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DISSERTATION

Postoperative Ergebnisse bei Patienten nach Aortenklappenersatz unter Verwendung der Labcor Dokimos Plus Prothese

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INHALTSVERZEICHNIS

ABSTRAKT (DEUTSCH)

Einleitung. Die Labcor Dokimos Plus (LDP) ist eine gestentete supraannulär implantierbare perikardiale Bioprothese für die Implantation in die Aortenposition, welche neu in Europa eingeführt wurde. Das Ziel dieser Studie ist, die intra- und postoperativen Ergebnisse sowie die hämodynamische Leistung dieser Klappenprothese zu evaluieren.

Methodik. Ein Hundert aufeinanderfolgende Patienten mit einem mittleren Alter von 65.9 ± 10.7 Jahren (Range 35 – 87) und einem mittleren EuroSCORE II von 3.1 ± 3.9 (Messbereich 0.67 – 24.5) erhielten einen Aortenklappenersatz mit der LDP. Die mittlere Prothesengröße betrug 25.2 ± 1.7 mm. Kombinierte Eingriffe wurden in 34% der Fälle ausgeführt. Postoperative klinische Daten wurden analysiert und die hämodynamische Prothesenleistung wurde mittels transthorakaler Echokardiographie evaluiert. Außerdem wurde zwei Jahre postoperativ eine Nachuntersuchung durchgeführt.

Ergebnisse. Intraoperativ traten keine Komplikationen auf. Die mittlere Aortenklemmzeit betrug für isolierte und kombinierte Eingriffe jeweils 74.5 ± 20.0 Min. und 103.7 ± 37.1 Min. Die Patienten wurden im Durchschnitt nach 9.4 ± 15.8 Stunden extubiert. Es zeigte sich kein postoperativer Schlaganfall. Eine postoperative thorakale Blutung entwickelte sich bei vier Patienten. Die 30-Tages-Mortalität betrug 2%. Es wurde eine frühpostoperative Prothesenendokarditis beobachtet. Echokardiographisch zeigten sich maximale und mittlere Druckgradienten über die Aortenklappenprothese jeweils von 18.1 ± 6.4 und 9.6 ± 3.7 mmHg. Entsprechend den Prothesengrößen 21, 23, 25 and 27 mm betrugen die mittleren Druckgradienten jeweils 17.3, 9.5, 8.5 and 10.2 mmHg, die effektiven Klappenöffnungsflächen waren 1.92, 1.79, 2.0, 2.16 cm^2 und die indizierten effektiven Klappenöffnungsflächen - 1.08, 0.95, 0.99 and 1.01 cm^2/m^2. Es wurde keine relevante Proteseninsuffizienz beobachtet. Die 2-Jahres-Überlebensrate betrug 87.5 ± 3.4%

Zusammenfassung. Die LDP zeigte intraoperativ keine Komplikationen und postoperativ zufriedenstellende klinische Ergebnisse mit niedriger Morbidität und Mortalität. Die hämodynamischen Eigenschaften der Prothese waren ebenfalls zufriedenstellend.

ABSTRACT (ENGLISH)

Introduction. The Labcor Dokimos Plus (LDP) is a stented externally mounted pericardial aortic bioprosthesis, which was recently introduced in Europe. Aims of the study are evaluation of operative and postoperative results as well as hemodynamic performance.

Methods. One hundred consecutive patients with a mean age of 65.9 ± 10.7 years (range 35–87) and a mean EuroSCORE II of 3.1 ± 3.9 (range 0.67–24.5) underwent aortic valve replacement with the LDP. Mean valve-size was 25.2 ± 1.7 mm. Concomitant procedures were performed in 34% of the cases. Postoperative clinical data were analyzed and hemodynamic performance of the prostheses was evaluated by transthoracic echocardiography. In addition, a follow-up was performed two years postoperatively.

Results. Intraoperatively no peculiarities occurred. Mean cross clamp times for isolated and complex procedures were 74.5 ± 20.0 min and 103.7 ± 37.1 min, respectively. Patients were extubated after a mean of 9.4 ± 15.8 h. There were no perioperative strokes. Bleeding events occurred in 4 patients. 30-day-mortality was 2%. One case of early endocarditis occurred. Echocardiography showed maximum and mean pressure gradients of 18.1 ± 6.4 and 9.6 ± 3.7 mmHg, respectively. Correspondingly to valve sizes 21, 23, 25 and 27 mm, mean pressure gradients were 17.3, 9.5, 8.5 and 10.2 mmHg, effective orifice areas were 1.92, 1.79, 2.0, 2.16 cm^2 and indexed effective orifice areas were 1.08, 0.95, 0.99 and 1.01 cm^2/m^2, respectively. No relevant regurgitations occurred. After two years, overall survival was 87.5 ± 3.4%

Conclusions. The LDP showed operatively no peculiarities and a satisfactory clinical outcome with low perioperative morbidity and mortality. The hemodynamic performance of the implanted valve sizes was satisfactory.

1. EINLEITUNG

Seit der ersten Herzklappenimplantation 1960 von Harken (1) wurden die Herzklappenprothesen kontinuierlich weiterentwickelt. Heutzutage zeigen die modernen Aortenklappenprothesen deutlich bessere hämodynamische und klinische Ergebnisse. Im Jahr 2014 wurden nach der DGTHG-Leistungsstatistik 11.764 konventionelle herzchirurgische Aortenklappenersatz-Operationen (AKE) in Deutschland vorgenommen(2). Dennoch sind die heutigen Prothesen nicht perfekt und müssen weiterentwickelt werden.

Die Aortenklappenstenose ist mit 43% die häufigste Form der Herzklappenerkrankungen (3-5). Die durchschnittliche Überlebensrate beträgt nach 2 Jahren ca. 50 Prozent und nach 5 Jahren ca. 20 Prozent (6, 7). Eine medikamentöse Therapie kann die Progression der Aortenklappenstenose nicht vermeiden (8, 9). Ein umgehender operativer Aortenklappenersatz sollte allen symptomatischen Patienten mit schwerer Aortenklappenstenose dringend empfohlen werden, wenn sie für eine Operation geeignet sind (10, 11). Die Aortenklappenisuffizienz tritt deutlich seltener als die Aortenklappenstenose auf und besteht bei ca. 20% der Patienten mit Aortenklappenerkrankungen (12). Die Operation ist bei symptomatischen Patienten (ab NYHA II) indiziert, die eine schwere Aortenklappeninsuffizienz aufweisen (13). In der Regel wird die erkrankte Klappe durch eine Prothese ersetzt. Heutzutage zeigt das TAVI-Verfahren deutliche Vorteile im Vergleich zu konventioneller Aortenklappenchirurgie bei hochmorbiden Patienten (14-16), wobei ein chirurgischer Aortenklappenersatz immer noch als Goldstandard in Behandlung von erworbenen Aortenklappenvitien gilt. Ziel dieser klinischen Studie ist es, die hämodynamischen Eigenschaften der neuen gestenteten biologischen Aortenklappenprothese Labcor Dokimos Plus postoperativ zu evaluieren und den klinischen Verlauf der Klappenpatienten zu beurteilen. Wir erwarten somit anhand der vorliegenden Arbeit wesentliche Vor- und Nachteile der Dokimos-Bioprothese zu identifizieren sowie Aussagen zum hämodynamischen Flussprofil, Prothesenfunktion als auch Anfälligkeit für Komplikationen zu treffen. In dieser Studie berichten wir sowohl über die früh postoperativen Ergebnisse, als auch über die Ergebnisse der klinischen Nachuntersuchung zwei Jahre nach der Operation.

2. METHODIK

2.1. Studienkollektiv

Einschlusskriterien. In die Studie wurden 100 aufeinanderfolgende Patienten eingeschlossen, die von Oktober 2013 bis Februar 2015 aufgrund eines Aortenklappenvitiums einen Aortenklappenersatz mit einer Labcor Dokimos Plus Prothese in der Klinik für Kardiovaskuläre Chirurgie der Charité – Universitätsmedizin Berlin erhielten. Während dieser Zeit unterzogen sich 358 Patienten einem Aortenklappenersatz. Die Entscheidung, diese Bioprothese zu implantieren, wurde von dem Operateur anhand der aktuellen Leitlinien (17) getroffen.

Patientenkollektiv. Das Patientenalter lag zwischen 35 und 87 Jahren und betrug im Durchschnitt 65.9 +/- 10.7 Jahre. Die Studiengruppe bestand zu 77% aus Männern und zu 23% aus Frauen. 55 Patienten hatten präoperativ eine Aortenklappenstenose, 25 Patienten litten an einer Aortenklappeninsuffizienz und 20 Patienten an einem kombinierten Aortenklappenvitium. Neun Patienten aus diesem Kollektiv hatten eine aktive Endokarditis.

2.2. Studiendesign

Die Patienten wurden prospektiv in die Studie eingeschlossen. Es handelt sich somit um eine klinische nicht randomisierte, monozentrische Studie mit einer Follow-Up Untersuchung.

Datenerhebung. Nach Genehmigung der Ethikkomission wurden folgende prä-, intra- und postoperative Daten ausgewertet:

1. Präoperative Daten: Alter (Jahre), Geschlecht (männlich, weiblich), Hauptdiagnose (AS, AI, kombiniertes Aortenklappenvitium, aktive Endokarditis), Körpergröße (cm), Körpergewicht (kg), Körperoberfläche (m^2), Body mass index, Herzrhythmus, kardiale Nebenerkrankungen, arterielle Hypertonie, Diabetes Mellitus, Euro SCORE II (%).
2. Intraoperative Daten: Eingriff (isoliert / kombiniert), Sternotomietechnik (konventionell / minimalinvasiv), Prothesengröße (21-27 mm), Implantationstechnik (intra- / supraannulär), Operationsdauer (min), Dauer der

extrakorporalen Zirkulation mittels Herz-Lungen-Maschine (min), Aortenklemmzeit (min), Low Cardiac Output Syndrom, weitere Komplikationen.

3. Postoperative Daten: Rethorakotomie wegen Blutung bzw. Tamponade, Re-Aortenklappenersatz, Schrittmacherimplantation, Schlaganfall, dialysepflichtiges akutes Nierenversagen, beatmungspflichtige Pneumonie, tiefe Wundinfektion, Prothesenendokarditis, Nachbeatmungszeit (h), Aufenthalt auf der Intensivstation (d), Krankenhausaufenthaltsdauer (h), 30-Tages-Mortalität (18).

Echokardiographie. Bei allen Patienten wurde vor der Entlassung eine transthorakale Echokardiographie mit dem Gerät GE Vivid 7 Dimension (General Electric, Fairfield, Connecticut, USA) durchgeführt. Die folgenden Parameter wurden ausgewertet: morphologische und funktionelle Beurteilung der implantierten Klappenprothese im 2-D-Echo (Klappenposition, Beweglichkeit der Klappensegel), Vorhandensein einer trans- bzw. paravalvulären Protheseninsuffizienz mittels Farb-Doppler, linkventrikuläre Ejektionsfraktion (%) im 4-Kammerblick, maximale und mittlere Flussgeschwindigkeit über der Aortenklappe (m/s) mittels CW-Doppler, maximale und mittlere Druckgradienten über der Aortenklappe (mm Hg) mittels CW-Doppler, maximale und mittlere Druckgradienten im linksventrikulären Ausflusstrakt (LVOT) (mmHg) mittels PW-Doppler, Aortenklappenöffnungsfläche (cm^2), berechnet nach der Kontinuitätsgleichung, indizierte Aortenklappenöffnungsfläche (cm^2/m^2) (iEOA, indexed effective orifice area

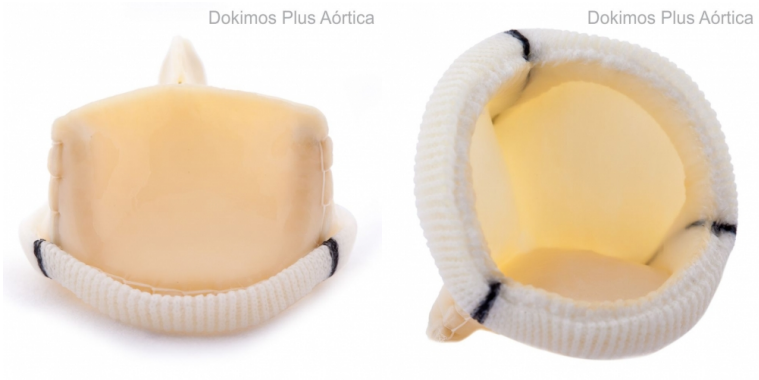
Follow-up. Im Verlauf erfolgte eine Nachuntersuchung des Patientenkollektives. Es handelte sich um eine aktives, prospektives Follow-up. Der Zeitpunkt der Untersuchung betrug im Durchschnitt 1.7 ± 0.5 Jahre. Die Nachuntersuchung erfolgte zum größten Teil (69 Patienten) in der herzchirurgischen Ambulanz der Klinik für Kardiovaskuläre Chirurgie der Charite und bestand aus dem Anamnesegespräch, aus der körperlichen Untersuchung und der transthorakalen Echokardiographie. 28 Patienten konnten zur Nachuntersuchung nicht kommen. Diese, oder deren Angehörige, wurde telefonisch kontaktiert und befragt.

