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Kumulative Habilitationsschrift
zur Erlangung der Venia legendi
für das Fach Herzchirurgie

Chirurgie der Atrioventrikularklappen im Kindesalter

Vorgelegt von
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Inhaltsverzeichnis

Einleitung

Chirurgische Eingriffe im Bereich der Atrioventrikularklappen (AV-Klappen) im Kindesalter gehören mit zu den komplexesten Prozeduren in der Kinderherzchirurgie. Vitien dieser Klappen stellen aufgrund der multifaktoriell bedingten, hochkomplexen Morphologie und Heterogenität eine besondere Herausforderung für die chirurgischen Rekonstruktionsmöglichkeiten in der Kinderherzchirurgie dar. Pathologische Veränderungen der AV-Klappen bei neonatologischen und pädiatrischen Patienten liegen häufig in Kombination mit weiteren angeborenen Fehlbildungen (z.B. hypoplastisches Linksherzsyndrom, Shone-Syndrom, kompletter atrioventrikulärer Septumdefekt) vor, sodass eine Standardisierung der chirurgischen Rekonstruktionsverfahren dieser Klappen nur schwer möglich ist, im Gegensatz zur systematisierten AV-Klappenrekonstruktion nach Carpentier im Erwachsenenalter [1]. Ein weiterer, wichtiger Unterschied zur AV-Klappenchirurgie im Erwachsenenalter, ist, dass neben der Klappenpathologie, vor allem das Alter des Kindes und die strukturelle Integrität des Klappenapparates zum Zeitpunkt des AV-Klappeneingriffes eine entscheidende Rolle spielt. Somit wird die Haltbarkeit der AV-Klappenrekonstruktion im Kindesalter neben der Morphologie des Klappenvitiums maßgeblich durch das somatische Wachstum des Kindes, sowie der vergesellschafteten kongenitalen Anomalien beeinflusst. Bisherige Studien zur Haltbarkeit nach chirurgischer AV-Klappenrekonstruktion sind gekennzeichnet durch kleine, inhomogene Patientenkollektive hinsichtlich der Klappenpathologien, der weiteren angeborenen Fehlbildungen, und der verwendeten chirurgischen Techniken [2-4]. So variieren die publizierten Angaben bezüglich der Haltbarkeitsdauer nach AV-Klappenrekonstruktion: eine Freiheitsrate von Reoperation 20 Jahre nach kongenitaler Mitralklappenrekonstruktion von 77% [5], eine 21 %-ige Inzidenz von Reoperation 12 Jahre nach Trikuspidalklappenrekonstruktion bei Kindern mit hypoplastischem Linksherzsyndrom [6] oder eine Freiheitsrate von Reoperation 10 Jahre nach Rekonstruktion der gemeinsamen Atrioventrikularklappe beim kompletten atrioventrikulären Septumdefekt von 62% [7]. Eine Rekonstruktion der AV-Klappe sollte jedoch immer angestrebt werden, da der prothetische Klappenersatz mit deutlichen Nachteilen für das Kind verbunden ist. Zum einen mit einer stark erhöhten perioperativen Mortalität von 14-29% [8, 9] und zum anderen mit einem 15-44% erhöhten Risiko für die Notwendigkeit eines permanenten Herzschrittmachers [8, 9]. Zusätzlich kommt es durch das Wachstum des Kindes

zwangsläufig zu einem Patienten-Prothesen-Mismatch, woraufhin eine größere Klappenprothese implantiert werden muss. Bei einem mechanischen Klappenersatz ist zudem die lebenslange orale Antikoagulation mit erhöhtem Einblutungsrisiko als Nachteil zu nennen. Um eine klare Aussage über das Ergebnis verschiedener chirurgischer Rekonstruktionstechniken der AV-Klappen im Kindesalter zu treffen, wurden an unserer Klinik Studien mit gezielten Fragestellungen initiiert:

I. Mitralklappenrekonstruktion bei Kindern unter 10 Jahren: Problem oder Erfolg?
II. Trikuspidalklappenrekonstruktion bei Kindern mit hypoplastischem Linksherzsyndrom: Einfluss des Zeitpunktes und des Mechanismus auf das Ergebnis
III. Chirurgie der gemeinsamen Atrioventrikularklappe bei Kindern mit funktionell singulärem Ventrikel
IV. Chirurgie der Atrioventrikularklappen bei Patienten mit univentrikulärem Herz und zwei getrennten Atrioventrikularklappen

Studie I

Mitralklappenrekonstruktion bei Kindern unter 10 Jahren:
Problem oder Erfolg?

Originaltitel:

Mitral Valve Repair in Children Below Age 10 Years: Trouble or Success?

Publiziert in *The Annals of Thoracic Surgery* 2020

Erkrankungen der Mitralklappe im Kindesalter können entweder angeboren sein oder als Spätfolge eines rheumatischen Fiebers auftreten. Angeborene Erkrankungen der Mitralklappe sind selten mit einer weltweiten Inzidenz von 0.5% und treten häufig in Kombination mit weiteren angeborenen Anomalien wie einem Ventrikelseptumdefekt, einer subvalvulären Aortenstenose, oder einer Aortenisthmusstenose auf [10-12]. Pathologische Mitralklappenveränderungen rheumatischer Genese sind in den Industrieländern mittlerweile selten, in Entwicklungsländern jedoch weiter häufig vorkommend [13]. Krankhafte Veränderungen der Mitralklappe im Kindesalter betreffen unterschiedliche Klappenstrukturen. Sollte ein fibrotischer Ring oberhalb der Klappensegel vorliegen, spricht man von einem supramitralen Ring, eine Sonderform der angeborenen Mitralklappenstenose. Aufgrund der hohen morphologischen Komplexität und Variabilität der kindlichen Mitralklappenvitien bedarf es modifizierter Rekonstruktionstechniken. Inzwischen konnten gute Ergebnisse bei der Mitralklappenrekonstruktion von angeborenen Vitien (6-Jahres Überleben: 85-86%, 6-Jahres Freiheitsrate von Reoperation: 68-88%) [2, 5] und rheumatisch bedingten Vitien (10-Jahres Überleben: 87%, 15-Jahres Freiheitsrate von Reoperation: 68%) [14] veröffentlicht werden.

Wir haben in einer retrospektiven Studie die Ergebnisse nach Mitralklappenrekonstruktion bei 50 Kindern, die zum Operationszeitpunkt jünger als 10 Jahre waren, analysiert. Bei 40 Kindern

lagen angeborene Mitralklappenvitien vor und bei 10 Kindern erworbene Vitien. Bei den angeborenen Vitien lag bei 78% (31/40) eine Insuffizienz und bei 22% (9/40) eine Stenose vor. Ursächlich für eine Insuffizienz war vor allem eine Spaltbildung (Cleft) im Klappensegel, wohingegen bei der Stenose die Pathologien gleich verteilt waren (Tabelle 1). Verantwortlich für eine erworbene Mitralklappeninsuffizienz waren funktionelle Ursachen (ALCAPA-Syndrom) oder endokarditisch bedingte Veränderungen (Tabelle 2). Die Mitralklappe wurde bei allen 50 Kindern initial rekonstruiert (Tabelle 2 und 3).

Tabelle 1: Charakteristika und Details der Pathologie der angeborenen Mitralklappenvitien [15].

Characteristic	Value
Median age, y (range, days-years)	1.2 (14-9.8)
Median weight, kg (range)	8.2 (2.9-41.9)
Male sex	16 (40)
Mitral regurgitation	31 (77.5)
Mitral stenosis	9 (22.5)
Associated cardiac malformations	32 (80)
Ventricular septal defect	11 (27.5)
Aortic stenosis (valvar/subvalvar)	6 (15)
Atrial septal defect II (ostium secundum)	4 (10)
Shone's complex	3 (7.5)
Pulmonary atresia + intact ventricular septum	2 (5)
Tricuspid regurgitation	2 (5)
Transposition of the great vessels	2 (5)
Persistent foramen ovale	1 (2.5)
Patent ductus arteriosus	1 (2.5)
Mitral valve regurgitation	31 (77.5)
Type I (normal leaflet motion)	21 (52.5)
Annular dilatation	3 (7.5)
Cleft leaflet	17 (42.5)
Leaflet defect	1 (2.5)
Type II (leaflet prolapse)	3 (7.5)
Elongated chordae	3 (7.5)
Type III (restricted leaflet motion)	7 (17.5)
Short chordae	5 (12.5)
Fused commissures	1 (2.5)
Others	1 (2.5)
Mitral valve stenosis	9 (22.5)
Type A (normal papillary muscle)	6 (15)
Supravalvar ring	3 (7.5)
Papillary muscle–commissural fusion	3 (7.5)
Type B (abnormal papillary muscle)	3 (7.5)
Parachute valve	3 (7.5)

Tabelle 2: Charakteristika und chirurgische Techniken bei Kindern mit erworbenen Mitralklappenvitien [15].

