiac cycle need to be considered for more detailed evaluation of SG performance.

According to the extracted results, only a few of all the nowadays available MGs and SGs have been in vitro tested. It seems like Advanta V12/Viabahn as SG and Endurant/Excluder as MG or Zenith as fenestrated device display vigorous in vitro evidence. However, other off-the-shelf available devices are being indistinctively used for the endovascular treatment of jAAA lacking any in vitro evidence. Future studies are needed to evaluate the rest of clinically employed devices and their in vitro performance for the treatment of jAAA. In vitro testing should also consider the current clinical evidence to further elucidate points of attention that are difficult or impossible to investigate in vivo connecting this way the strengths of each modality.

Limitations

The limitations of in vitro testing and the relatively small sample size per arm hinder the recommendation of a SG as a dedicated device for each technique. Following the main goal of the present revision, the outcomes per se of each study were not presented. Complete harmonization in the presentation of the included studies was burdensome due to the different nature and evaluation method of each technique. Seven studies declared obtaining industry funds,[10,11,13,15,19,22,26] and 9 stated potential conflicts of interest,[15–20,23,24,26] while conflicts/funding status was not cited in 1 study.[8] Due to the nature and design of the included studies, a validated quality assessment binding in systematic reviews[21,42] was not possible.

Conclusions

The present systematic review presents a broad analysis of the current in vitro methods evaluating the endovascular treatment of jAAA precluding an uniform comparison between studies, while underlying the need for standardized in vitro evaluation manifesting the relevance of our paper. Despite the limitations, fundamental issues have been benchtop tested in both FEVAR and PGs. However, other important questions regarding these techniques have not been in vitro evaluated yet. The analysis of the included studies allowed to recommend an optimal testing design. In vitro testing is a potential tool to further elucidate points of attention hard to investigate in vivo to finally enhance the endovascular treatment outcomes. Future in vitro studies are needed to evaluate the in vitro performance of all indistinctively used devices in the clinical practice.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Supplemental Material

Supplemental material for this article is available online.

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