2.3. Prothesenbeschreibung und chirurgische Technik

Die Labcor Dokimos Plus Aortenklappenprothese (weiter LDP) ist eine gestentete biologische Prothese aus bovinem Perikard (Abb. 5.), hergestellt in den Labcor Laboratories, Belo Horizonte, Brazil. Das Perikard wird nach der Reducer® Antikalzifizierungmethode behandelt, die die biologische Stabilität des Gewebes erhöht. Die Segel werden in einer gepufferten Glutaraldehydlösung bei Nulldruck fixiert, um die Integrität der Kollagenfasern zu erhalten. Die Segel sind auf einem flexiblen, mit Polyestermaterial überzogenen Azetalkopolymer-Stent befestigt.

Der Stent weist ein niedriges Profil auf. Die Flexibilität des Stents bietet Beweglichkeit auf der Kommissurenebene, wodurch die Verschlußbelastung der Kommissuren reduziert wird. Die Nahtmanschette besteht aus einem Silikongummiring, der ebenfalls mit Polyestermaterial überzogen ist. Die Prothese wird in den Größen 19, 21, 23, 25 und 27 hergestellt. Sowohl eine intra- als auch supraannuläre Implantation ist möglich.

Abb. 1 - Labcor Dokimos Plus Bioprothese



Chirurgische Technik. Es erfolgte entweder eine obere partielle oder eine mediane Sternotomie. Danach wurde die Aorta ascendens und der rechte Vorhof standardmäßig kanüliert. Die Ausnahmen waren zwei Patienten, die eine zusätzliche Rekonstruktion der Trikuspidalklappe brauchten, bei ihnen erfolgte eine bikavale Kanülierung. Die meisten Eingriffe wurden in Normothermie durchgeführt, aber bei wenigen komplexen Kombinationseingriffen wurde eine milde Hypothermie (32-34 ^{o}C) verwendet. Nach dem Abklemmen der Aorta und Erzeugung des Herzstillstandes mittels antegrader

Blutkardioplegie nach Calafiore erfolgte eine Aortotomie ca. 1-2 cm über den Komissuren. Nach der Resektion der erkrankten Aortenklappe erfolgte die Ausmessung des Aortenannulus.

Danach wurde die geeignete Prothese mittels 12 bis 20 Filznähten entweder intraannulär oder supraannulär implantiert. Der Verschluß der Aorta wurde zweireihig fortlaufend, d.h. mit ener Matratzennaht und einer zusätzlichen fortlaufenden überwendlichen Naht, durchgeführt. Zur Vermeidung von Luftembolien erfolgte während der Klappenimplantation eine CO_2-Insufflation. Die Funktion der Aortenklappenprothese wurde intraoperativ mittels transösophagealer Echokardiographie kontrolliert.

2.4. Statistische Auswertung und Datendarstellung

Die gesammelten Daten wurden vollständig mit Hilfe des Tabellen- und Kalkulationsprogramms Microsoft Excel® archiviert. Die statistische Auswertung der Daten erfolgte mit Hilfe des Statistikprogrammes SPSS Statistics Version 22.0.0. (SPSS Inc., Chicago, Illinois). Es wurde eine deskriptive Statistik erstellt, welche die Berechnung der Mittelwerte, der Standardabweichungen, der Mediane sowie der Messbereiche beinhaltet. Alle Werte wurden auf eine Normalverteilung geprüft. Die Überlebenskurve wurde nach Kaplan-Meier berechnet.

2.5. Evaluation der Labcor Dokimos Prothese in anderen Studien

Die LDP-Patientenkohorte wurde außerdem in zwei weiteren Studien unserer Klinik evaluiert (19, 20). Erstens, wurde die Labcor Dokimos Prothese mit zwei anderen Prothesen: Medtronic 3f® (Medtronic Inc., Fridley, MN, USA) und Perceval® (Sorin Biomedica Cardio S.r.l., Saluggia VC, Italy) bei Patienten verglichen, die einen Aortenklappenersatz über den minimal-invasiven Zugang erhielten. Zweitens, erfolgte ein Vergleich der LDP mit der Sorin Freedom Solo Prothese hinsichtlich der prozeduralen, klinischen und hämodynamischen Eigenschaften.

3. ERGEBNISSE

3.1. Präoperative Daten

In Tabelle 1 sind alle wichtigen präoperativen Charakteristiken des Patientenkollektivs enthalten.

Tab. 1. Präoperative Patientendaten

Patientenanzahl (n)	100
Herzrhythmus	
Sinusrhythmus (n)	73
Vorhofflimmern (n)	27
Kardiale Nebenerkrankungen	
Koronare Herzerkrankung (n)	38
Arterielle Hypertonie (n)	67
Pulmonale Hypertonie (n)	7
Myokardinfarkt	4
Nichtkardiale Nebenerkrankungen	
Niereninsuffizienz (n)	32
Diabetes mellitus (n)	22
Adipositas (n)	30
pAVK	11
COPD	7
NYHA Klasse	2.6 ± 0.7
EuroSCORE II	3.1 ± 3.9
Range	0.7 - 24.5
Für isolierte Eingriffe	2.0 ± 1.7
Range	0.7 - 8.2
Für kombinierte Eingriffe	5.9 ± 3.8
Range	0.7 - 24.5

3.2. Operative Daten

Eingriffeinteilung. Von insgesamt 100 Patienten erhielten 61 (61%) einen isolierten Aortenklappenersatz durch die LDP als Ersteingriff. Bei fünf Patienten (5%) erfolgte eine Reoperation eines Aortenklappenersatzes (Re-AKE). Die restlichen Eingriffe wurden zusätzlich mit koronarer Bypass-Operation (CABG), Vorhofablation, Mitralklappenersatz/-rekonstruktion (MKE / MKR), Trikuspidalklappenrekonstruktion (TKR) und Erweiterung des Aortenannulus kombiniert. Die genaue Verteilung der Eingriffe wird in Tabelle 2 dargestellt.

Tab. 2. - Prozeduren

Eingriff	**Anzahl**
Isolierte Eingriffe:	
AKE (Ersteingriff)	61
Re-AKE	5
Kombinierte Eingriffe:	
CABG 1-fach / 2-fach/ 3-fach	8 / 8 / 5
MKR / MKE	3 / 5
Vorhofablation	3
TKR	2
Aortenannuluserweiterung	2

Häufigkeit der Prothesengrößen. Die Dokimos Plus Prothese wurde in vier verschieden Größen implantiert: 21, 23, 25 und 27 mm. Die Anzahl innerhalb der Größen ist im Diagramm 1 dargestellt. Die Größe 21 wurde am seltensten implantiert, denn die internen Richtlinien der Klinik empfehlen die Verwendung von gerüstfreien Prothesen bei Patienten mit kleinem Aortenannulus.

Minimalinvasive Technik. 43 von 61 isolierten Eingriffen (70.5 %) wurden in minimalinvasiver Technik durch eine partielle obere Sternotomie mit J-förmiger Querinzision in den 3. oder 4. Interkostalraum nach rechts durchgeführt (21-24). Die andere Eingriffe wurden durch eine mediane Sternotomie durchgeführt.

Implantationstechnik. Bei 60 Patienten (60%) erfolgte die Implantation der Prothese intraanulär und bei 40 Patienten (40%) supraanulär. Die intraannuläre Implantation wurde bei Patienten mit einem großen Aortenannulus (>29 mm, n = 23), möglicher Koronarobstruktion (n = 18) und ausgeprägter Kalzifizierung der Sinus Valsalvae (n =19) durchgeführt.

Operationsdauer, Zeit der extrakorporalen Zirkulation und Ischämiezeit. Die mittlere Operationsdauer des gesamten Patientenkollektivs betrug 212.4 ± 57.7 Minuten. Die Herz-Lungen-Maschinen-Zeit lag bei 113.6 ± 40.6 Minuten. Die mittlere Abklemmzeit der Aorta betrug 84.8 ± 30.0 Minuten. Bei isolierten Eingriffen betrug die mittlere Operationsdauer 189.2 ± 36.3 Minuten, die mittlere Herz-Lungen-Maschinen-Zeit 96.6 ± 25.3 Minuten und die mittlere Abklemmzeit der Aorta 74.2 ± 20.0 Minuten. Bei kombinierten Eingriffen betrug die mittlere Operationsdauer 257.2 ± 65.4 Minuten, die mittlere Herz-Lungen-Maschinen-Zeit 140.2 ± 45.7 Minuten und die mittlere Abklemmzeit der Aorta 103.7 ± 37.1 Minuten.

3.3. Postoperativer Verlauf

Die durchschnittliche Beatmungszeit betrug 9.4 ± 15.8 Stunden. Zehn Patienten (10%) hatten eine Beatmungszeit über 24 Stunden, dementsprechend wurden 90 Patienten (90%) am ersten postoperativen Tag extubiert.

Der durchschnittliche Aufenthalt auf der Intensivstation postoperativ war 2.8 ± 3.5 Tage. 57 Patienten (57%) blieben auf der ITS weniger als 24 Stunden.

Der postoperative Krankenhausaufenthalt der Dokimos Patienten betrug 10.5 ± 6.9 Tage.

Postoperative Komplikationen. Bei keinem Patienten trat postoperativ ein Schlaganfall, eine beatmungspflichtige Pneumonie oder eine tiefe Wundinfektion auf. Im Verlauf wurden vier Patienten (4%) wegen einer Blutung rethorakotomiert. Alle diese Patienten konnten erfolgreich versorgt werden. Sechs Patienten (6%) erhielten postoperativ einen permanenten Schrittmacher. Bei fünf von diesen sechs Patienten

war die Schrittmacherimplantation aufgrund eines postoperativen AV-Blocks III. Grades indiziert, bei einem Patienten bestand die Indikation in einem Sick-Sinus-Syndrom.

Acht Patienten (8%) erlitten postoperativ ein temporäres dialysepflichtiges akutes Nierenversagen. Bei vier von diesen Patienten bestand bereits präoperativ eine Niereninsuffizienz. Bei einem Patienten (1%) zeigte sich eine früh postoperative Prothesenendokarditis. Am 30. postoperativen Tag erhielt dieser Patient einen Ersatz der Prothese. Er konnte erfolgreich versorgt werden.

Die 30-Tages-Mortalität bei Patienten, die einen isolierten Aortenklappenersatz erhielten, betrug 0%. Die 30-Tages-Krankenhaus-Mortalität betrug im gesamten Patientenkollektiv 2% (zwei Patienten). Beide verstorbene Patienten erhielten einen Kombinationseingriff. Der erste Patient (EuroSCORE II von 7.6%) erhielt einen Aortenklappenersatz in Kombination mit einer Mitralklappenrekonstruktion und einer Vorhofablation. Er verstarb am sechsten postoperativen Tag an Herzversagen. Der zweite Patient (EuroSCORE II von 13.1%) erhielt einen Aortenklappenersatz in Kombination mit einer Mitralklappenrekonstruktion und CABG. Er verstarb am neunten postoperativen Tag ebenfalls am therapierefraktären Herzversagen.

3.4. Ergebnisse der postoperativen echokardiografischen Untersuchung

93 Patienten (93%) erhielten eine postoperative transthorakale Echokardiographie vor Entlassung. Sieben Patienten konten aufgrund der eingeschränkten Schallbedingungen (n = 4), des früh postoperativen Todes (n = 2) und der Endokarditis (n=1) nicht untersucht werden.

Druckgradienten über der Aortenklappe. Der durchschnittliche maximale Druckgradient über der Aortenklappenprothese im gesamten Patientenkollektiv lag bei 18.1 ± 6.4 mm Hg. Der mittlere Druckgradient betrug im Durchschnitt 9.6 ± 3.7 mm Hg. In Tabelle 3 sind die Druckgradienten der einzelnen Prothesengrößen aufgelistet.