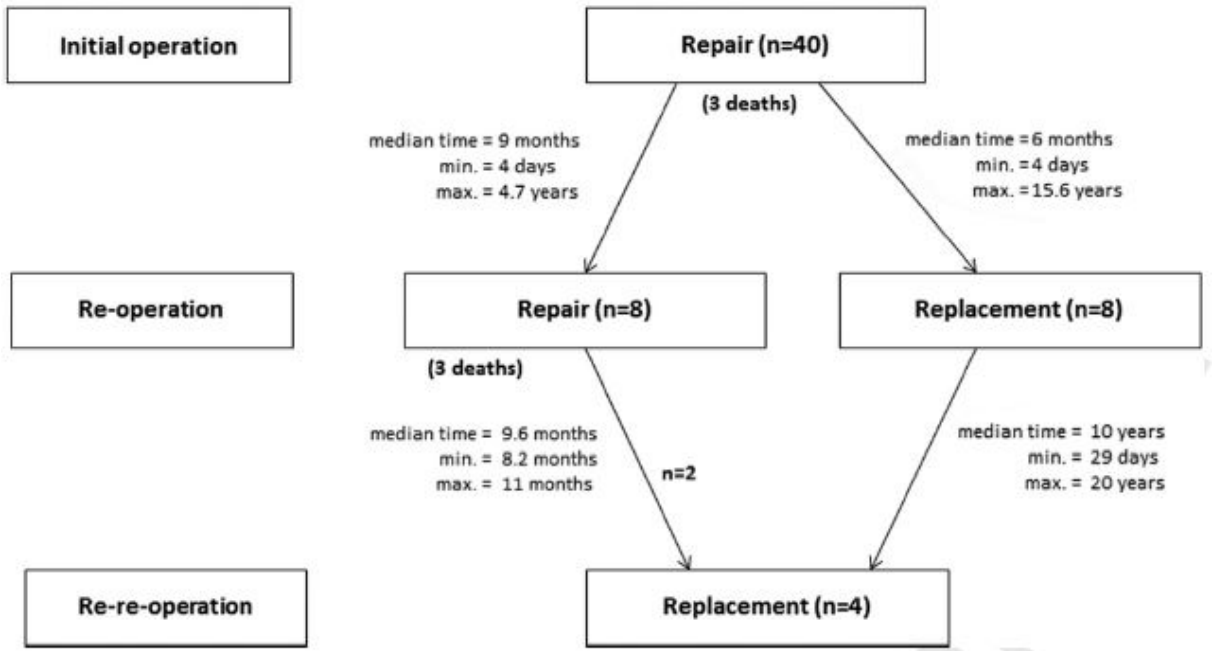
Characteristic	Value
Median age, y (range, days-years)	1.9 (10-9.9)
Median weight, kg (range)	10.6 (3.8-30.4)
Male sex	5 (50)
Mitral regurgitation	10 (100)
Endocarditis	5 (50)
Functional	3 (30)
Iatrogenic	2 (20)
Type I leaflet defect	4 (40)
Type I cleft leaflet	2 (20)
Type II elongated chordae	1 (10)
Type II ruptured chordae	1 (10)
Type III fused commissures	1 (10)
Type III others	1 (10)
Associated cardiac malformations	6 (60)
Anomalous left coronary artery originating from the pulmonary artery	3 (50)
Atrial septal defect II (ostium secundum)	2 (33)
Ventricular septal defect	1 (17)
Leaflet suture	4 (40)
Cleft suture	2 (20)
Leaflet augmentation	2 (20)
Chordal replacement	1 (10)
Chordal shortening	1 (10)

Tabelle 3: Chirurgische Techniken bei Kindern mit angeborenen Mitralklappenvitien [15].

Surgical Technique	No. of Cases (%)
Supravalvar repair	3 (7.5)
Resection of a supramitral membrane	3 (7.5)
Valvar repair	32 (80)
Ring annuloplasty	4 (10)
Rigid, complete ring	1 (2.5)
Semirigid, complete ring	2 (5)
Semirigid, partial ring	1 (2.5)
Leaflet procedure	22 (55)
Leaflet/cleft suture	19 (47.5)
Triangular leaflet resection	1 (2.5)
Leaflet augmentation	2 (5)
Alfieri stitch	3 (7.5)
Commissurotomy	3 (7.5)
Subvalvar repair	5 (12.5)
Chordal replacement	1 (2.5)
Papillary muscle splitting	4 (10)

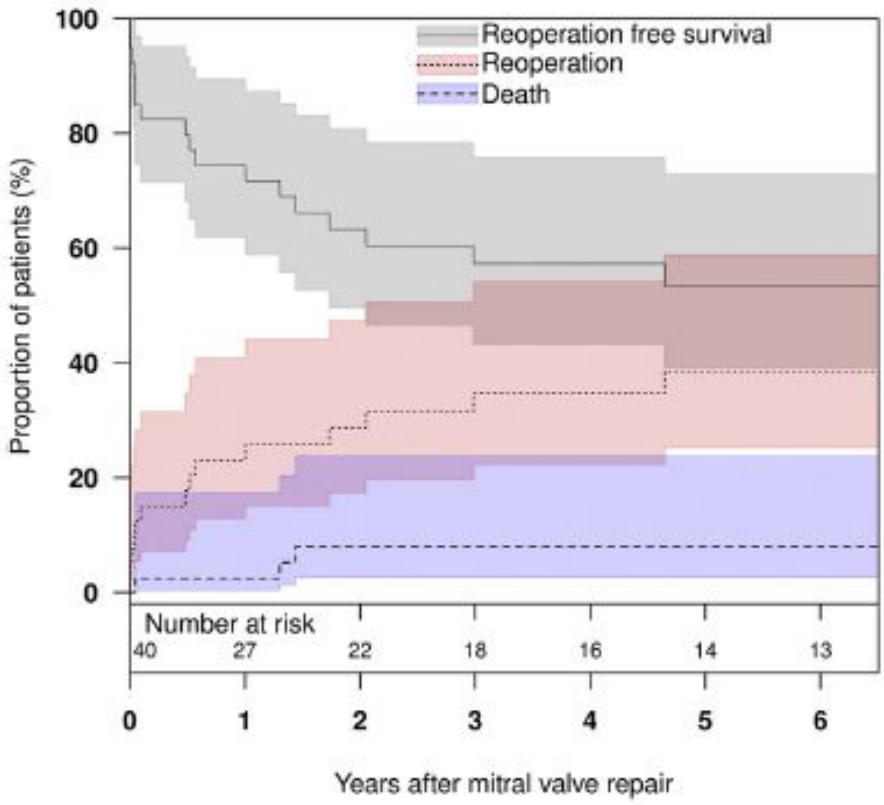
Sechs Jahre nach Rekonstruktion der angeborenen Mitralklappenvitien betrug das Überleben 79%. Patienten mit Mitralklappeninsuffizienz zeigten ein geringen Überlebensvorteil im Gegensatz zu Patienten mit Mitralklappenstenose (85% vs 60%, p= 0.1). Die operative Mortalität und Spätmortalität betrug 5% und 10%. Nach angeborener Mitralklappenrekonstruktion musste die Klappe bei 20% der Kinder mittels einer mechanischen Prothese ersetzt werden (Abbildung 1).

Abbildung 1: Klinischer Verlauf bei Kindern nach angeborener Mitralklappenrekonstruktion [8].



Sechs Jahre nach Rekonstruktion von angeborenen Mitralklappenvitien überlebten 53% der Kinder ohne erneute Operation und in 39% der Fälle war eine Reoperation notwendig (Abbildung 2). Acht Prozent der Kinder verstarben nach dem primären Eingriff ohne erneute Operation.

Abbildung 2: Kompetitive Risikoanalyse für Tod und Reoperation bei Kindern mit angeborenen Mitralklappenvitien [15].



Nach Rekonstruktion der Mitralklappe bei erworbenen Vitien musste bei 3 von 10 Kindern die Mitralklappe erneut rekonstruiert werden. Die Mortalität in dieser Gruppe betrug 0%.

Fazit – Studie I

Unsere Studie bestätigt, dass bei der Mitralklappenchirurgie im Kindesalter am Deutschen Herzzentrum München vor allem angeborene Klappenvitien, wie die Spaltbildung im Bereich des Klappensegels, eine relevante Rolle spielen. Erworbene Vitien aufgrund endokarditischer Veränderungen oder funktioneller Genese sind nur bei einem Bruchteil der Patienten nachweisbar. Die Rekonstruktion der Mitralklappe ist, sowohl bei angeborenen als auch erworbenen Vitien, sicher durchführbar und mit einer niedrigen Mortalität vergesellschaftet. Jedoch müssen über ein Drittel der Kinder nach initialer Mitralklappenrekonstruktion erneut an der Mitralklappe operiert werden.

Studie II

Trikuspidalklappenrekonstruktion bei Kindern mit hypoplastischem Linksherzsyndrom: Einfluss des Zeitpunktes und des Mechanismus auf das Ergebnis

Originaltitel:

Tricuspid valve repair in children with hypoplastic left heart syndrome: impact of timing and mechanism on outcome

Publiziert in *European Journal of Cardio-Thoracic Surgery* 2020

Das hypoplastische Linksherzsyndrom (HLHS) ist ein angeborener Herzfehler mit Hypoplasie des linken Ventrikels, Mitral- als auch Aortenklappenstenose/atresie, und hypoplastischer Aorta ascendens sowie Aortenbogen. Der rechte Ventrikel ist bei diesem Krankheitsbild verantwortlich sowohl für die pulmonale als auch systemische Zirkulation. Die Trikuspidalklappe funktioniert bei diesem Krankheitsbild als systemische Atrioventrikularklappe (AV-Klappe). Aufgrund der erhöhten chronischen Volumenbelastung des rechten Systemventrikels kommt es zu einer progressiven rechtsventrikulären Dilatation mit konsekutiver Erweiterung des Trikuspidalklappenringes, was zu einer deutlichen funktionellen Trikuspidalklappeninsuffizienz führt [16, 17]. Neben der Klappenringdilatation spielen vor allem strukturelle Veränderungen der Klappensegel und des Klappenhalteapparates eine wichtige Rolle bei der Entstehung einer signifikanten Trikuspidalklappeninsuffizienz [18, 19]. Hauptsächliche morphologische Veränderungen sind entweder ein Segelprolaps oder eine Restriktion im Segelbereich [18, 20]. Somit ist die Entstehung einer relevanten Trikuspidalklappeninsuffizienz multifaktoriell bedingt und kann jederzeit im Rahmen der univentrikulären Palliation des HLHS entstehen. Eine mittel- oder höhergradige Trikuspidalklappeninsuffizienz ist bei knapp 25% der Kinder mit HLHS nachweisbar und stellt ein deutliches Risiko für eine erfolgreiche Palliation dieser Kinder dar [3, 21, 22]. Für die Rekonstruktion dieser Klappe stehen verschiedene chirurgische Techniken

zur Verfügung (Partielle Annuloplastie, Kommissurenplastik, Edge-to-Edge Repair, etc.) [23]. Jedoch gibt es aktuell keine klaren Richtlinien bezüglich des optimalen Zeitpunktes für die Rekonstruktion der Trikuspidalklappe bei Kindern mit HLHS.

Unsere Studie an 44 Kindern mit HLHS und Trikuspidalklappenrekonstruktion untersucht retrospektiv die Entstehungsmechanismen für eine Trikuspidalklappeninsuffizienz und den Einfluss von Risikofaktoren auf das Überleben und Reoperationen an der Trikuspidalklappe. Wir führten eine uni- und multivariate Regressionsanalyse zur Identifikation von Risikofaktoren für Mortalität, Reoperation und Trikuspidalklappenersatz durch.

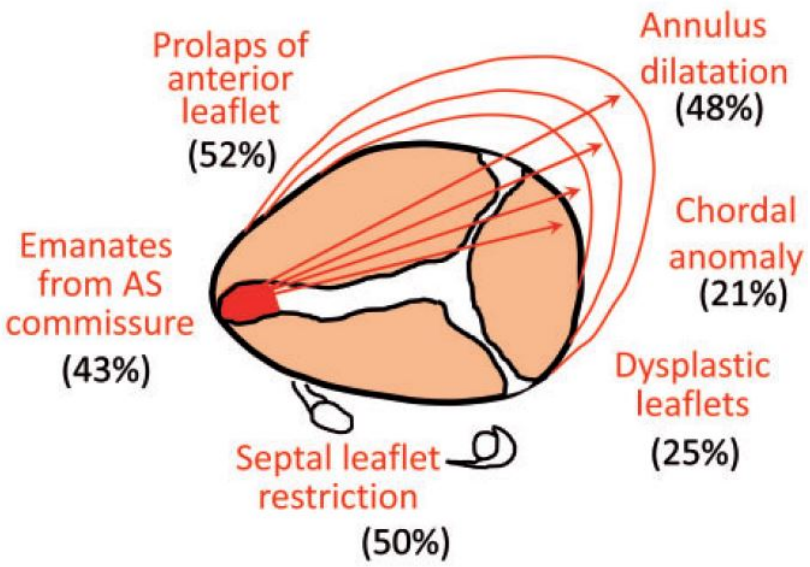
Von 249 Kindern mit HLHS, bei denen zwischen 1999 und 2018 eine univentrikuläre Palliation erfolgte, wurde bei 44 Kindern eine Trikuspidalklappenrekonstruktion durchgeführt (Tabelle 1). Am häufigsten (n=23, 52%) wurde die Trikuspidalklappe während des zweiten Schrittes der univentrikulären Palliation, der oberen bidirektionalen cavopulmonalen Anastomose (BCPS), rekonstruiert.

Tabelle 1: Patientencharakteristika und Zeitpunkt der initialen Trikuspidalklappenrekonstruktion [24].

Variables	
Total number of patients	44
Total number of TV procedures	62
Primary diagnosis	
Aortic atresia, *n* (%)	29 (65.9)
Mitral atresia, *n* (%)	17 (38.6)
Diameter of ascending aorta (mm), median (IQR)	3.0 (2.0–3.8)
Pre-Norwood echocardiography	
TR, median (IQR)	1.0 (0.8–2.0)
TAPSE, median (IQR)	12 (10–12)
Reduced RV function, *n* (%)	2 (4.5)
Premature birth, *n* (%)	3 (6.8)
Associatied extracardiac anomaly, *n* (%)	6 (13.6)
Norwood operation	
Age at Norwood (days), median (IQR)	9 (7–11)
Weight at Norwood (kg), median (IQR)	3.2 (2.9–3.6)
Operation time (min), median (IQR)	274 (236–304)
CPB time (min), median (IQR)	143 (110–163)
AXC time (min), median (IQR)	50 (41–59)
BT shunt, *n* (%)	24 (54.5)
RV–PA conduit, *n* (%)	20 (45.5)
Time of initial TV procedure, *n* (%)	
Before stage II (BCPS)	4 (9.1)
Stage II	23 (52.3)
Between stages II and III	3 (6.8)
Stage III (Fontan)	14 (31.8)
Age at first TV procedure (months), median (IQR)	5 (3–19)

Die Hauptursachen für die Entstehung einer Trikuspidalklappeninsuffizienz waren ein Prolaps des anterioren Segels bei 52% (n=23) und eine Restriktion des septalen Segels bei 50% (n=22) (Abbildung 1). Somit entstand ein Insuffizienzjet vor allem im Bereich der anteroseptalen Kommissur.

Abbildung 1: Mechanismus der Trikuspidalklappeninsuffizienz bei Kindern mit HLHS [24].



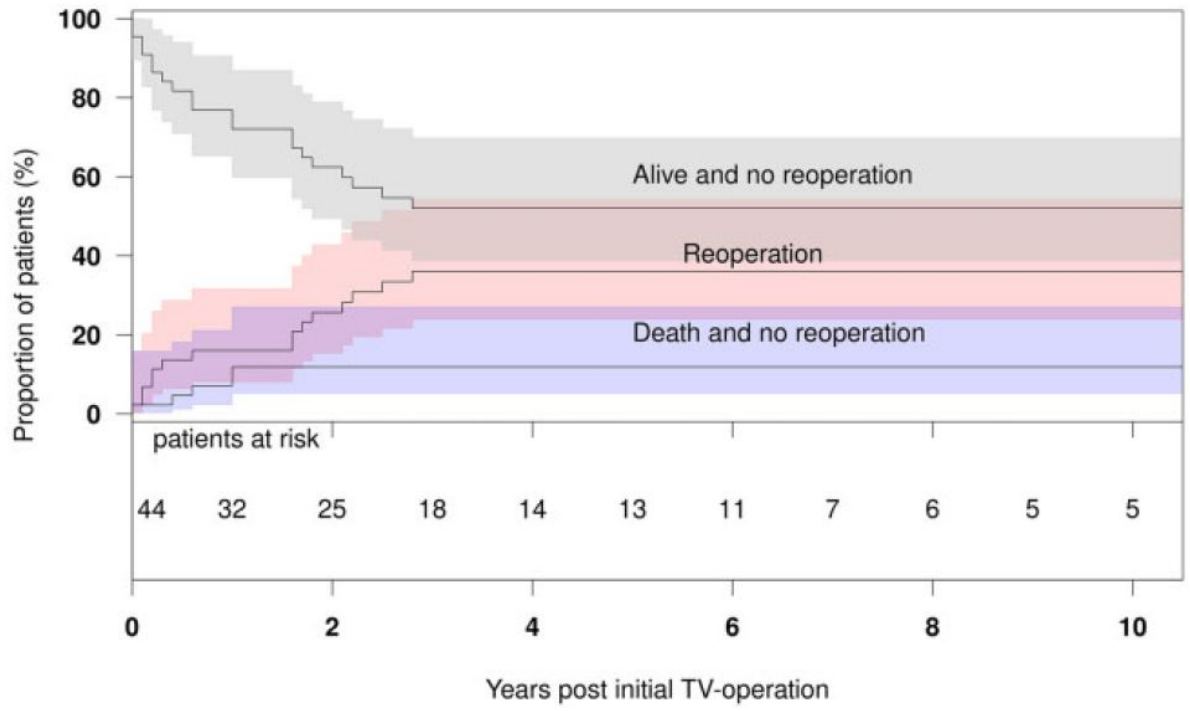
Die am häufigsten verwendete Rekonstruktionstechnik war der Verschluss der anteroseptalen Kommissur (n=27, 61%), gefolgt von der Segeladaptation (n=20, 46%) und der Annuloplastie (n=11, 25%) (Tabelle 2).