Tab. 3 - Die maximalen / mittleren Druckgradienten über der Aortenklappe für einzelne Prothesengrößen:

Parameter	Größe 21	Größe 23	Größe 25	Größe 27
Max. Druckgradient über AK (mm Hg)	29.7 ± 12.1	19.3 ± 4.9	16.5 ± 5.8	19.1 ± 5.8
Mittl. Druckgradient über AK (mm Hg)	17.3 ± 6.7	9.6 ± 3.0	8.5 ± 3.1	10.2 ± 3.6

Effektive Öffnungsfläche der Aortenklappenprohese (AKÖF). Mittlere AKÖF und die so genannte Indexed Effective Orifice Area (EOAI) betrugen postoperativ jeweils 2.01 ± 0.52 cm^2 und 0.99 ± 0.25 cm^2/m^2. Zwei Patienten zeigten ein schwergradiges Patient-Prothesen-Mismatch (PPM) (iEOA < 0.65 cm^2/m^2), diese hatten einen mittleren BMI von 33.3. Außerdem zeigten 21 Patienten (21%) ein mittelgradiges PPM (iEOA > 0.65 cm^2/m^2 und < 0.85 cm^2/m^2). In Tabelle 4 sind die AKÖF und EOAI der einzelnen Prothesengrößen aufgelistet.

Tab. 4 Die AKÖF und iEOA für einzelne Prothesengrößen:

Parameter	Größe 21	Größe 23	Größe 25	Größe 27
AKÖF (cm^2)	1.92 ± 0.44	1.79 ± 0.36	2.0 ± 0.6	2.16 ± 0.47
EOAI (cm^2/m^2)	1.08 ± 0.33	0.95 ± 0.18	0.99 ± 0.29	1.01 ± 0.24

Protheseninsuffizienz. In der postoperativen Echokardiographie zeigte sich bei keinem der 100 Patienten eine relevante trans- oder paravalvuläre Klappenprotheseninsuffizienz, eine Dysfunktion der Prothese oder eine Prothesenthrombose.

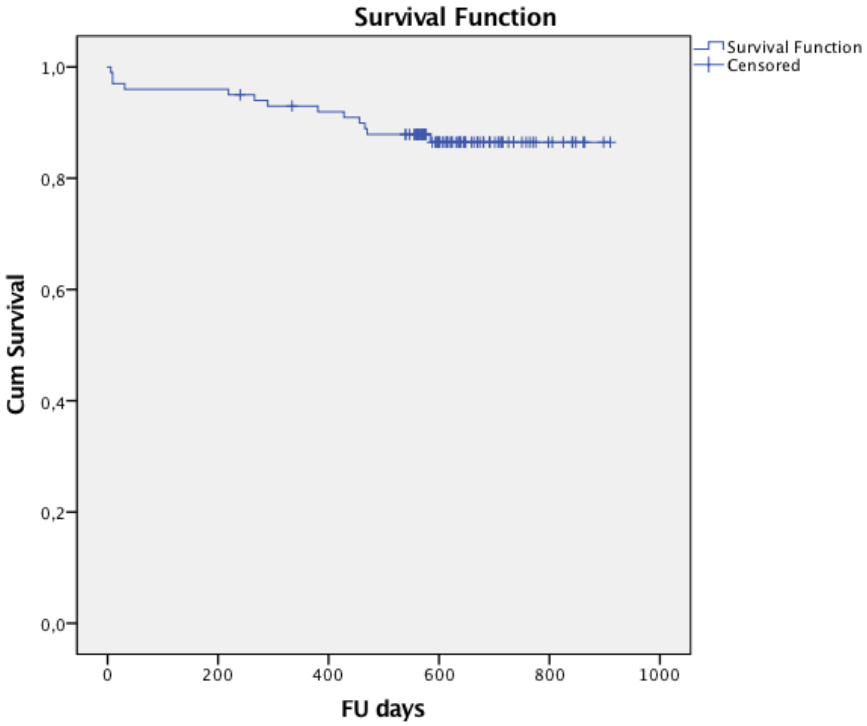
3.5. Ergebnisse der Nachuntersuchung

Die 2-Jahres-Überlebensrate betrug 87.5 ± 3.4%. Die Überlebenskurve nach Kaplan-Meier wird in Abbbildung 2 dargestellt. Die Todesursachen waren:

- Multiorganversagen – 6 Patienten;
- Karzinom – 3 Patienten
- Lungenembolie – 1 Patient;
- Sepsis (nicht kardial) – 1 Patient;

- Nierenversagen – 1 Patient
- Unklare Ursache – 1 Patient.

Abb. 2 Überlebenskurve nach Kaplan-Meier



Drei Patienten entwickelten im Verlauf einen Schlaganfall (3%). Insgesamt vier Patienten (4%) mussten bei Prothesenendokarditis reoperiert werden. Sie erhielten einen Wechsel der Prothese. Es ergaben sich keine weitere Komplikationen. Die wichtigsten Ergebnisse der echokardiografischen Nachuntersuchung sind in Tabelle 5 enthalten.

Tab. 5 Ergebnisse der echokardiografischen Nachuntersuchung (2-Jahres Follow-up)

Parameter	Nachuntersuchung
LVEF (%)	56.2 ± 4.1
Max. Druckgradient über AK (mm Hg)	14.6 ± 6.1
Mittl. Druckgradient über AK (mm Hg)	6.9 ± 3.3
AKÖF (cm^2)	2.2 ± 0.4
EOAI (cm^2/m^2)	1.08 ± 0.2

4. DISKUSSION

Ein konventioneller Aortenklappenersatz ist immer noch der Goldstandard für Patienten mit fortgeschrittener Aortenklappenerkrankung ohne erhöhtes Risikoprofil. Die Bioprothesen sind für Patienten über 65 Jahre oder für die Patienten, die eine Kontraindikation zu einer systemischen Antikoagulation haben, indiziert (25-27). Gestentete Bioprothesen sind einfach zu implantieren (im Verlgleich zu gerüstfreien Prothesen) und zeigen gute hämodynamische Ergebnisse. Trotz der kontinuierlichen Entwicklung der technischen Ausrüstung sowie der zunehmenden Erfahrung der Herzchirurgen sind solche Klappenprothesen weiter zu verbessern bezüglich der hämodynamischen Eigenschaften, klinischen Ergebnisse und der Haltbarkeit. Die Labcor Dokimos Plus Prothese wurde in Europa im Jahr 2013 eingeführt. Innovatives Design und die Antikalzifizierungsmethode machen die LDP zu einer attraktiven Alternative auf dem Markt der Herzklappenprothesen. Nach unserem Wissen ist es die erste Studie, die die postoperativen Ergebnisse des Aortenklappenersatzes mit der Dokimos Plus Prothese evaluiert (28).

Unsere Studie ist durch die Studienpopulationsgröße limitiert. Diese betrug 100 Patienten, was die statistische Aussagekraft der Daten einschränkt. Diese Patientenanzahl ist durch zwei Faktoren erklärbar. Als Dauer des Einschlusses der Patienten in die Studie legten wir 18 Monate fest, was der durchschnittlichen Dauer ähnlicher prospektiver klinischer Studien entspricht. Darüber hinaus implantierten wir in diesem Zeitraum in unserer Klinik parallel andere Aortenklappenprothesen, dies reduzierte die Anzahl der Dokimos Implantationen.

Hinsichtlich der Patientendemographie handelt es sich in der Studie um ein typisches Patientengut, wenn man die Daten des Aqua-Instituts zugrunde legt (29). Die Verteilung der Komorbiditäten bei dem Studienkollektiv ist auch mit der Bundesauswertung vergleichbar. Zur Beurteilung der Funktion der Prothese verwandten wir postoperativ die transthorakale Echokardiographie. Die relevanten Parameter wurden hierbei ausführlich ausgewertet. Limitierend für diese Art der Untersuchung sind eingeschränkte Schallbedingungen früh postoperativ, wie z.B. die Notwendigkeit der Rückenlage nach erfolgter Sternotomie und Luftausfüllung des Brustkorbes. Zudem

gestaltete sich die Untersuchung besonders mühsam bei Patienten mit Adipositas. Dennoch wird das TTE standardmäßig als Methode der ersten Wahl zur Beurteilung der Prothese eingesetzt (30).

Zum Vergleich der Studienergebnisse wurden vor allem die Daten aus der Bundesauswertung des AQUA-Instituts zum Erfassungsjahr 2014 verwendet. Außerdem wurde ein Vergleich mit den anderen Studien durchgeführt, die sich auf ähnliche gestentete Klappenprothesen beziehen und ein ähnliches Studiendesign haben (31-35).

Die intraprozedularen Charakteristiken wie mittlere Operationsdauer, mittlere Herz-Lungen-Maschinen-Zeit sowie mittlere Abklemmzeit der Aorta sind sowohl bei dem gesamten Patientenkollektiv, als auch bei den isolierten Eingriffen mit den anderen Studien vergleichbar. Die früh postoperativen klinischen Ergebnisse und die Ergebnisse der 2-Jahres-Nachuntersuchung nach der LDP-Implantation waren zufriedenstellend. Die meisten Patienten zeigten einen unauffälligen Verlauf. Innerhalb desselben Aufenthaltes ergab sich keine Indikation zu einem Re-Aortenklappenersatz wegen einer Prothesendysfunktion. Dieser Wert spricht für eine gute Qualität der Prothese und ist als erfolgreich zu bewerten.

Ein Schlaganfall im frühpostoperativen Verlauf entwickelte sich in unserer Studiengruppe ebenfalls nicht. Das Risiko eines Schlaganfalles wird bei einem Aortenklappenersatz vor allem dadurch erhöht, dass bei der Exzision einer verkalkten Aortenklappe ein Absprung eines Kalksegmentes in den linken Ventrikel mit nachfolgendem Transport in die supraaortale Gefäße möglich ist. Die 30-Tages-Krankenhaus-Mortalität betrug im gesamten Patientenkollektiv 2%. Dieser Wert war niedriger als die präoperativ berechnete voraussichtliche Letalität von 3.1 ± 3.9 % in EuroSCORE II. Die 30-Tages-Mortalität bei der Bundesauswertung betrug 4.5 % für kombinierte Eingriffe und 2.7 % für isolierte AKE. Die 1- und 2-Jahres-Überlebensraten waren ebenso vertretbar. Eine Rethorakotomie wegen einer postoperativen Blutung oder Tamponade wurde bei vier Patienten (4%) durchgeführt. Zwei von vier rethorakotomierten Patienten bekamen einen isolierten Aortenklappenersatz als Initialeingriff. Der dritte Patient erhielt einen Aortenklappenersatz und eine

Trikuspidalklappenrekonstruktion. Die Revision wurde jeweils eine Stunde postoperativ durchgeführt, wobei keine chirurgische Blutung festgestellt wurde. Der vierte Patient entwickelte eine drohende Tamponade am dritten postoperativen Tag auf der Intensivstation bei seit der primären Operation laufendem ECMO-System. Bei der Revision wurde keine chirurgische Blutungsquelle gefunden. Die Patienten, die ein ECMO-System benötigen, weisen erfahrungsgemäß eine höhere Blutungsrate auf, weil das Gerinnungssystem häufig eingeschränkt ist.

6 % der Patienten in der Dokimos-Gruppe erhielten postoperativ einen permanenten Schrittmacher. Es zeigt sich eine höhere Schrittmacherimplatationsrate in unserem Kollektiv im Vergleich zu den anderen Studien und Datenbanken. Sieben von 100 Patienten erlitten postoperativ ein dialysepflichtiges akutes Nierenversagen (7%). Dieser Wert liegt im durchschnitlichen Bereich im Vergleich zu ähnlichen Studien.

Die Labcor Dokimos Prothese zeigte auch gute hämodynamische Ergebnisse. Die durchschnittlichen Druckgradienten über der Aortenklappenprothese, die Öffnungsfläche der Prothese sowie die s.g. EOAI waren vergleichbar und teilweise besser als solche Parameter bei anderen biologischen Aortenklappenprothesen (36-38). Bei der Auswertung der EOAI ist es zu erwähnen, dass die durchschnittliche Körperoberfläche in unserem Patientenkollektiv relativ hoch war (2.0 ± 0.2), was diesen Wert entsprechend reduzierte. Allerdings zeigten sich in der Studiengruppe nur zwei Fälle eines schwergradigen PPM. Diese Patienten hatten eine Adipositas und erhielten die Prothesen Größe 25. Acht von 21 Patienten mit einem mittelgradigen PPM hatten auch eine Adipositas (BMI über 30). Aus der früh postoperativen Echokardiographie bei allen 100 Patienten ergab sich keine trans- oder paravalvuläre Insuffizienz der Klappenprothese. Dies spricht für eine gute Prothesenfunktion und Implantierbarkeit der Prothese. Die weiteren Vergleichsstudien unserer Klinik wiesen auch gute vertretbare Ergebnisse der Dokimos Plus Prothese auf.

Zusammenfassung.

Die bovine gestentete Labcor Dokimos Plus Aortenklappenprothese ist leicht implantierbar und weist zufriedenstellende intra- und früh postoperative klinische und hämodynamische Ergebnisse auf.

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6. LEBENSLAUF

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

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RESEARCH ARTICLE Open Access

Clinical outcome and hemodynamic behavior of the Labcor Dokimos Plus aortic valve

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Abstract

Background: The Labcor Dokimos Plus (LDP) is a stented externally mounted pericardial aortic bioprosthesis, which was recently introduced in Europe. Aims of the study are evaluation of operative and postoperative results as well as hemodynamic performance.