Tabelle 2: Rekonstruktionstechniken während der univentrikulären Palliation [24].

Variables	N (%)	Norwood or post	At BCPS	Post-BCPS	At Fontan
Initial repair technique		4 (9.1)	23 (52.3)	3 (6.8)	14 (31.8)
Valve reconstruction					
Leaflet adaptation	20 (45.5)	1 (25)	13 (56.5)		6 (42.9)
Cleft closure	10 (22.8)	1 (25)	7 (30.4)		2 (14.3)
Alfieri stitch	7 (15.9)	1 (25)	3 (13)		3 (21.4)
Bicuspidization	4 (9.1)		1 (3.3)	1 (33.3)	2 (14.3)
Pericard patch augumentation	5 (11.4)		5 (21.9)		
Commisural approximation					
AS commussure	27 (61.4)	1 (25)	14 (60.9)	2 (66.7)	10 (71.4)
AP commissure	9 (20.5)	2 (50)	4 (17.4)	1 (33.3)	2 (14.3)
SP commissure	11 (25.0)	1 (25)	8 (34.8)		2 (14.3)
Chordae reconstruction	10 (22.7)		6 (26.1)	1 (33.3)	4 (28.6)
Annuloplasty	11 (25.0)		6 (26.1)	1 (33.3)	4 (28.6)
DeVega	4 (9.1)		1 (4.3)	1 (33.3)	2 (14.3)
Partial annuloplasty	7 (15.9)		5 (21.5)		2 (14.3)

Nach Trikuspidalklappenrekonstruktion verstarben 2 Kinder (5%) im Krankenhaus und 9 Kinder (21%) während des 5-Jahres-Follow-up. Die kumulative Inzidenz von Reoperationen an der Trikuspidalklappe betrug 36% fünf Jahre nach initialer Rekonstruktion (Abbildung 2). Bei 8 Kindern konnte die Trikuspidalklappe erneut rekonstruiert werden und bei 6 Kindern musste die Trikuspidalklappe mittels einer mechanischen Prothese ersetzt werden. Das reoperationsfreie Überleben fünf Jahre nach Trikuspidalklappenrekonstruktion betrug 52%.

Abbildung 2: Ergebnis nach Trikuspidalklappenrekonstruktion bei Kindern mit HLHS. Die rote Kurve stellt die kumulative Inzidenz von Reoperation dar und die lila Kurve die kumulative Inzidenz von Tod ohne Reoperation. Die graue Kurve zeigt das reoperationsfreie Überleben [24].



Kinder, bei denen eine Trikuspidalklappenrekonstruktion vor dem zweiten univentrikulären Palliationseingriff (BCPS) durchgeführt wurde, zeigten ein signifikant erhöhtes Risiko sowohl für eine erneute Operation (Hazard ratio [HR] 5.5, p=0.04) als auch für einen späteren Klappenersatz (HR 36.9, p=0.01) (Tabelle 3). Bei diesen Patienten konnte ebenso eine deutlich erhöhte Mortalität nach Trikuspidalklappenrekonstruktion (HR 6.1, p=0.01) nachgewiesen werden. Eine Restriktion im septalen Segelbereich war mit einem erhöhten Reoperationsrisiko (HR 4.7, p=0.02) vergesellschaftet. Lagen Anomalien im Bereich des anterioren (HR 4.7, p=0.04) oder posterioren (HR 7.3, p=0.02) Sehnenfadens vor, so war das Risiko für einen Klappenersatz deutlich erhöht.

Tabelle 3: Uni- und multivariate Risikoanalyse für Mortalität, Reoperation und Klappenersatz nach Trikuspidalklappenrekonstruktion [24].

	Univariate model			Multivariate model		
Variables	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Mortality						
Pre-stage II (BCPS)	6.092	1.587–23.381	0.008			
Age at initial TV procedure	0.874	0.749–1.019	0.085			
Weight at initial TV procedure	0.738	0.550–0.992	0.044	0.738	0.550–0.992	0.044
Reoperation						
TR pre-Norwood	1.490	0.941–2.360	0.089			
TAPSE pre-Norwood	0.731	0.508–1.051	0.091			
Z-score TAPSE pre-Norwood	0.694	0.454/1.060	0.091			
Pre-stage II (BCPS)	6.813	1.286–36.086	0.024	5.510	1.063–29.620	0.042
At stage II	3.043	0.962–9.625	0.058			
TR at initial TV procedure	2.393	0.860–6.663	0.095			
Age at initial TV procedure	0.912	0.840–0.990	0.027			
Weight at initial TV procedure	0.768	0.626–0.944	0.012	0.769	0.623–0.950	0.015
Restrictive septal leaflet	4.723	1.326–16.814	0.017			
Pericard patch augumentation	3.558	1.120–11.304	0.031			
TV replacement						
TR pre-Norwood	2.163	1.178–3.924	0.013			
Pre-stage II (BCPS)	51.762	5.104–524.94	0.001	36.917	2.165–629.63	0.013
Anterior leaflet chordal anomalies	4.382	1.095–17.541	0.037			
Posterior leaflet chordal anomalies	7.371	1.473–36.877	0.015			

Fazit – Studie II

Ein Prolaps des anterioren Segels und eine Restriktion des septalen Segels konnten wir in unserer Studie als Hauptmechanismen für eine Trikuspidalklappeninsuffizienz bei Kindern mit HLHS identifizieren. Bei restriktivem septalem Segel und Sehnenfadenanomalien zeigte sich ein deutlich erhöhtes Risiko für Reoperation und Klappenersatz. Wenn die Trikuspidalklappe bei Kindern mit HLHS bereits vor dem zweiten univentrikulären Palliationsschritt rekonstruiert werden muss, dann ist dies mit einem deutlich erhöhten Risiko für Mortalität, Reoperation und späterem Klappenersatz verbunden.

Studie III

Chirurgie der gemeinsamen Atrioventrikularklappe bei Kindern mit funktionell singulärem Ventrikel

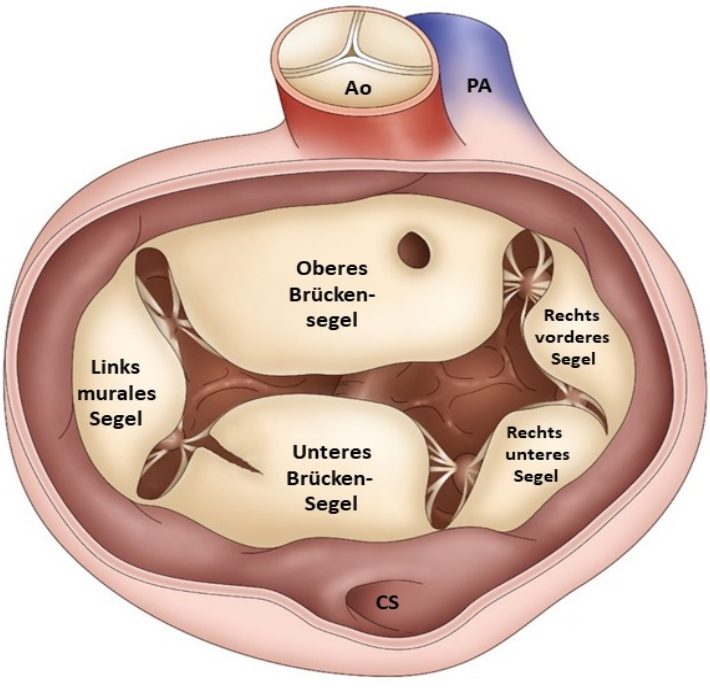
Originaltitel:

Common atrioventricular valve surgery in children with functional single ventricle

Publiziert in *European Journal of Cardio-Thoracic Surgery* 2021

Eine gemeinsame Atrioventrikularklappe (CAVV) ist vorhanden bei Kindern mit einem kompletten atrioventrikulären Septumdefekt (CAVSD) oder bei Kindern mit univentrikulärem Herz [25]. Bei dem Krankheitsbild des CAVSD liegt sowohl ein Vorhofseptumdefekt als auch ein Ventrikelseptumdefekt vor. Die Klappenringe der Atrioventrikularklappen sind nicht getrennt angelegt und die linke und rechte Atrioventrikularklappe sind miteinander in Form eines oberen und unteren Brückensegels verbunden (Abbildung 1).

Abbildung 1: Gemeinsame Atrioventrikularklappe [26].



Dies ist häufig verbunden mit einer abnormen Anlage der Sehnenfäden, welche in beide Ventrikel herunterreichen, jedoch auch die Ventrikelseiten kreuzen können (Straddling). Sollte bei diesem Krankheitsbild eine Ventrikelseite unterentwickelt sein, entsteht eine ventrikuläre Imbalance und man spricht von einem unbalancierten CAVSD (uCAVSD). Bei Kindern mit uCAVSD oder Straddling der gemeinsamen Atrioventrikularklappe ist eine biventrikuläre Korrektur nicht möglich und eine univentrikuläre Palliation ist indiziert. Jedoch besteht bei 15-30% der Kinder mit uCAVSD eine relevante Insuffizienz der gemeinsamen Atrioventrikularklappe (CAVVR), was einen Risikofaktor für Mortalität und Nichterreichen der univentrikulären Palliation dieser Kinder darstellt [27-29]. Die Ursachen für eine Insuffizienz dieser Klappe sind multifaktoriell bedingt und vor allem intrinsische Veränderungen der Klappensegel spielen eine entscheidende Rolle. Jedoch bestehen bis heute keine klaren Richtlinien über den optimalen Zeitpunkt der CAVV-Rekonstruktion. Ein Großteil der kinderherzchirurgischen Zentren führen die Rekonstruktion dieser Klappe entweder während des zweiten Schrittes der univentrikulären Palliation [30] oder während des letzten Schrittes [4] durch. In unserem Zentrum rekonstruieren wir die gemeinsame Atrioventrikularklappe während des zweiten Palliationsschrittes, da somit eine Volumenüberlastung des Ventrikels mit konsekutivem Remodeling und Einschränkung der Pumpfunktion verhindert werden kann.

In unserer Studie wurde in einem Zeitraum von 1984 bis 2019 bei 30 Kindern mit ventrikulärer Imbalance und univentrikulärer Palliation die gemeinsame Atrioventrikularklappe chirurgisch behandelt. Wir untersuchen retrospektiv die Entstehungsmechanismen für eine Insuffizienz der gemeinsamen Atrioventrikularklappe und das Überleben sowie die Reoperationsrate nach initialer Klappenrekonstruktion.

Bei dem Großteil der Kinder (n=25, 83%) lag ein uCAVSD vor und bei 10 % (n=3) ein balancierter CAVSD mit Straddling der Klappe (Tabelle 1). Indikation für eine CAVV-Rekonstruktion war eine mittel- (n=12, 40%) oder hochgradige Insuffizienz (n=18, 60%). Das mediane Gewicht zum Operationszeitpunkt betrug 6.5 kg und 53% der Kinder (n=16) waren jünger als ein Jahr. Am häufigsten (n=12, 40%) wurde die gemeinsame Atrioventrikularklappe während des zweiten Schrittes der univentrikulären Palliation rekonstruiert.

Tabelle 1: Patientencharakteristika und Zeitpunkt der initialen CAVV-Rekonstruktion [26].

Total	30
Age (years)	0.9 (0.3–1.8)
Weight (kg)	6.5 (3.9–8.7)
Male gender	16 (53)
Primary diagnosis	
Unbalanced CAVSD	25 (83.3)
Right ventricular dominance	23 (76.7)
Left ventricular dominance	2 (6.7)
Balanced CAVSD	3 (10)
Univentricular heart	2 (6.7)
Associated cardiac defects	
Heterotaxy	12 (40)
DORV	8 (26.7)
PS	8 (26.7)
TAPVD	8 (26.7)
Heterotaxy and TAPVD	7 (23.3)
Chromosomal anomalies	3 (10)
Preoperative CAVV regurgitation	
Moderate	12 (40)
Severe	18 (60)
CAVV straddling	3 (10)
Timing of CAVV surgery	
At stage I	6 (20)
Between stage I and II	3 (10)
At stage II	12 (40)
Between stage II and Fontan	1 (3.3)
At Fontan	8 (26.7)
Initial stage I palliation	
MBTS	4 (13.3)
Central shunt	4 (13.3)
PA banding	11 (36.7)
Norwood	4 (13.3)
RV–PA conduit	1 (3.3)
No stage I palliation	6 (20)

Die häufigsten Ursachen für eine Insuffizienz der gemeinsamen Atrioventrikularklappe waren strukturelle Veränderungen im Bereich der Klappensegel, wie zum Beispiel ein Cleft (n=8, 27%) oder eine Insuffizienz im Bereich der Kommissuren (n=7, 23%) (Tabelle 2). Deutlich geringer war der Anteil der Kinder (n=5, 17%) mit funktioneller Genese im Sinne einer Annulusdilatation.

Tabelle 2: Pathologien der gemeinsamen Atrioventrikularklappe [26].

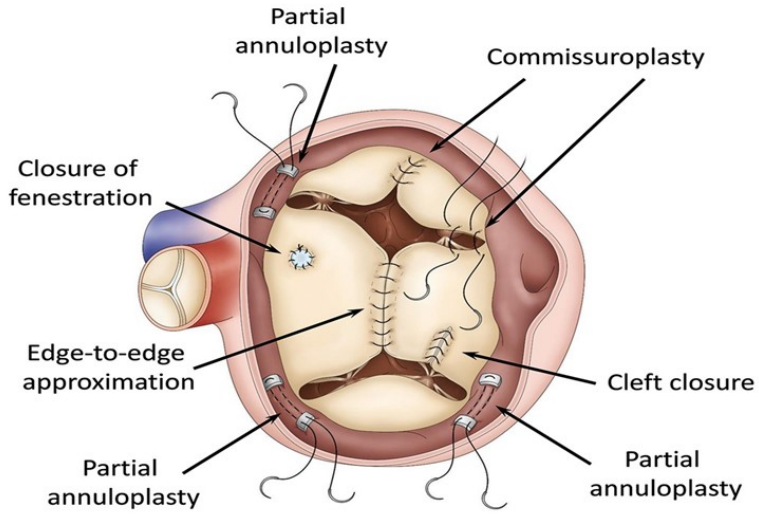
Leaflet cleft	8 (26.7)
BL right inferior	2 (6.7)
BL left superior + inferior	2 (6.7)
BL right superior + inferior	1 (3.3)
BL right superior + anterior	1 (3.3)
Location undetermined	2 (6.7)
Commissural regurgitation	7 (23.3)
BL right superior + inferior	2 (6.7)
BL left superior + inferior	2 (6.7)
BL right superior + anterior	1 (3.3)
BL superior	1 (3.3)
BL left mural	1 (3.3)
Lack of coaptation	6 (20)
Annular dilatation	5 (16.7)
Circular	2 (6.7)
Right inferior	1 (3.3)
Left inferior	1 (3.3)
Location undetermined	1 (3.3)
Leaflet fenestration BL superior	1 (3.3)
Leaflet prolapse BL inferior	1 (3.3)

Analog zu den Pathologien wurde somit am häufigsten ein Cleftverschluss durchgeführt, gefolgt von einer Adapatation der Segel im Bereich der Kommissuren (Tabelle 3) (Abbildung 2). Bei 2 Kindern (7%) war eine Rekonstruktion der Klappe, aufgrund von massiver Dysplasie der Klappe, nicht möglich, sodass ein mechanischer Klappenersatz durchgeführt werden musste.

Tabelle 3: Chirurgische Eingriffe an der gemeinsamen Atrioventrikularklappe [26].