Methods: One hundred consecutive patients with a mean age of 65.9 ± 10.7 years (range 35–87) and a mean EuroSCORE II of 3.1 ± 3.9 (range 0.67–24.5) underwent aortic valve replacement with the LDP. Mean valve-size was 25.2 ± 1.7 mm. Concomitant procedures were performed in 34% of the cases. Postoperative clinical data were analyzed and hemodynamic performance of the prostheses was evaluated by transthoracic echocardiography. Clinical follow-up was 100%, echocardiographic follow-up was 93% complete.

Results: Intraoperatively no peculiarities occurred. Mean cross clamp times for isolated and complex procedures were 74.5 ± 20.0 min and 103.7 ± 37.1 min, respectively. Patients were extubated after a mean of 9.4 ± 15.8 h. There were no perioperative strokes. Bleeding events occurred in 4 patients. 30-day-mortality was 2%. One case of early endocarditis occurred. Echocardiography showed maximum and mean pressure gradients of 18.1 ± 6.4 and 9.6 ± 3.7 mmHg, respectively. Correspondingly to valve sizes 21, 23, 25 and 27 mm, mean pressure gradients were 17.3, 9.5, 8.5 and 10.2 mmHg, effective orifice areas were 1.92, 1.79, 2.0, 2.16 cm^2 and indexed effective orifice areas were 1.08, 0.95, 0.99 and 1.01 cm^2/m^2, respectively. No relevant regurgitations occurred.

Conclusions: The LDP showed operatively no peculiarities and a satisfactory clinical outcome with low perioperative morbidity and mortality. The hemodynamic performance of the implanted valve sizes was satisfactory.

Keywords: Stented aortic valve replacement, Biological prosthesis, Valve replacement, Echocardiography

Background

Recently, a new bovine pericardial stented bioprosthesis for the aortic position, the Labcor Dokimos plus (LDP), became available in Europe. The design features are a low profile stent with externally mounted leaflets [1]. Yet, no contemporary data about clinical outcome and hemodynamic performance are available. We report about our perioperative experience with this substitute, the early clinical outcome and hemodynamic performance.

Methods

Patients

From October 2013 to February 2015 100 consecutive patients underwent aortic valve replacement with LDP prostheses, while a total of 358 patients received an aortic valve replacement at our institution. The decision to implant the bioprosthesis was made according to the actual guidelines [2, 3]. Baseline preoperative characteristics are displayed in Table 1.

Prosthesis

The LDP prosthesis, manufactured in Labcor Laboratories, Belo Horizonte, Brazil is a CE-marked stented bovine pericardial bioprosthesis and available in sizes from 19 to 27 mm (Fig. 1). Special features of this prosthesis

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Table 1 Baseline characteristics and risk stratification

Characteristic	Number
Number of patients (*n*)	100
• Age in years ± standard deviation	65.9 ± 10.7
Gender	
• Male (*n*)	77
• Female (*n*)	23
Body surface area ± standard deviation (m^2)	2.0 ± 0.2
Aortic valve lesion	
• Stenosis (*n*)	55
• Regurgitation (*n*)	25
• Mixed lesion (*n*)	20
• Active endocarditis (*n*)	9
Predominant cardiac rhythm	
• Sinus rhythm (*n*)	73
• Atrial fibrillation (*n*)	27
Concomitant disease	
• Coronary artery disease (*n*)	38
• Arterial hypertension (*n*)	67
• Pulmonary hypertension (*n*)	7
• Renal dysfunction (*n*)	32
• Diabetes mellitus (*n*)	22
• Obesity (*n*)	30
NYHA class (Mean ± standard deviation)	2.6 ± 0.7
EuroSCORE II	3.1 ± 3.9 Range: 0.7-24.5
• Isolated aortic valve replacement	2.0 ± 1.7 Range 0.7-8.2
• Complex procedures	5.9 ± 3.8 Range 0.7-24.5

Fig. 1 Lateral view and front view of the Labcor Dokimos Plus

are a low profile, an acetal copolymer stent covered with polyester, externally mounted pre-molded leaflets fixed with glutaraldehyde at zero pressure as well as a so called Reducer® anti-calcification treatment.

Surgical technique

A right upper hemisternotomy in the 4th intercostal space was performed for isolated aortic valve replacement and full sternotomy for combined procedures. Standard cannulation of the ascending aorta and the right atrium was performed in all cases except in two patients with additional tricuspid valve repair. In these cases bicaval cannulation was performed. Usually normothermic perfusion was used. However, in complex cases with impaired ventricular function mild hypothermia (32–34 °C) was applied. After clamping of the aorta, intermittent antegrade blood cardioplegia according to Calafiore was performed. The ascending aorta was transversely opened 1–2 cm above the commissures for half of its circumference. After resection of the diseased valve and thorough annular decalcification, sizing with ball-sizers and LDP-sizers was performed. The appropriate prosthesis was implanted with 12–20 horizontal felt-armed mattress sutures. The prosthesis was positioned either supra-annularly or intra-annularly depending on the distance between the aortic annulus and the coronary ostia, the position of the coronary ostia, calcifications in the coronary sinus and the size of the annulus and the sinus coronarius. The intra-annular position was chosen in patients with tubular sinuses, possible coronary obstruction by the bioprosthesis and in patients with aortic annuli above 29 mm. In smaller annuli (≤21 mm), stentless valves were implanted (according to institutional guidelines), what represents a selection bias for this study. Mitral valve procedures (with or without left atrial ablation), distal coronary anastomoses and aortic annular enlargement were performed before implantation of the LDP. Tricuspid procedures were performed on the beating heart after the aortic valve replacement. Aortic annular enlargement was done using the Manouguian technique using a patch of bovine pericardium to reconstruct the extended aortotomy into the non-coronary cusp and the subaortic curtain. The function of the prosthesis was controlled by trans-esophageal echocardiography.

Clinical follow-up

After approval by the local Ethics Committee pre-, intra- and early postoperative (until discharge) data were prospectively collected. Hemodynamic performance was evaluated using transthoracic echocardiography at discharge. It was performed with a GE Vivid 7 Dimension (General Electric, Fairfield, Connecticut, USA) to check morphology and function of the implanted prostheses.

Two-dimensional and Doppler transthoracic echocardiography was performed. Mean values for each measurement were derived from three beats in sinus rhythm, and five beats in those in non-sinus rhythm. Transaortic flow velocities were assessed by continuous–wave Doppler, while flow velocities in the left ventricular outflow tract were assessed by pulsed–wave Doppler. Pressure gradients were calculated using the Bernoulli equation. The effective aortic valve orifice area (EOA) was calculated with the continuity equation and indexed by the body surface area of the patient (EOAI).

Statistics

All data were prospectively collected and analyzed with SPSS Statistics version 22.0.0 (SPSS Inc., Chicago, Illinois). Descriptive statistics are reported as the mean ± standard deviation for continuous variables and as absolute frequencies and percentages for categorical variables.

Results

Operative details are presented in Table 2. Smaller valve sizes (≤21 mm) were implanted rarely, due to institutional guidelines to implant stentless valves in these cases. Intra-annularly implantation of the LDP was performed due to a wide aortic annulus (>29 mm, $n = 23$), possible coronary obstruction ($n = 18$) and calcification or anatomical anomalies of the Valsalva sinuses ($n = 16$). Supra-annularly implantation was performed in the rest of the patients. No intraoperative complications occurred and intraoperative mortality was 0%. Patients were extubated after a mean of 9.4 ± 15.8 h. Three patients developed a low cardiac output syndrome postoperatively and therefore received extracorporeal life support (ECLS) within the first 24 h after the operation. These patients had undergone complex combined procedures and suffered preoperatively from an impaired left ventricular function with a left ventricular ejection fraction ≤ 35%. ECLS could be weaned in two patients at the 4th and 5th day postoperatively, respectively. However, both patients died due to intractable ventricular fibrillation and septic multi-organ failure at the 9th and 44th postoperative day, respectively. The third patient died at the 6th postoperative day due to multi-organ failure. No other fatalities occurred. Hence, in patients with complex procedures the 30-day mortality was 5.9% and the hospital mortality 8.8%. For patients undergoing isolated valve replacement the 30-day mortality was 0%.

Postoperative complications included re-exploration for bleeding, which had to be performed in four patients. Furthermore, eight patients developed acute renal insufficiency and required temporary dialysis. Insertion of a permanent pacemaker became necessary in six patients. There were no strokes or deep sternal wound infections.

Table 2 Operative characteristics

Procedure	Number
Isolated aortic valve replacement (*n*)	66
Combined procedures (*n*)	34
• Coronary artery bypass grafting (*n*)	21
• Mitral Valve Replacement (*n*)	5
• Mitral Valve Repair (*n*)	3
• Left atrial ablation (*n*)	3
• Ascending Aorta Replacement (*n*)	2
• Tricuspid Valve Reconstruction (*n*)	2
• Aortic Annular Enlargement (*n*)	2
Implanted valve sizes	
• 21 mm (*n*)	3
• 23 mm (*n*)	20
• 25 mm (*n*)	41
• 27 mm (*n*)	36
Technique of implantation	
• Supra-annularly (*n*)	40
• Intra-annularly (*n*)	60
Duration of procedure (min)	212.4 ± 57.7
• Isolated procedures (min)	189.2 ± 36.3
• Combined procedures (min)	257.2 ± 65.4
Cardiopulmonary bypass time (min)	113.6 ± 40.6
• Isolated procedures (min)	96.6 ± 25.3
• Combined procedures (min)	140.2 ± 45.7
Aortic cross clamp time (min)	84.8 ± 30.0
• Isolated procedures (min)	74.5 ± 20.0
• Combined procedures (min)	103.7 ± 37.1

One case of early postoperative endocarditis occurred, which led to a successful secondary valve replacement at the 30th postoperative day. Patients were discharged after a mean of 10.5 ± 6.9 days.

Echocardiography was analyzed for 93% of the cases. Excluded were data of 7 patients, due to insufficient conditions early postoperatively ($n = 4$), death ($n = 2$; patients with ECLS, who died on the 6th and 9th day postoperatively) and endocarditis (n = 1). Maximum and mean prosthetic pressure gradients at discharge were 18.1 ± 6.4 and 9.6 ± 3.7 mmHg, respectively. Mean EOA and mean EOAI were 2.01 ± 0.52 cm^2 and 0.99 ± 0.25 cm^2/m^2, respectively. Two cases of severe patient-prosthesis mismatch (EOAI < 0.65 cm^2/m^2) were observed (mean body mass index in these patients was 33.3). Twenty-one cases of moderate prosthesis-mismatch (EOAI > 0.65 cm^2/m^2 and < 0.85 cm^2/m^2) were observed. No relevant central or para-valvular regurgitation was evident. No structural or nonstructural valve dysfunctions and no valve thrombosis could be

observed. Table 3 provides the detailed hemodynamic data according to the different valve sizes.

Discussion

Conventional aortic valve replacement is still a gold standard for patients with relevant aortic valve disease without excessive risk profile. Biological substitutes are recommended for patients older than 65 years or those with contraindications to systemic anticoagulation [2, 3]. Stented biological substitutes are easy to implant and show acceptable hemodynamic performances. However, there is still the necessity to improve these valves concerning hemodynamic properties and clinical performance as well as durability. The LDP was launched in Europe in 2013. It´s innovative design combined with a novel anti-calcification treatment makes it a promising substitute in the category of stented bioprostheses. To our knowledge, this is the first study that reports early postoperative outcome and hemodynamic data in a European population.

Procedural data, including cross clamp times, were comparable to other stented bio-prosthetic heart valves and verify the simplicity and safety of the LDP-implantation [4–6]. However, one has to consider the low mean age and predicted risk of the study cohort, which was triggered by the increasing use of transfemoral aortic valve replacement in our institution in older high risk patients. Noticeably, intra-annularly implantation occurred very frequently. This is triggered by the institutional guideline to implant stentless valves in smaller annuli, which leaves the stented valves for larger annuli, where in turn intra-annularly implantation can be advantageous. This proceeding also led to a predominant male study population, by eliminating female patients with small annuli. Consequently, 64% of valve size 27 mm was implanted intra-annularly.

The early clinical results after implantation of the LDP were within normal limits for bioprostheses. The postoperative course of most patients was uneventful. However, the need of permanent pacemakers in six patients was slightly higher than reported for the SJM Trifecta [7]. Moreover, there were eight patients requiring temporary dialysis postoperatively. However, those patients were multi-morbid and all but one had undergone complex procedures. The 30-day mortality of 2.0% was lower than the EuroSCORE II predicted mortality (3.1 ± 3.9%), which is actually one of the best predictors for hospital mortality after aortic valve replacement [8].