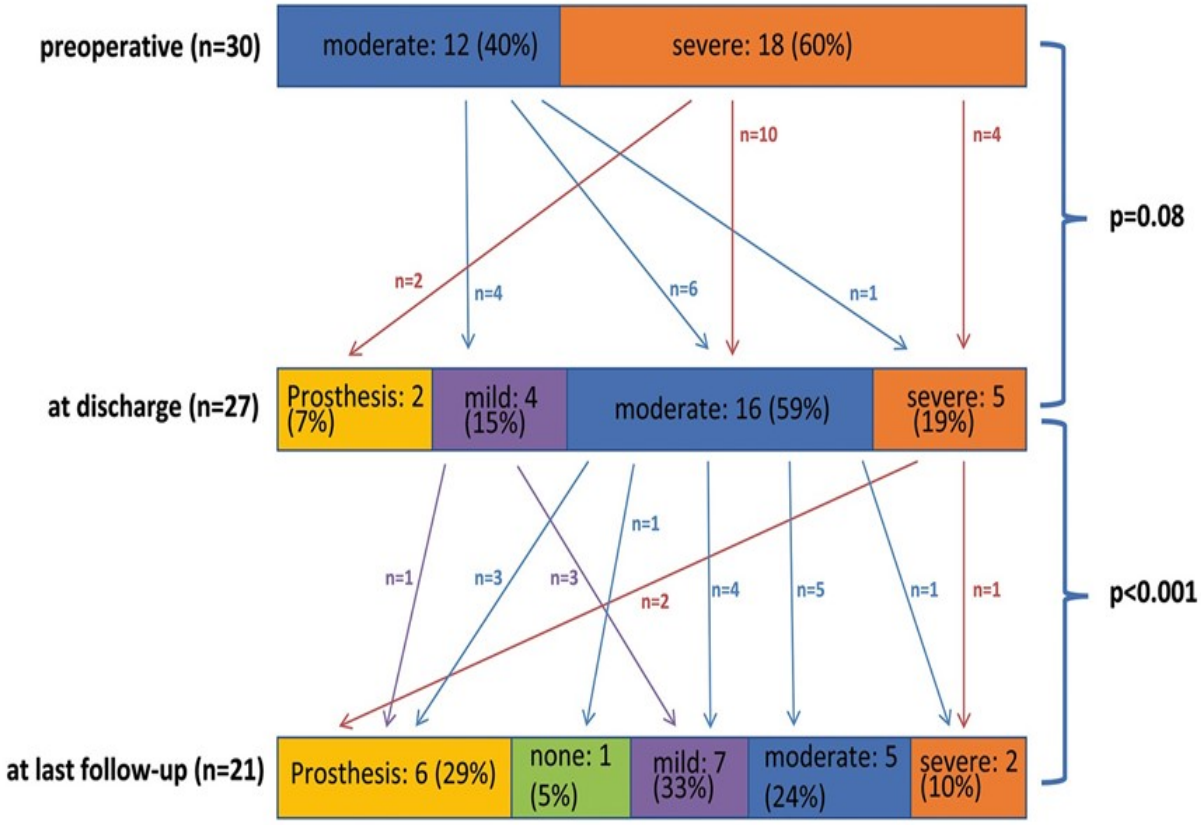
Techniques for first CAVV surgery	
CAVV repair	28 (93.3)
Cleft closure	8 (28.6)
Commissuroplasty	7 (25)
Edge-to-edge repair	6 (21.4)
Annuloplasty	5 (17.9)
De Vega plasty	2 (7.1)
Partial plasty	2 (7.1)
Kay-Wooler plasty	1 (3.6)
Fenestration closure	1 (3.6)
Chordal replacement	1 (3.6)
CAVV replacement	2 (6.7)
Techniques for second CAVV surgery	
CAVV redo repair	11 (36.7)
Cleft closure	4 (13.3)
Partial annuloplasty	3 (10)
Commissuroplasty	2 (6.7)
Edge-to-edge repair	1 (3.3)
Fenestration closure	1 (3.3)
CAVV redo replacement	2 (6.7)
Techniques for third CAVV surgery	
Partial annuloplasty	1 (3.3)
CAVV re-redo replacement	3 (10)

Abbildung 2: Rekonstruktionstechniken der gemeinsamen Atrioventrikularklappe [26].



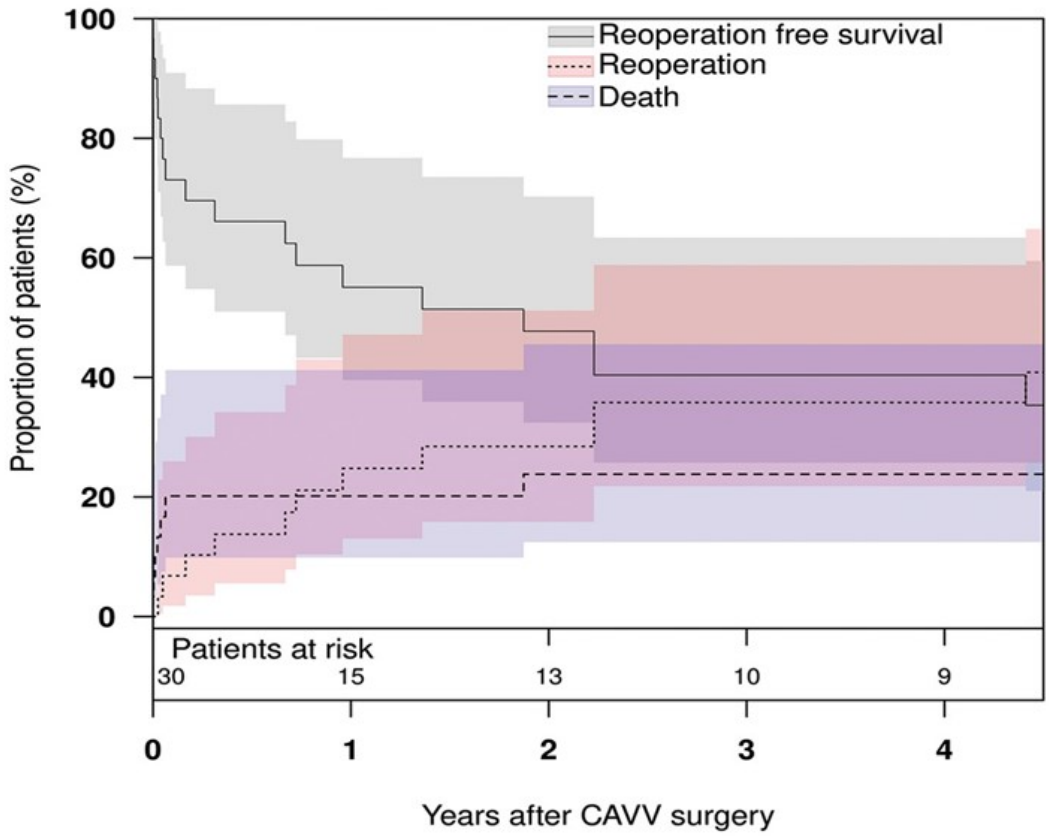
Nach Rekonstruktion der gemeinsamen Atrioventrikularklappe zeigte sich eine deutliche Verbesserung der Insuffizienz bei der echokardiographischen Untersuchung sowohl bei Entlassung (p=0.08) als auch zum letzten Nachsorgetermin (p<0.001) (Abbildung 3). Jedoch konnte die gemeinsame Atrioventrikularklappe bei 6 Kindern nicht mehr erhalten werden.

Abbildung 3: Echokardiographische Untersuchung der gemeinsamen Atrioventrikularklappe und Verlauf der Insuffizienz [26].



Nach Chirurgie der gemeinsamen Atrioventrikularklappe verstarben 7 Kinder (23%) im Krankenhaus und 2 Kinder (9%) während des 4-Jahres-Follow-up. Die kumulative Inzidenz von Reoperationen an der gemeinsamen Atrioventrikularklappe betrug 36% vier Jahre nach initialer Klappenchirurgie (Abbildung 4). Vier Jahre nach Rekonstruktion der gemeinsamen Atrioventrikularklappe betrug das reoperationsfreie Überleben 40%.

Abbildung 4: Kompetitive Risikoanalyse für Tod und Reoperation an der gemeinsamen Atrioventrikularklappe. Die graue Kurve zeigt das reoperationsfreie Überleben. Die rote Kurve stellt die kumulative Inzidenz von Reoperation dar und die blaue Kurve die kumulative Inzidenz von Tod ohne Reoperation [26].



Fazit – Studie III

Die Chirurgie der gemeinsamen Atrioventrikularklappe bei Kindern mit ventrikulärer Imbalance stellt die komplexeste Form der Atrioventrikularklappenchirurgie im Kindesalter dar. Pathologische Veränderungen dieser Klappe sind vor allem struktureller Natur, entweder die Klappensegel oder die Kommissuren betreffend, welche eine relevante Insuffizienz hervorrufen. Die Rekonstruktion der gemeinsamen Atrioventrikularklappe verringert den Schweregrad der Insuffizienz signifikant, jedoch ist eine komplett suffizient schließende Klappe nur in wenigen Fällen zu erreichen. Diese klappenchirurgischen Eingriffe sind bei Patienten mit nur einem funktionierenden Ventrikel mit einer hohen perioperativen Mortalität und einer hohen Reoperationsinzidenz assoziiert.

Studie IV

Chirurgie der Atrioventrikularklappen bei Patienten mit univentrikulärem Herz und zwei getrennten Atrioventrikularklappen

Originaltitel:

Atrioventricular valve surgery in patients with univentricular heart and two separate atrioventricular valves

Publiziert in *Cardiology in the Young* 2024

Eine mittel- oder höhergradige AV-Klappeninsuffizienz bei Kindern mit univentrikulärem Herz ist keine Seltenheit und stellt einen Risikofaktor für eine erhöhte Langzeitmorbidität und Mortalität dar [31-34]. Jedoch fokussieren sich die meisten Publikationen über relevante AV-Klappeninsuffizienzen im Rahmen der univentrikulären Palliation auf Kinder mit einer gemeinsamen AV-Klappe oder systemischen Trikuspidalklappe bei hypoplastischem Linksherzsyndrom [35, 36]. Kinder mit zwei getrennten AV-Klappen und univentrikulärem Herz, wie zum Beispiel beim Double Inlet Left Ventricle (DILV), unbalanziertem Double Outlet Right Ventricle (DORV), oder unbalanzierter congenital korrigierter Transposition der großen Gefäße (ccTGA) stellen eine wichtige Untergruppe dar, da es bei 26% dieser Kinder im Alter von 25 Jahren zu einem Versagen der AV-Klappenschlussfähigkeit kommt [37]. Beim DILV münden beide Vorhöfe in die linke Herzkammer und beim DORV besitzt sowohl die Aorta als auch die Pulmonalarterie eine morphologische Konnektion zum rechten Ventrikel, dabei kann ein Ventrikel zu klein sein. Bei der ccTGA sind die Ventrikel vertauscht und ein Ventrikel kann ebenfalls nur unzureichend entwickelt sein. Die Rekonstruktion der AV-Klappen bei diesen Kindern ist äußerst anspruchsvoll und Nakata und Kollegen beschreiben eine Freiheitsrate von Reoperation 5 Jahre nach AV-Klappenrekonstruktion von 57% [38]. Ist eine AV-Klappenrekonstruktion bei zwei getrennten AV-Klappen nicht möglich, so kann die unterentwickelte links- oder rechtsseitige AV-Klappe mittels Naht oder Patch verschlossen werden [39]. Zum aktuellen Zeitpunkt ist die Datenlage bezüglich des klinischen und

echokardiographischen Langzeitergebnisses nach AV-Klappenrekonstruktion und/oder Klappenverschluss bei Kindern mit zwei getrennten AV-Klappen und univentrikulärem Herz noch limitiert.

In unserer Studie untersuchten wir bei 32 Kindern mit zwei getrennten AV-Klappen und univentrikulärem Herzen retrospektiv die Entstehungsmechanismen einer relevanten links- oder rechtsseitigen AV-Klappeninsuffizienz oder Stenose, sowie das klinische und echokardiographische Ergebnis nach AV-Klappenrekonstruktion und AV-Klappenverschluss im Langzeitverlauf.

Von 202 Kindern mit univentrikulärem Herz und zwei getrennten AV-Klappen, bei denen zwischen 1994 und 2021 eine univentrikuläre Palliation erfolgte, wurde bei 32 Kindern ein Eingriff im Bereich der AV-Klappen durchgeführt. Bei 44% der Kinder (n=14) lag ein DILV vor, bei jeweils 22% (n=7) ein DORV oder eine kongenital korrigierte Transposition der großen Gefäße. Bei 69% der Kinder (n=22) wurden Eingriffe im Bereich der rechten AV-Klappe durchgeführt und bei 28% (n=9) Eingriffe im Bereich der linken AV-Klappe. Am häufigsten (n=17, 53%) wurde die links- und rechtsseitige AV-Klappe in Kombination mit der Komplettierung der Fontan-Zirkulation operiert (Tabelle 1).

Tabelle 1: Patientencharakteristika und Zeitpunkt der initialen CAVV-Rekonstruktion [40].

Total	32
Age, years	1.9 (0.9–5.7)
Weight, kg	10.6 (7.9–18.9)
Female sex	18 (56.3)
Primary diagnosis	
DILV	14 (43.8)
DORV	7 (21.9)
CCTGA	7 (21.9)
Shone Complex	2 (6.3)
Other	2 (6.3)
Left ventricular dominance	19 (59.4)
Right ventricular dominance	13 (40.6)
Associated cardiac defects	
CoA	9 (28.1)
PS subvalvular	8 (25)
LPSVC	6 (18.8)
Pulmonary atresia	3 (9.4)
Dextrocardia	3 (9.4)
TAPVD	1 (3.1)

Preoperative AVVR	
Moderate	23 (71.9)
RAVV	17 (53.1)
LAVV	6 (18.8)
Severe	9 (28.1)
RAVV	6 (18.8)
LAVV	3 (9.4)
Preoperative severe LAVVS	1 (3.1)
RAVV straddling	4 (12.5)
LAVV straddling	3 (9.4)
Timing of initial AVV surgery	
At stage I	
LAVV	1 (3.1)
At BCPS	
RAVV	8 (25)
LAVV	3 (9.4)
At Fontan	
RAVV	12 (37.5)
LAVV	4 (12.5)
LAVV + RAVV	1 (3.1)
Between stage I and BCPS	
LAVV	2 (6.3)
Between stage I and Fontan*	
RAVV	1 (3.1)
Initial stage I palliation	
Main PA banding	8 (26.7)
Central shunt	7 (21.9)
Norwood	5 (15.6)
MBTS	3 (9.4)
DKS + Central Shunt	1 (3.1)
DKS + MBTS	1 (3.1)
Aortic valve Repair + CoA Resection	1 (3.1)
No stage I palliation	6 (18.8)

Values are expressed as n (%) or median (interquartile range). AVV = atrioventricular valve; AVVR = atrioventricular valve regurgitation; BCPS = bidirectional cavopulmonary shunt; CCTGA = congenitally corrected transposition of the great arteries; CoA = coarctation of the aorta; DILV = double inlet left ventricle; DKS = Damus-Kaye-Stansel anastomosis; DORV = double outlet right ventricle; kg = kilogram; LAVV = left atrioventricular valve; LAVVS = left atrioventricular valve stenosis; LPSVC = persistent left superior vena cava; MBTS = modified Blalock-Taussig shunt; PA = pulmonary artery; PS = pulmonary stenosis; RAVV = right atrioventricular valve; TAPVD = total anomalous pulmonary venous drainage; VSD = ventricular septal defect.
*In this patient, Stage II bidirectional cavopulmonary shunt was not performed.

Die häufigsten Ursachen für eine relevante Insuffizienz der linksseitigen AV-Klappe war ein Cleft im Bereich der Segel (n=4, 13%) oder ein Segelprolaps (n=3, 9%). Bei der rechtsseitigen AV-Klappe war die häufigste Pathologie ein Segelprolaps (n=8, 25%), gefolgt von einer Insuffizienz im Bereich der Kommissuren (n=6, 19%) (Tabelle 2).

Tabelle 2: Pathologien der linken und rechten AV-Klappe [40].

Left atrioventricular valve regurgitation	9 (28.1)
Cleft	4 (12.5)
Anterior leaflet	2 (6.3)
Posterior leaflet	1 (3.1)
Anterior + posterior leaflet	1 (3.1)
Leaflet prolapse	3 (9.4)
Anterior leaflet	2 (6.3)
Posterior leaflet	1 (3.1)
Valve dysplasia	3 (9.4)
Annular dilatation	1 (3.1)
Leaflet fenestration anterior + posterior	1 (3.1)
Left atrioventricular valve stenosis	1 (3.1)
Valve dysplasia	1 (3.1)
Right atrioventricular valve regurgitation	23 (71.9)
Leaflet prolapse	8 (25)
Posterior	4 (12.5)
Anterior	3 (9.4)
Septal	1 (3.1)
Commissural regurgitation	6 (18.8)
Anteroseptal	4 (12.5)
Posteroseptal	2 (6.3)
Pseudo-commissure leaflet	5 (15.6)
Anterior	1 (3.1)
Posterior	1 (3.1)
Septal	1 (3.1)
Anteroseptal	1 (3.1)
Posteroseptal	1 (3.1)
Annular dilatation	5 (15.6)
Valve dysplasia	3 (9.4)
Lack of coaptation	2 (6.3)
Cleft septal leaflet	1 (3.1)
Cleft anterior leaflet	1 (3.1)
Data are expressed as n (%).	

Bei 5 Kindern (17%) konnte die linksseitige AV-Klappe rekonstruiert werden und bei 4 Kindern (13%) wurde die linksseitige AV-Klappe verschlossen (Naht: n=2; Gore-Tex Patch: n=2) (Abbildung 1). Im Rahmen der linksseitigen AV-Klappenrekonstruktion erfolgte entweder ein Cleftverschluss (n=2) oder eine Segeladaptation (n=2) (Tabelle 3). Bei 20 Kindern (63%) konnte die rechtsseitige AV-Klappe rekonstruiert werden und bei nur 2 Kindern (6%) musste die rechtsseitige AV-Klappe verschlossen werden (Naht: n=2). Haupttechniken zur AV-Klappenrekonstruktion rechts waren der Kommissurenverschluss (n=6, 19%) und die Annuloplastie (n=5, 16%). Bei einem Kind erfolgte ein kombinierter Eingriff im Bereich der linken (Cleft-Verschluss+Ring-Annuloplastie) und rechten (Klappenverschluss mit Dacron-Patch) AV-Klappe.