At first glance, hemodynamic data of the LDP in this study were conclusive. Mean results, regarding pressure gradients, EOA and EOAI were comparable or even better than other bioprostheses, like the St. Jude Medical Trifecta, the Sorin Mitroflow, the Medtronic Mosaic or the Sorin Freedom Solo [6, 9–11]. While analyzing these data it´s to consider, that the body surface area of our study population was relatively high (but normal and typical for German inhabitants), which lowered the EOAI results. Additionally, only two cases of severe patient-prosthesis-mismatch were evident. These cases occurred in obese patients with valve size 25 mm, where obesity biased (lowered) the EOAI by causing a higher body surface area. Notably, also 8 of the 21 patients with moderate-patient-prosthesis mismatch were obese (body mass index above 30). But at second glance, hemodynamic outcome with regard to the labelled valve sizes showed conflicting results in comparison to various other available bioprostheses. For this evaluation, data of the 21 mm LDP was not considered, due to the low number of cases. Data for valve-sizes 23 mm and 25 mm were comparable to data published for the SJM Trifecta regarding pressure gradients, EOA and EOAI [7, 12]. In contrast, data for size 27 mm showed inferior results than the SJM Trifecta. The comparison to the Sorin Mitroflow, a stented pericardial bioprostheses, showed comparable pressure gradients for valve-sizes 23 mm and 25 mm, whereas LDP size 27 mm showed higher gradients [9]. The EOAI of the Sorin Mitroflow was lower for all valve sizes, but the gap to the LDP was closest for the 27 mm prosthesis. The Medtronic Mosaic, a stented porcine bioprostheses, showed higher mean pressure gradients for valve sizes 23 mm and 25 mm and comparable values for size 27 mm [10]. Upon consideration of the EOA of the Medtronic Mosaic, values were comparable for valve sizes 23 mm and 25 mm, and higher for size 27 mm [10]. The first generation porcine stentless valves (Medtronic Freestyle,

Table 3 Echocardiographic results according to labeled valve sizes

Valve size (mm)	21	23	25	27
Number	3	18	39	33
Mean Pressure Gradient in mmHg	17.3 ± 6.7	9.6 ± 3.0	8.5 ± 3.1	10.2 ± 3.6
Maximum Pressure gradient in mmHg	29.7 ± 12.1	19.3 ± 4.9	16.5 ± 5.8	19.1 ± 5.8
Effective Orifice Area in cm^2	1.92 ± 0.44	1.79 ± 0.36	2.0 ± 0.6	2.16 ± 0.47
Indexed Effective Orifice Area in cm^2/m^2	1.08 ± 0.33	0.95 ± 0.18	0.99 ± 0.29	1.01 ± 0.24

SJM Toronto) showed a clear disadvantage in terms of pressure gradients and EOA [13, 14]. On the contrary, the latest generation of pericardial stentless valves showed lower transvalvular gradients compared to our data [11]. Even so, the EOAI of these valves was only slightly above results of the LDP, but once again with the widest gap for valve size 27 mm [11]. According to the comparison with these studies, valve sizes 23 mm and 25 mm showed excellent hemodynamic properties, while a slightly impaired function of valve size 27 mm was evident. Possibly, the high percentage of intra-annularly implanted valves in this size has an impact, due to the change of the hemodynamic flow pattern caused by the stent in the aortic annulus. However, our results showed no difference between the intra-annular and the supra-annular position for valve size 27, possibly due to the low number of cases. Hence, further studies with larger cohorts and a higher number of implants per size are required. Additionally, longer follow-up is necessary to confirm these findings in mid-term and long-term follow-up.

Conclusion

The Labcor Dokimos Plus was easy to implant, offered operatively no peculiarities and patients showed a satisfactory clinical outcome. Hemodynamic results were pleasing.

Abbreviations

ECLS: Extracorporeal life support; EOA: Effective aortic valve orifice area; EOAI: Indexed effective aortic valve orifice area; LDP: Labcor Dokimos Plus

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Availability of data and material

The datasets generated during and/or analyzed during the current study are not publicly available due to reasons of data protection but are available from the corresponding author on reasonable request.

Authors' contributions

TC analyzed and interpreted the patient data and wrote the manuscript. KZ performed data acquisition and was a major contributor in writing the manuscript. WK and SH were major contributors in writing the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The Study was approved by the Ethics committee of the Charité-Universitätsmedizin Berlin (Reference number EA1/053/15). Patients consented into participation in the study.

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Initial Experience with Aortic Valve Replacement via a Minimally Invasive Approach: A Comparison of Stented, Stentless and Sutureless Valves

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Background: This study aimed to compare the short-term outcomes of MIS-AVR among 3 different types of biological heart valves.

Material/Methods: Complete data were obtained from 79 patients who underwent MIS-AVR between January 2010 and June 2015. Patients were divided into 3 groups: 27 patients (group A) received Medtronic 3f® (Medtronic Inc., Fridley, MN, USA), 36 patients (group B) received DokimosPlus® (LabCor Laboratórios Ltda., Belo Horizonte, Brazil) and 16 patients (group C) received Perceval® (Sorin Biomedica Cardio S.r.l., Saluggia VC, Italy) valves.
Operative and postoperative parameters such as duration of operation, bypass time, duration of ventilation, morbidity, and mortality were statistically analyzed using the Kruskal-Wallis test. Hemodynamic assessment with transthoracic echocardiography was performed before discharge.

Results: The EuroSCORE II ranged between 0.67 and 6.94 with no significant difference between the groups. The median operative time was 166 min (range 90–230 min) in total, with significantly shorter times in group C (120 min [range 90–200]). The median total ventilation time was significantly lower in group C and significantly higher in group A. Hemodynamic evaluation demonstrated a mean maximal velocity (v_{max}) over the aortic valve of 2.3 m/s (range 0.9–4.3 m/s) with average mean and peak pressure gradient values of 10 mmHg (range 3–24 mmHg) and 20 mmHg (range 5–42 mmHg), respectively. Group A showed the highest values for v_{max} (H>5.99).
No significant difference was found regarding duration of hospitalization. Mortality was 3%.

Conclusions: In conclusion, all 3 valves showed good perioperative results, satisfying hemodynamic performance, and low complication rates.

MeSH Keywords: Aortic Valve • Aortic Valve Insufficiency • Surgical Procedures, Minimally Invasive

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Background

Aortic valve disease is a major problem, especially in the aging population, due to degenerative processes. Severe aortic valve stenosis, which is a common form of valvular heart disease [1], usually requires surgical or interventional treatment for mechanical relief. Similarly, active infective endocarditis often needs to be treated operatively, as suggested by the current guidelines [2]. However, with increasing age and multimorbidity, a growing fraction of patients is burdened with a very high operative risk. In fact, before the establishment of transaortic valve replacement (TAVR), it had been estimated that one-third of all patients over 75 years of age with severe aortic stenosis would be rendered inoperable [3]. However, TAVR also bears complex complications and has several limitations [4].

Due to limited trauma, minimally invasive surgery of the aortic valve (MIS-AVR) reduces operative risk and possible complications [5–9], yet retains the advantage of open-heart surgery, including complete removal of the diseased valve, accurate implantation, and better longevity of the prosthesis. To further reduce operative time, the rapid deployment system (RDAVR) was introduced and proved to be suitable for MIS-AVR [10–13]. Furthermore, it may be a suitable technique for high-risk patients who are obliged to undergo surgery of the aortic valve due to conditions such as endocarditis [14].

The aim of this study was to compare the intra- and early postoperative results of patients after MIS-AVR.

Material and Methods

Study population

From January 2010 to June 2015, a total of 1133 patients underwent aortic valve replacement (AVR) at the Charité Hospital, Medical University Berlin. Out of all MIS-AVRs, a patient cohort of 79 patients was selected after applying final exclusion criteria, which were additional cardiac procedures and reoperation.

The patient cohort was subdivided into 3 groups: group A (n=27) received a stentless pericardial valve (3f®; Medtronic Inc., Fridley, MN, USA), group B (n=36) received a stented bioprosthesis (Dokimos®; LabCor Laboratories, Belo Horizonte, Brazil), and group C (n=16) received a sutureless system (Perceval valve®; Sorin Biomedica Cardio S.r.l., Saluggia VC, Italy).

Initially, patients were assessed regarding morbidities and health status. This included general data such as age, sex, body mass index, renal function, and mobility, as well as a list of pre-existing medical conditions such as arterial hypertension, chronic pulmonary disease, metabolic syndrome, malignant neoplasia, autoimmune defects, and infectious diseases.

Renal function was assessed by calculating creatinine clearance using the Cockroft-Gault formula and divided into 4 groups: unimpaired (>85 ml/h), moderately impaired (51–85 ml/h), severely impaired (<50 ml/h), and renal impairment requiring dialysis.

A risk profile was established for each patient by calculating their EuroSCORE II [15].

The patients were operated on only by qualified surgeons capable of performing all 3 MIS-AVR methods, were previously discussed in a heart team, and were fully informed of all options and procedures before giving written consent.

The choice of the bioprosthesis was left to the discretion of the operating surgeon. Pure aortic regurgitation was seen as a contraindication for sutureless prostheses (group C).

Surgical technique

Our group has published the detailed surgical techniques for MIS-AVR in 1996 [16], which has been used with minor modifications regarding venous cannulation.

In brief, all patients were operated on under general anesthesia and orotracheal intubation. After limited skin incision of approximately 7 cm, a right upper hemisternotomy ("J Sternotomy") was performed between the jugular notch and the 3rd or 4th intercostal space. Cardiopulmonary bypass was established by standard cannulation of the aorta and the right atrium. Intermittent antegrade warm blood cardioplegia was used. The ascending aorta was opened transversely 10–20 mm above the sino-tubular junction for the implantation of a stented or stentless bioprostheses, and 35 mm above the right coronary artery for the sutureless bioprosthesis. The diseased heart valve was precisely explanted, followed by debridement of the annulus as well as decalcification, which was extended up to the mitral valve if necessary.

Following precise sizing, the selection and implantation of a suitable prosthesis was performed.

Group A received the 3f® valve, which was implanted using a standard continuous 3-0 polypropylene suture and 4-0 polypropylene sutures were used for adaptation of the commissural hinge points.

Group B received the Dokimos® valve, which was implanted with 15–20 horizontal felt-armed 2-0 mattress sutures.

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Group C received the Perceval® valve. This sutureless valve was implanted by initially placing three 3-0 polypropylene guiding sutures, then cautiously lowering the valve into the annulus and expanding a balloon for 30 s at a pressure of 4 mBar, finally allowing the nitinol stent to adapt to the annulus under a continuous flow of 37°C sterile physiologic solution before removing the guiding sutures.

Intraoperative transesophageal echocardiography was performed for control of proper hemodynamic function of the prosthesis and possible air residues. High-flow CO_2 (2–4 L/min) was used to ease deairing. After sufficient reperfusion time, adequate hemostasis, and chest closure, patients were transferred to the intensive care unit. The postoperative care followed institutional guidelines, including platelet aggregation inhibition with 100 mg acetylsalicylic acid and low-molecular-weight heparin.

Intraoperative parameters were duration of the operation from first incision to chest closure, total cross-clamp time, total cardiopulmonary bypass time, and acute intraoperative complications including low cardiac output (LCO) as well as the use of intra-aortic balloon pump (IABP) or extra-corporeal membrane oxygenation (ECMO) implantation.

The postoperative clinical course was compared using the amount of transfusions needed, incidence of arrhythmias, permanent pacemaker implantation, neurological complications, hospital-acquired pneumonia (HAP), acute kidney failure or dialysis, systemic inflammatory response syndrome (SIRS), wound infections and sepsis, as well as need for reexploration, further significant complications, and death. The duration of ventilation was recorded and divided into short-time ventilation (<48 h) and longtime ventilation (>48 h). Furthermore, the duration of intensive care and total hospitalization days were assessed.

Postoperative hemodynamic performance of the prostheses was tested by transthoracic echocardiography using a GE Vivid 7 Dimension ultrasound scanner (General Electric, Fairfield, CT, USA) at discharge. General and regional heart contractility, cardiac output, morphology of the valve, regurgitation, and maximal velocity, as well as transaortic peak and mean gradient, were evaluated with standard views by experienced echocardiographers according to an internal protocol. Mean values were obtained during a span of 3 (sinus rhythm) or 5 (non-sinus rhythm) heartbeats. Transaortic valve gradients were calculated using the Bernoulli equation.

Regurgitation was ranked from grade I° (slight regurgitation) to grade III° (severe regurgitation).

Statistics

All data were retrospectively collected from hospital charts and reported as numeric percentages for categorical variables and as median with range for continuous variables. To determine significant differences among the 3 independent groups, the Kruskal-Wallis test was performed for each ordinal variable. The Kruskal-Wallis test compares datasets of 3 or more independent groups and generates a ranking of the data among the groups in ordinal numbers without units. An H value was determined to assess the significance, and if H exceeded the critical χ^2 value of 5.99 (at 2 degrees of freedom and a p value of 0.05), the difference between the datasets of the 3 groups could be accepted as significant. For H calculation and the ranking, the online software *http://vassarstats.net/kw3.html* was used [17]. Further statistical analyses were done using IBM SPSS 23 (SPSS Inc., Chicago, IL, USA) and Microsoft Excel (Microsoft Inc., Redmond, WA, USA).

Results

Median patient age was 69 years (range 35–86 years), distributed among groups A, B, and C with median 71.1, 62.3 and 70.6 years (range 54–86, 35–80 and 58–83 years), respectively; 40% (n=32) were female and 60% (n=47) were male. Group C had the highest fraction of female patients, with 81% (n=13); and group B had significantly more male patients (75%). Median BMI was 27.6 (range 18.7–51.6) and was evenly distributed among all groups. Twelve patients had been diagnosed with cancer; most cases were in Group C (n=7, 41%), 1 patient in group B presented with advanced terminal prostate cancer and infective endocarditis subsequent to port infection. One patient from group A suffered from neurological immobility due to myotonic disease. A summary of general preoperative status can be seen in Table 1.

The operative risk was assessed with the EuroSCORE II, which ranged between 0.67 and 6.94. The Kruskal-Wallis test showed no overall difference of EuroSCORE II among the 3 groups (H >5.99).

In group A, 2 patients suffered from insulin-dependent diabetes mellitus, and pulmonary hypertension was present in 15 patients (19%).

Renal function was unimpaired in 41 patients and severely impaired in 10 patients (13%). Additionally, 2 patients required long-term dialysis beforehand.

Eleven patients suffered from chronic obstructive pulmonary disease with steroid treatment, with the fewest patients in group B (3%). Of all patients, 10% were admitted with

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Table 1. General preoperative findings of the study cohort.

Parameter*	Group A n=27		Group B n=36		Group C n=16	
Nicotine abuse	9	(33%)	6	(17%)	6	(37%)
Ethanol abuse	6	(22%)	4	(11%)	1	(6%)
Arterial hypertension	22	(81%)	23	(64%)	13	(81%)
Hyperlipoproteinaemia	13	(48%)	7	(19%)	8	(50%)
Malignant neoplasia	1	(4%)	4	(11%)	7	(44%)
Automimmune defects	2	(7%)	3	(8%)	2	(13%)
Metabolic defects	5	(19%)	7	(19%)	4	(25%)
Anaemia	8	(30%)	9	(28%)	5	(31%)
Infectious diseases	2	(7%)	5	(13%)	3	(19%)
Extracardial operations	12	(44%)	15	(42%)	12	(75%)

* Total number of patients for each individual parameter is expressed as a percentage of the subtotal of each group in parenthesis.

extracardiac arteriopathy, including a history of peripheral artery disease, amputations, and vessel interventions.

Median NYHA class of all patients was II and ranged from I to IV with no significant difference between the 3 groups. One patient from group B presented with low cardiac output prior to the procedure. Further risk factors according to EuroSCORE II are shown in Table 2.

Pre-existing additional cardiologic conditions were found in 60% of all patients, most commonly slight mitral insufficiency (35%), followed by arrhythmias (20%) and coronary artery disease (CAD) (18%), in which stenoses were either irrelevant or had been treated earlier (n=11).

Aortic valve stenosis and mixed disease (26%) were the leading reasons for aortic valve dysfunction, distributed evenly among all 3 groups. Pure aortic valve regurgitation was found in 8% of patients, distributed in groups A and B only, as it poses a contraindication for the sutureless system.

Two patients were in a critical preoperative condition; causes were low cardiac output in one and acute renal and hepatic failure in the other. All operations were elective, except for 6 (8%) urgent patients with active endocarditis; 4 of them were in group B and 2 in group C. Table 3 shows the distribution of cardiac preconditions in detail.

The median operative time was 166 min (range 90–230 min) distributed among groups A, B, and C, with median times of 170 min (range 140–230 min), 175 min (range 120–215), and 120 min (range 90–200), respectively. The total cross-clamp time was lowest in group C (30.3 min, range 20–53 min), followed by groups A and B (68 min [range 48–109 min] and 70.5 min [range 31–107 min]), respectively. The Kruskal-Wallis test confirmed significant differences among the 3 groups regarding total operative time, bypass time, and cross-clamp time. Group C ranked lowest in all 3 parameters. No conversion to full sternotomy was necessary.

Two patients suffered from low cardiac output (1 patient from group A and 1 from group B). The patient in group A received an IABP as circulatory support, which could be weaned and removed in the subsequent clinical course.

Two patients were ventilated for >48 h due to postoperative complications (220 h and 346 h; both from group A). Apart from the 2 long-term ventilated patients, median total ventilation time was 4.75 h (range 1–37 h), distributed in groups A, B, and C, with median times of 6, 3, and 3 h, respectively. Kruskal-Wallis analysis revealed a significant difference among the 3 groups, with group C ranking lowest (lowest ventilation time) and group A ranking highest (longest ventilation time).

Detailed information regarding intraoperative results is shown in Table 4.

Overall, patients spent a mean of 1 day (range 0–9 days) in the intensive care unit and were discharged from the hospital after a mean of 9 days (range 3–38 days). Patients from group A spent the most time in intensive care and until discharge (median 2 days [range 1–23] and 9 days [range 4–17 days], respectively). Kruskal-Wallis test results confirmed a difference in length of intensive care treatment: group C ranked lowest

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Table 2. Risk factors according to EuroSCORE II.

Parameters*	Group A (3F)	Group B (Dokimos)	Group C (Perceval)	Total
Number of patients	27	36	16	79
Age (years)**	71, 54–86	64, 35–80	73, 58–83	71, 35–86
Female	10 (37%)	9 (25%)	13 (81%)	32 (40%)
Renal Impairment: Creatinine clearance (ml/h)				
Moderately impaired (50–85 ml/h)	15 (56%)	4 (11%)	7 (44%)	26 (33%)
Severely impaired (<50 ml/h)	4 (15%)	3 (8%)	3 (19%)	10 (13%)
Dialysis	1 (4%)	1 (3%)	0	2 (3%)
Previous cardiac surgery	0	0	0	0
Chronic lung disease	4 (15%)	2 (6%)	5 (31%)	11 (14%)
Active endocarditis	0	4 (11%)	2 (13%)	6 (8%)
Critical pre-OP	1 (4%)	1 (3%)	0	2 (3%)
Diabetes on Insulin	2 (7%)	0	0	2 (3%)
Pulmonary hypertension	6 (22%)	5 (14%)	4 (25%)	15 (19%)
Urgency				
Elective	27 (100%)	32 (89%)	14 (88%)	73 (91%)
Urgent	0	4 (11%)	2 (13%)	6 (9%)
NYHA class	2; 1–4	3; 1–3	2; 1–3	3; 1–4
LVEF (%)				
Moderate (31–50%)	1 (4%)	6 (17%)	0	7 (9%)
Poor (21–30%)	0	1 (2%)	0	1 (1%)
Very poor (<20%)	0	0	0	0

* Total number of patients for each individual parameter is expressed as a percentage of the subtotal of each group in parenthesis;
** expressed in median and range. NYHA – New-York Heart Association; LVEF – left ventricular ejection fraction.

and group A ranked highest (H >5.99). No significant difference regarding overall hospitalization was found (H <5.99).

Major postoperative adverse effects were defined as mortality, surgical reexploration, and permanent neurological deficits. Hospital mortality was 3% (n=2); both patients were from group A, and died due to septic multi-organ failure on the 8th and 23rd postoperative day, respectively. Reexploration due to bleeding was necessary in 2 patients (3%); 1 patient from group A and 1 from group C. Moreover, 17 patients (21%) were delirious in the early postoperative phase, 11 of which had admitted a history of chronic alcohol abuse; however, no strokes or permanent neurological deficits were observed.

Other postoperative complications included new-onset arrhythmias, hospital-acquired pneumonia, and need for dialysis. New-onset atrial fibrillation occurred in 21% (n=17), which were converted pharmaceutically or electrically in 12 patients. In 5 patients (6%), a permanent pacemaker was implanted due to new-onset persisting non-sinus rhythm. Of those, 3 patients were in group A and 2 in group B.

Hospital-acquired pneumonia (HAP) occurred in 6 patients (8%): 4 patients in group A and 2 in group B. Four patients (5%) had renal dialysis postoperatively, 2 of which had been on dialysis preoperatively and 1 had a transplant failure. Overall, 4 patients (5%) developed sepsis due to HAP, prosthetic endocarditis, urinary tract infection, and in 1 patient with unclear focus. Two patients died in progress of septic multi-organ failure (group A). No patient had to be readmitted after discharge for related causes such as recurrent endocarditis and thromboembolic complications. Details are shown in Table 5. Valve sizing did not differ significantly among the groups (H <5.99).

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Table 3. Preoperative cardiac diagnoses.

Parameter *	Group A	Group B	Group C
Aortic valve	27 (100%)	36 (100%)	16 (100%)
Regurgitation		4 (11%)	0
Stenosis		21 (58%)	14 (88%)
Mixed		11 (31%)	2 (12%)
Mitral valve disease	11 (31%)	8 (22%)	9 (56%)
Regurgitation	11 (31%)	8 (22%)	6 (38%)
Stenosis	0	0	3 (18%)
Tricuspid disease	6 (22%)	7 (19%)	2 (3%)
Regurgitation	6 (22%)	6 (17%)	2 (3%)
Prior interventions	7 (26%)	3 (8%)	1 (6%)
Arrhythmias	7 (26%)	5 (15%)	4 (25%)
Recent mi	1 (4%)	0	0
Coronary artery disease	6 (22%)	3 (8%)	6 (37%)
1 Vessel disease	3 (11%)	2 (6%)	4 (25%)
2 Vessel disease	3 (11%)	1 (3%)	2 (13%)
3 Vessel disease	0	0	0

* Total number of patients for each individual parameter is expressed as a percentage of the subtotal of each group in parenthesis.

Table 4. Intraoperative results.

Parameters	Group A	Group B	Group C
Duration (h)*	02: 50 (2: 20–3: 50)	02: 55 (2: 00–3: 35)	2: 00 (01: 30–03: 20)
Bypass time (min)*	90.0 (61–139)	94.0 (45–130)	48.0 (36–87)
Ischaemiea (min)*	68.0 (48–109)	70.5 (69–107)	30.3 (20–53)
LCO**	1 (3.7%)	1 (2.7%)	0
IABP**	1 (3.7%)	0	0
Operative mortality	0	0	0

* Expressed as median and range, range is given in parentheses; ** number of patients and percentage. LCO – low cardiac output; IABP – intra-aortic balloon pump, total number of patients is expressed as a percentage of the subtotal of each group in parenthesis.

Furthermore, the median amount of erythrocyte concentrate, thrombocyte concentrate, and fresh frozen plasma needed showed no significant difference (H <5.99).

Median total postoperative left ventricular function was 60% (range 25–75%) in all groups.

Mean maximal velocity (v_{max}) over the aortic valve was 2.3 m/s (range 0.9–4.3 m/s) with average mean and peak pressure gradient values of 10 mmHg (range 3-24 mmHg) and 20 mmHg (range 5–42 mmHg), respectively. Group A showed the highest values for v_{max}, with median values of 2.6 m/s (range 1.8–4.3 m/s) The Kruskal-Wallis test confirmed these findings, with group A ranking highest and group B ranking lowest (H >5.99). More details are shown in Table 6.

Overall, 3 patients (4%) had slight regurgitation (<I°–I°), all from group A, with no need for further intervention. In all groups, no paravalvular leakage was observed.

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Table 5. Postoperative course, complications, mortality and morbidity.

Parameters*	Group A (n=27)	Group B (n=36)	Group C (n=16)
Transfusions: units of red blood cells**	1 (0–10)	0 (0–4)	2 (0–5)
Transfusions: units of platelets**	0 (0–3)	0 (0–16)	0 (0–4)
Transfusions: units of fresh frozen plasma**	0 (0–8)	0 (0–8)	0 (0–2)
Reintubation	3 (11%)	0	1 (6%)
Tracheostomy	1 (4%)	0	0
Bleeding requiring reexploration	1 (4%)	0	1 (6%)
Delirium	8 (29.6%)	6 (16.7%)	3 (18.8%)
Pneumothorax	2 (7%)	1 (3%)	0
Stroke	0	0	0
HAP	4 (15%)	0	2 (13%)
Pleural effusion	3 (11%)	2 (6%)	0
Acute kidney failure	1 (4%)	3 (8%)	0
Dialysis	2 (7%)	2 (6%)	0
Pericardial effusion	2 (7%)	0	2 (13%)
SIRS	6 (22%)	20 (56%)	6 (38%)
Sepsis	3 (11%)	0	1 (6%)
New-onset arrhythmias	6 (22%)	2 (6%)	7 (44%)
Total duration of hospitalization (days)*	9 (4–17)	7,5 (1–38)	11 (5–31)
Duration Intensive Care Unit (days)**	2 (0–23)	1 (1–7)	1 (1–9)
Mortality	2 (7%)	0	0

* Total number of patients for each individual parameter is expressed as a percentage of the subtotal of each group in parenthesis; ** expressed as median and range, range is given in parentheses. HAP – health-care acquired pneumonia; SIRS – Systemic Inflammatory Response Syndrome.

Table 6. Echocardiographic findings in the three study groups before discharge.

Parameters	Group A (n=27)	Group B (n= 36)	Group C (n=16)
Size of prosthesis (mm)*	25 21–27	25 21–27	25 21–27
Ejection fraction (%)*	60 (40–65)	55 (25–75)	60 (45–73)
Peak gradient over aortic valve (mmHg)*	29 (10–42)	17 (5–41)	17 (11–29)
Mean gradient over aortic valve (mmHg)*	16 (6–24)	8 (3–23)	9 (4–18)
Valvular insufficiency** ≤I°	2 (13%)	0	0

* Total number of patients for each individual parameter is expressed as a percentage of the subtotal of each group in parenthesis; ** expressed as median and range, range is given in parentheses.

Discussion

Severe aortic valve stenosis with hemodynamic relevance is a diagnosis that requires timely surgical or interventional action for mechanical relief as treatment, and it has been shown that patients had almost normal life expectancy after surgical treatment [1]. For patients with a low-to-moderate risk profile, surgical AVR remains the criterion standard.

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However, Yan et al. reported that almost 25% of all patients with severe aortic stenosis were deemed inoperable because of a high operative risk due to morbidity and age [3]. Recently, transcatheter aortic valve replacement (TAVR) has been introduced as an alternative for conventional operation, and proves to be a good technique in patients rendered inoperable or with extremely high risk. However, drastic complications may arise from TAVR implantation, such as strokes, aortic dissection, severe regurgitation, endocarditis, and major ventricular tachyarrhythmia [18]. In fact, Mohr et al. reported that 1–2% of complications needed immediate surgical correction, with a mortality of 50% during surgery [18].

The risk of misplacement can be vastly reduced by open-heart surgery, and the minimally invasive approach adds the benefits of limited surgical trauma to the ability to remove the diseased valve and adjust the prosthesis position visually for optimal placement. Thus, minimally invasive surgery reduces the risk for low- and intermediate-risk patients compared to conventional surgery [11], and improves survival [8,19].

However, due to the circumstances of reduced operative field and the increased technical demands, MIS-AVR is often associated with longer operative and cross-clamp times [8], as well as associated postoperative complications that may arise. However, there are also studies that contradict this finding, presenting results showing that MIS-AVR has a shorter operative time [20,21]. However, sutureless valves reduce the time and complications of MIS-AVR, and are thus a good option for MIS-AVR implants [12,13,21,22].

This study compared 3 different bioprostheses from a total study cohort of 79 patients after MIS-AVR, and assessed the overall hemodynamic function, operative duration, and early postoperative complications.

Preoperative data showed that the general health status was divided relatively homogenously among the 3 groups. Regarding previous diagnoses, group C presented with multiple cancer patients (44%). Therefore, these patients were subjected to sutureless MIS-AVR in order to reduce operating and ventilation time and thus reduce the postoperative risk profile of these morbid patients. Conventional AVR would have been contraindicated due to the high-risk profile as well as length and quality of the remaining life.

Furthermore, group B included a palliative cancer patient with multiple metastases and active endocarditis following a septic port inflammation. The operation was uneventful, with duration of 205 min. The patient was discharged on the 7th postoperative day, with 1 day spent in intensive care and no postoperative incidents or complications. These excellent results demonstrate that even high-risk patients, who cannot be treated appropriately with conventional antibiotic therapy, could benefit from MIS-AVR regarding length and quality of the remaining life.

Regarding cardiovascular risk stratification, EuroSCORE II showed no significant differences in preoperative risk. However, groups A and C had fewer extremely high-risk patients than group B. As opposed to groups A and B, group C had no patients with pure aortic regurgitation, as this is a contraindication for sutureless implants.

However, patients were not matched. This leads to a certain risk of bias, especially because sex imbalance between the groups may shift the risk for early postoperative outcome [23]. Overall, good perioperative and early postoperative results were obtained in all 3 patient groups.

Compared with conventional AVR, the cross-clamp times proved to be slightly shorter in this MIS-AVR approach (73.5±19.3 min in AVR *vs.* 70.3±17.4 min in MIS-AVR) [8].

The Perceval valve with the sutureless deployment system significantly reduced operative, bypass, cross-clamping, and ventilation times compared to groups A and B. This is important because reduced operative and ventilation times can decrease the risk of hospital-acquired infections (HAI) and associated morbidity.

Postoperatively, the group C presented with the fewest complications, with the exception of temporary arrhythmias, which occurred in 44% of the total patient cohort. However, of those patients, all arrhythmias were temporary and could be resolved pharmaceutically without permanent pacemaker implantation. This is notable, as ballooning of the valve does not lead to more permanent arrhythmias as reported before, supporting findings of other groups [21].

Compared to results of Fischlein et al. [14], it can be seen that the hemodynamic performance of the Perceval valve was similar, with a median mean pressure gradient over the aortic valve of 9 mmHg (range 4–18 mmHg). Furthermore, the hemodynamic function of the Dokimos valve is flawless compared to the other 2 groups, with the lowest v_{max} over the aortic valve.

Patients in group C seemingly had the most complications. Both ventilation time and mortality showed comparably poor results at first glance, even though the preoperative EuroSCORE II showed no significant differences against the other groups. However, the 2 longtime ventilated patients were in fact the patients who died on the 8th and 23rd postoperative days due to multiple organ failure and were multimorbid elderly women aged 80 and 83 years, both having noninsulin-dependent diabetes mellitus (NIDDM), arterial hypertension,

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coronary 1 vessel disease, impaired kidney function, and a high EuroSCORE II. Both developed septic organ failure after a urinary tract infection in one patient and unclear focus in the other. Not taking these 2 patients into account, the 3f cohort showed a similar uneventful clinical course as the other 2 groups. Hemodynamically, the 3f presented with higher peak and mean gradients over the aortic valve compared to the other groups, yet values remained in acceptable limits, a finding that has been shown earlier by our group [21].

Compared to the findings of our group using the 3f in conventional AVR, the cross-clamp time was notably longer in the MIS-AVR approach than in standard AVR (70.6 ± 14.4 min compared to 51.6±8.2 min, respectively) [24]. The 3f valve is a freehand-sewn stentless valve, and longer duration of the operation can be explained by the tedious and complex implantation. On the other hand, this ensures optimal and safe positioning, and the 10-year follow-up of Christ et al. showed a very low rate of reoperation, proving the 3f valve to be a sustainable implant [25–28].

Study limitations

The limitations of the study are the small sample size (n=79), the uneven size of the subdivided groups, and the inhomogeneity of sex distribution. This article presents our initial experience with minimally invasive aortic valve replacement using bioprostheses with specific stentless or sutureless designs. The patients from different groups had not been matched; as an example, pure aortic valve regurgitation was not present in group C, as this is a contraindication for sutureless systems. However, according to EuroSCORE II, patients had a similar risk profiles.

Furthermore, this study only analyzed the short-term perioperative results and was conducted at a single hospital, in which a sutureless valve program had just been established.

Conclusions

In conclusion, MIS-AVR can be safely performed with all types of bioprostheses. Good performance concerning intra- and perioperative results, hemodynamic performance, and low complication rates were achieved. Overall, our findings show the benefit of reduced operating time and associated reduced postoperative complications and morbidity for low- to medium-risk patients with severe aortic stenosis and regurgitation. Furthermore, individual results of high-risk and terminally ill patients may open new doors for treatment with advanced sutureless and stented valves. There is a clear trend towards the feasibility and intraoperative risk reduction of sutureless implants, but this needs to be verified in larger randomized multi-center studies.

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None of the authors have any financial and personal relationships with other people or organizations that could potentially and inappropriately influence (bias) their work and conclusions.

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Original Article

Hemodynamics of Pericardial Aortic Valves: Contemporary Stented versus Stentless Valves in a Matched Comparison

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Purpose: Hemodynamic performance of aortic valve bioprostheses is essential for reliable function and durability. So far, the supra-annularly implanted stentless Sorin Freedom Solo (SFS) demonstrated unsurpassed hemodynamic properties. As contemporary stented and externally mounted pericardial bioprostheses, like the Labcor Dokimos Plus (LDP), also improve hemodynamic performance, these types of valves were compared in this study.
Methods: A total of 218 patients, who underwent aortic valve replacement with the LDP or the SFS, were matched retrospectively 1:1 on variables affecting hemodynamic measurements: implanted valve size, age, sex, and body surface area (BSA). With matching tolerance for valve size and gender of 0%, for age and BSA of 5%, 57 patient-pairs were yielded. Operative data, clinical, and hemodynamic outcome were analyzed.
Results: Except for slightly higher left ventricular function and lower procedural times in the SFS group, preoperative, operative, and postoperative characteristics of patient-pairs did not differ significantly. Mean pressure gradients, effective orifice areas (EOAs), and indexed EOAs were comparable. Corresponding to valve sizes of 21, 23, 25, and 27 mm, the indexed EOAs of the LDP and SFS prostheses were 1.08 ± 0.33, 0.92 ± 0.19, 0.93 ± 0.24, 0.99 ± 0.13 cm^2/m^2 and 0.81 ± 0.13, 0.92 ± 0.28, 0.95 ± 0.20, 1.04 ± 0.27 cm^2/m^2, respectively.
Conclusion: Contemporary stented and stentless pericardial bioprostheses showed excellent hemodynamic properties without significant differences in EOAs and indexed EOAs.

Keywords: biological prosthesis, valve replacement, echocardiography, hemodynamics

Introduction

The hemodynamic performance of aortic valve prostheses has a relation to patients' outcome with inferior survival in patients with a patient-prosthesis-mismatch.[1] Previously, stentless aortic bioprostheses showed excellent hemodynamic properties, especially the third-generation supra-annularly implantable Sorin Freedom Solo (SFS) valve.[2,3] However, conventional stented bioprostheses have been constantly improved and the latest generation of these valves also impressed with their hemodynamic profile.[4–6] The Labcor Dokimos Plus (LDP) valve is one of these stented pericardial bioprosthesis with a low profile stent and externally mounted leaflets for the supra-annular position.[7] **Table 1** shows the geometric dimensions of both prostheses. Technically, both types of valves (SFS or LDP) could be implanted in the same patient. The aim of this study was to compare the hemodynamic performance of contemporary stented and stentless bovine pericardial prostheses based on a retrospectively matched comparison of the LDP and the SFS valve.

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Table 1 Geometric dimensions of the Labcor Dokimos Plus and the Sorin Freedom Solo

Labcor Dokimos Plus[1]					
Labeled valve size	19	21	23	25	27
Sewing ring diameter (mm)	23	25	27	29	31
Orifice diameter (mm)	16	18	20	22	24
Sorin Freedom Solo[2]					
Labeled valve size	19	21	23	25	27
Sewing ring diameter (mm)	21	23	25	27	29
Orifice diameter (mm)	19	21	23	25	27

[1]Data according to Labcor Laboratories, Nova Granada, Brazil. [2]Data according to LivaNova PLC, London, United Kingdom

Methods

Patients

The local Ethics Committee approved the study and waived patients' individual consent. All patients who underwent aortic valve replacement from 2009 until 2015 with the stented LDP or the stentless SFS were evaluated regarding availability of a comprehensive echocardiographic examination at discharge. Thus, 93 patients with LDP prostheses and 125 patients with SFS prostheses were identified. Retrospective matching was done 1:1 on variables known to affect hemodynamic measurements: size of implanted valve, age, sex, and body surface area (BSA).[1)] LDP and SFS are equally oversized in comparison to the aortic annulus. The size of the measured annulus matches the labeled valve size for implantation in both valves. Therefore, sizing was done by ball sizers to assure accurate matching and avoid bias of differences in the actual size of the by the manufacturers provided sizers. Matching tolerance for valve size and gender was 0%, whereas for age and BSA it was 5%. Thereby, 57 matched patient-pairs were yielded. In all cases, bioprostheses were implanted after explicit patient education and informed consent according to the actual guidelines.[8)]

Operation

All procedures were performed using partial (isolated procedures) or complete (complex procedures) sternotomy, cardiopulmonary bypass, cardioplegic arrest (blood cardioplegia), excision of the diseased aortic valve including thorough decalcification, and sizing of the annulus using ball sizers. The LDP valve was implanted with 12–15 horizontal Teflon felt-armed mattress sutures. The SFS was implanted supra-annularly using three running polypropylene sutures according to the technique of Beholz to prevent a protruding flange.[9)] The procedures were performed by six surgeons and operative setting did not change in the study period. The choice of the bioprosthesis was left to the discretion of the surgeon.

Clinical follow-up

Pre-, intra-, and early postoperative data were prospectively collected. Hemodynamic performance was evaluated using transthoracic echocardiography, using a GE Vivid 7 Dimension (General Electric, Fairfield, CT, USA), at discharge. Standard two-dimensional and Doppler transthoracic echocardiography was performed. Mean values for each measurement were derived from three beats in sinus rhythm, and five beats in those in non-sinus rhythm. Trans-aortic flow velocities were assessed by continuous-wave Doppler, whereas flow velocities in the left ventricular outflow tract were assessed by pulsed-wave Doppler. Pressure gradients were calculated using the Bernoulli equation. The effective orifice area (EOA) was calculated with the continuity equation and indexed by the BSA of the patient indexed effective orifice area (EOAI).

Statistics

All data were analyzed with SPSS Statistics version 22 (IBM Corporation, Armonk, NY, USA). Descriptive statistics are reported as mean ± standard deviation for continuous variables and as absolute frequencies and percentages for categorical variables. For comparison of baseline and operative characteristics independent-samples Student's t-tests and Fisher's exact tests were used, respectively. For comparison of hemodynamic outcome and clinical outcome, paired-samples Student's t-tests and Fisher's exact tests were used, respectively. Due to the limited number of cases, no equal variances were assumed. All p values were two-sided. Statistical significance was set at a p value of less than 0.05.

Table 2 Baseline characteristics and risk stratification

Characteristic	LDP group	SFS group	p value
Number of patients (n)	57	57	1
• Age in years ± standard deviation	70.9 ± 7.2	71.1	0.64
Gender			1
• Male (n)	43	43	
• Female (n)	14	14	
Body surface area ± standard deviation (m^2)	1.99 ± 0.23	1.97 ± 0.23	0.11
Left ventricular ejection fraction	53.6	56.9	**<0.01**
• Left ventricular ejection fraction <40%	1	0	0.32
Predominant cardiac rhythm			0.28
• Sinus rhythm (n)	40	46	
• Atrial fibrillation (n)	17	11	
Concomitant disease			
• Coronary artery disease (n)	26	35	0.13
• Arterial hypertension (n)	48	52	0.39
• Pulmonary hypertension (n)	6	1	0.13
• Renal dysfunction (n)	20	12	0.14
• Peripheral arterial disease	8	8	1
• Diabetes mellitus (n)	11	17	0.28
• Chronic lung disease (n)	5	6	1

LDP: Labcor Dokimos Plus; SFS: Sorin Freedom Solo

Results

Matching resulted in two almost equal groups regarding baseline characteristics (**Table 2**). There was only a dissimilarity of 3.3% in mean left ventricular ejection fraction. This is clinically not relevant. Additionally, there was no significant difference between the groups regarding the presence of severely impaired left ventricular function. Operative characteristics revealed a distinct advantage in procedural times in the SFS group, whereas other procedural features were not significantly different (**Table 3**). Clinical outcome was uneventful and similar in both groups (**Table 4**).

Echocardiography showed no significant differences between the LDP and the SFS with respect to pressure gradients, EOA, and indexed EOA. In none of the patients, relevant aortic regurgitation occurred. Detailed results, corresponding to valve sizes 21, 23, 25, and 27 mm, are presented in **Table 5**. Except for a higher maximum pressure gradient of the 27 mm LDP valve, all parameters were comparable. Only three matched cases with valve size less than 23 mm were analyzed in the comparison.

Discussion

There is still a controversial debate about the use of stentless aortic valve prostheses. Although they demonstrate excellent hemodynamic performance, their implantation is more demanding implantation procedure and the long-term durability remains limited.[10,11] In contrast, conventional stented valves, exhibiting a proven durability, are simple to implant, while their hemodynamic performance is limited by the stent, which narrows the orifice area. The last generation of stentless and stented pericardial aortic bioprostheses is characterized by supra-annular implantation. The supra-annular position together with thinner stent design of newer stented bioprostheses preserves or even enlarges the orifice area. Additionally, externally mounted leaflets further increase the orifice area. However, both types of prostheses are constructed from fixed pericardium, which is not as pliable as the leaflets of the native aortic valve and consequently impairs transvalvular blood flow.

The results of this study are interesting regarding several aspects. The disadvantage of a demanding implantation procedure of the first generation of stentless valves, which resulted in prolonged procedural times,[10,11] disappeared due to the simplified single suture line implantation technique of the SFS[9] leading to shorter procedural times. In contrast, the LDP valves were associated with prolonged implantation time in our series. However, these differences did not affect the clinical outcome of the patients, which was uneventful in both groups. A repeatedly reported complication after implantation of the SFS is thrombocytopenia.[12,13] In our matched study

Table 3 Operative characteristics

Characteristic	LDP group	SFS group	p value
Procedure			
Isolated aortic valve replacement (n)	37	30	0.25
Combined procedures (n)	20	27	
• Coronary artery bypass grafting (n)	14	22	
• Mitral valve replacement (n)	2	0	
• Left atrial ablation (n)	2	5	
• Ascending aorta replacement (n)	2	0	
• Tricuspid valve reconstruction (n)	1	0	
Implanted valve sizes			
• 21 mm (n)	3	3	1
• 23 mm (n)	13	13	1
• 25 mm (n)	24	24	1
• 27 mm (n)	17	17	1
Duration of procedure (min)	210.6 ± 51.9	170.3 ± 47.3	**<0.01**
• Isolated procedures (min)	193.7 ± 37.4	148.4 ± 36.3	**<0.01**
• Combined procedures (min)	241.8 ± 60.9	194.6 ± 46.7	**0.01**
Aortic cross clamp time (min)	83.4 ± 51.9	68.9 ± 21.8	**<0.01**
• Isolated procedures (min)	78.2 ± 20.1	61.6 ± 21.0	**<0.01**
• Combined procedures (min)	93.2 ± 30.6	77.0 ± 20.0	**<0.05**

LDP: Labcor Dokimos Plus; SFS: Sorin Freedom Solo

Table 4 Clinical outcome

Characteristic	LDP group	SFS group	p value
Hospital mortality (n)	0	0	1
Redo valve replacement (n)	0	0	1
Myocardial infarction (n)	0	0	1
Stroke (n)	0	0	1
Relevant bleeding (n)	2	3	0.68
Thrombocytopenia (<100/nL) at discharge (n)	3	11	**0.04**

LDP: Labcor Dokimos Plus; SFS: Sorin Freedom Solo

cohort, it occurred in 11 patients of the SFS group and three patients of the LDP group. However, it was not accompanied with bleeding complications or thromboembolic events in both groups.

The main focus of the study was the hemodynamic performance of the different valves. Several publications about older generations of stented and stentless valves demonstrated a hemodynamic advantage of stentless bioprostheses, which was also confirmed in a meta-analysis.[14–16] Until now, there is no data available regarding contemporary stented, externally mounted pericardial bioprostheses, and third-generation stentless valves. Previously, the stented bioprosthesis LDP showed excellent hemodynamic results, which are comparable to other contemporary stented pericardial valves like the Edwards Perimount Magna (Edwards Lifesciences, Irvine, CA, USA) and the St. Jude Trifecta (Medtronic Inc., Minneapolis, MN, USA).[4–6] Similarly, the stentless SFS showed excellent hemodynamic properties.[2,3] Furthermore, a significant advantage in hemodynamics of the SFS compared to Edwards Perimount stented bioprostheses (Edwards Lifesciences) could be shown.[17] Considering the geometric dimensions of the LDP and the SFS (**Table 1**), with a higher orifice diameter of the SFS in the same labeled valve size (3 mm), one would expect a distinct advantage of the stentless valve in our study results. However, results of our matched analysis showed no significant difference in EOA or EOAI. Considering that the EOA is the EOA of the blood flow and not the geometric orifice area of the valve, apparently the stent of the LDP seems not to obstruct the effective blood flow. Consequently, no difference between stentless and stented valves could be found in our data. Due to the study population containing only three matched pairs of patients with valve size 21 mm, this finding is based on the comparison of larger valve sizes (≥23 mm). Comprehensibly,

Table 5 Echocardiographic outcome

Valve size in mm	21		23		25		27	
Type of valve	LDP	SFS	LDP	SFS	LDP	SFS	LDP	SFS
Number of patients	3	3	13	13	24	24	17	17
Mean PG in mmHg	17.3 ± 6.7	9.6 ± 5.4	9.6 ± 2.4	13.4 ± 8.4	8.1 ± 3.0	9.1 ± 4.1	9.0 ± 7.8	7.8 ± 3.2
Paired T-test	p = 0.39		p = 0.15		p = 0.27		p = 0.29	
Maximum PG in mmHg	29.7 ± 12.1	18.7 ± 9.7	19.7 ± 4.6	23.7 ± 14.9	15.4 ± 4.5	16.5 ± 6.8	17.8 ± 6.6	13.9 ± 5.9
Paired T-test	p = 0.48		p = 0.38		p = 0.41		**p = 0.04**	
EOA in cm^2	1.92 ± 0.44	1.41. ± 0.29	1.70 ± 0.36	1.67 ± 0.44	1.87 ± 0.47	1.87 ± 0.37	2.04 ± 0.27	2.15 ± 0.56
Paired T-test	0.23		0.87		0.99		0.55	
Indexed EOA in cm^2/m^2	1.08 ± 0.33	0.81 ± 0.13	0.92 ± 0.19	0.92 ± 0.28	0.93 ± 0.24	0.95 ± 0.20	0.99 ± 0.13	1.04 ± 0.27
Paired T-test	p = 0.29		p = 0.94		p = 0.77		p = 0.53	

PG: pressure gradient; EOA: effective orifice area; LDP: Labcor Dokimos Plus; SFS: Sorin Freedom Solo

in larger aortic annuli, the stent and sewing ring fit better in to the supra-annular aortic sinus. In smaller annuli, this could be different because the dimension of the stent is identical in all valve sizes. Thus, the proportion of the geometric orifice area which is reduced by the stent gets larger in smaller aortic roots. Therefore, results might differ in smaller valves sizes. Whether this mathematical assumption is clinical relevant or not has to be proved in further studies involving smaller valves.

Conclusion

The stented LDP and the stentless SFS showed comparable hemodynamic performance. In line with other publications, hemodynamic properties of contemporary stented pericardial bioprostheses, in particular in larger valve sizes, are not inferior to those of contemporary stentless pericardial bioprostheses. However, further studies are necessary to confirm the hemodynamic outcome in long-term follow-up and to evaluate the outcome in smaller valve sizes.

Disclosure Statement

The authors declare no conflict of interest.

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Eidesstattliche Versicherung

„Ich, Konstantin Zhigalov, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: „Postoperative Ergebnisse bei Patienten nach Aortenklappenersatz unter Verwendung der Labcor Dokimos Plus Prothese“ selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

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Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§156,161 des Strafgesetzbuches) sind mir bekannt und bewusst.“

Datum _____

Unterschrift

Anteilserklärung an den erfolgten Publikationen

Konstantin Zhigalov hatte folgenden Anteil an den folgenden Publikationen:

Publikation 1: Christ T*, Zhigalov K*, Konertz W, Holinski S. *Clinical outcome and hemodynamic behavior of the Labcor Dokimos Plus aortic valve*. J Cardiothorac Surg. 2016 Nov 29;11(1):160. (* - geteilte Erstautorschaft)
Beitrag im Einzelnen: Fragestellung, Studiendesign, Datenerhebung, statistische Auswertung, Dateninterpretation, Literaturrecherche, Manuskriptvorbereitung.

Publikation 2: Konertz J, Zhigalov K, Weymann A, Dohmen PM. *Initial Experience with Aortic Valve Replacement via a Minimally Invasive Approach: A Comparison of Stented, Stentless and Sutureless Valves.* Med Sci Monit. 2017 Apr 5;23:1645-1654.
Beitrag im Einzelnen: Studiendesign, Datenerhebung, Dateninterpretation.

Publikation 3: Christ T, Holinski S, Zhigalov K, Zielinski CB, Grubitzsch H. *Hemodynamics of Pericardial Aortic Valves: Contemporary Stented versus Stentless Valves in a Matched Comparison.* Ann Thorac Cardiovasc Surg. 2017 Sep 8. doi: 10.5761/atcs.oa.17-00061.
Beitrag im Einzelnen: Datenerhebung.

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