Abbildung 1: Klinischer Verlauf nach AV-Klappenchirurgie [40].

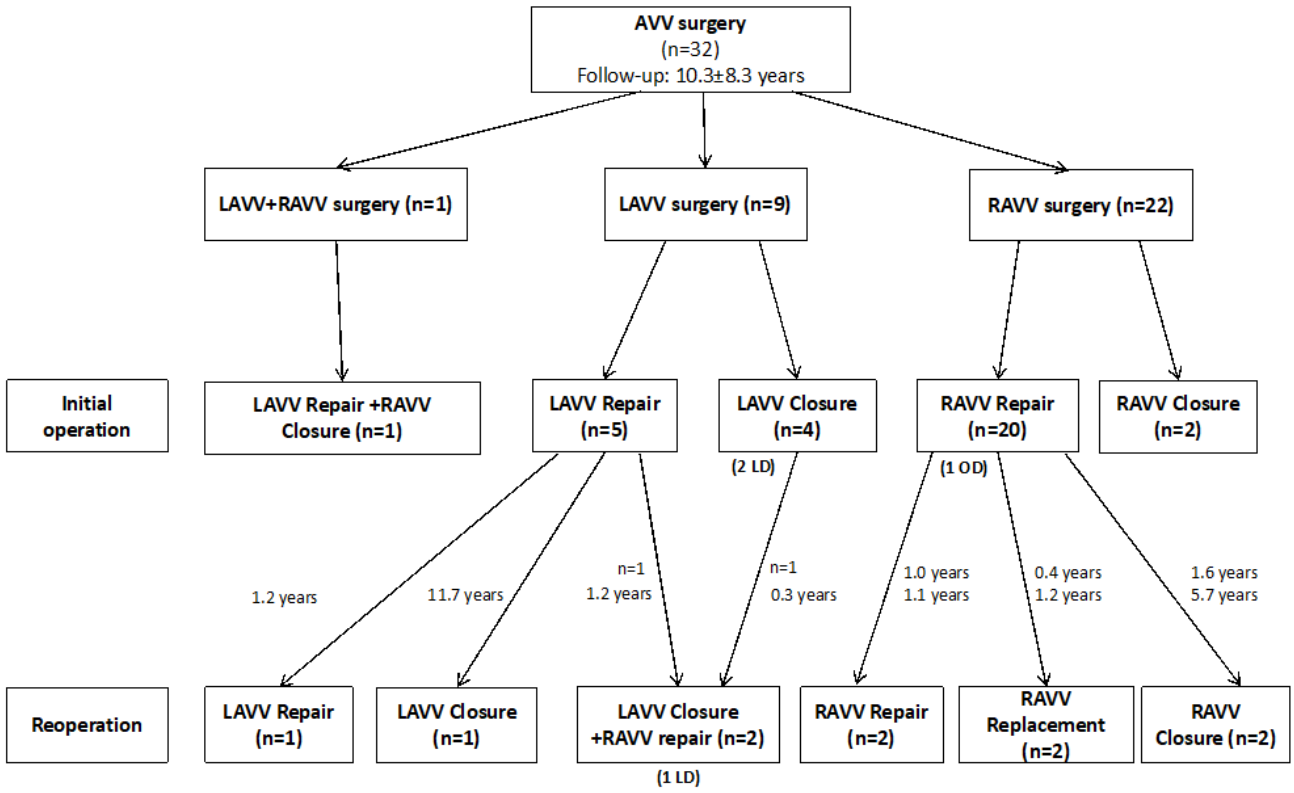


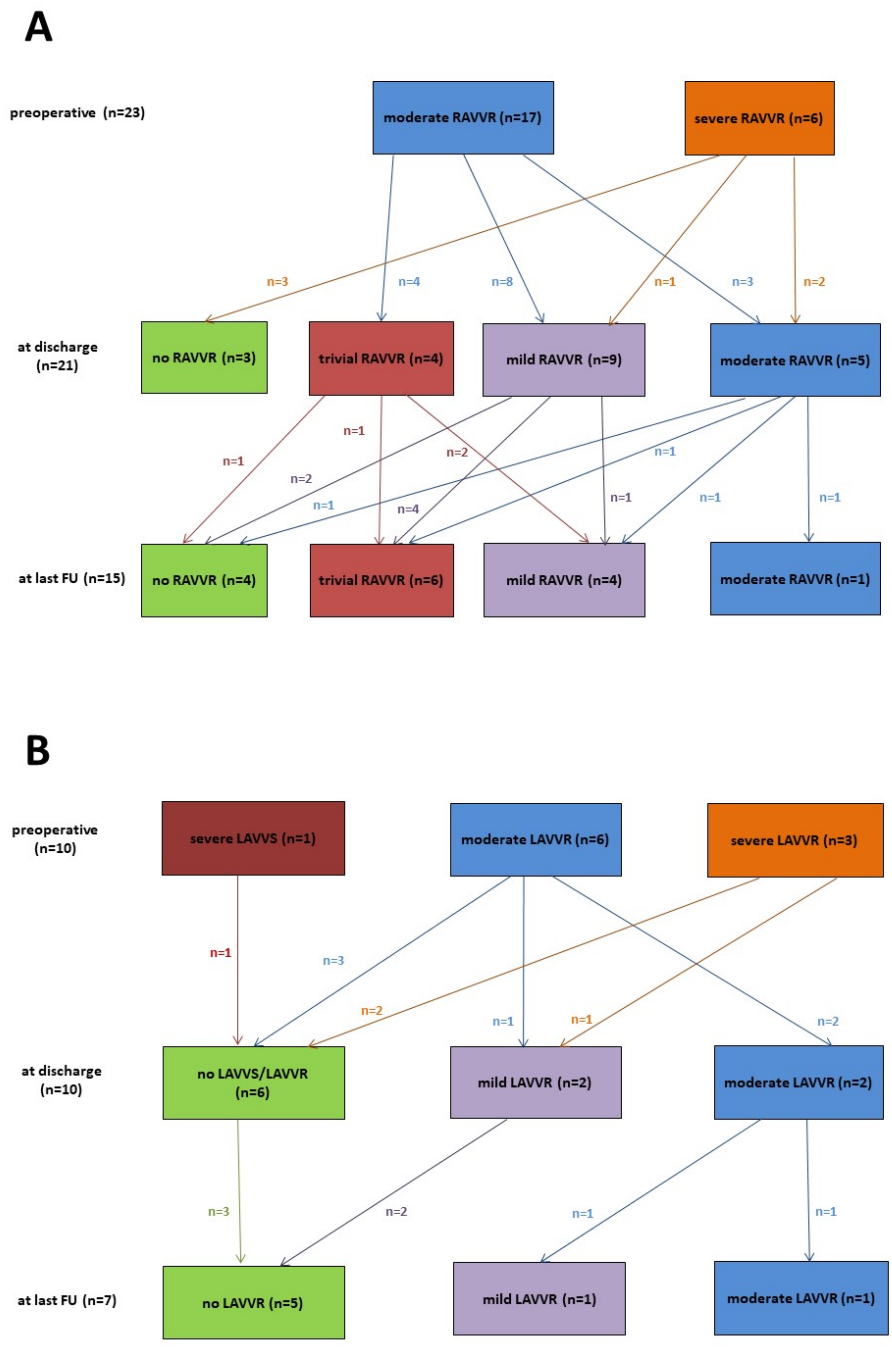
Tabelle 3: Verwendete chirurgische Techniken im Bereich der linken und rechten AV-Klappe [40].

Variable	N (%)	Stage I	Stage I - BCPS	BCPS	Stage I – Fontan*	Fontan
LAVV surgery in pts	9 (28.1)	1 (3.1)	1 (3.1)	3 (9.4)		4 (12.5)
Valve repair in pts	5 (15.6)			3 (9.4)		2 (6.3)
Cleft closure	2 (6.3)			1 (3.1)		1 (3.1)
Closure of fenestration	1 (3.1)					1 (3.1)
Leaflet adaptation	2 (6.3)			1 (3.1)		1 (3.1)
Edge-to-edge repair	1 (3.1)			1 (3.1)		
Valve closure in pts	4 (12.5)	1 (3.1)	1 (3.1)			2 (6.3)
Suture	2 (6.3)	1 (3.1)				1 (3.1)
Gore-Tex patch	2 (6.3)		1 (3.1)			1 (3.1)
RAVV surgery in pts	22 (68.8)		1 (3.1)	8 (25)	1 (3.1)	12 (37.5)
Valve repair in pts	20 (62.5)		1 (3.1)	8 (25)	1 (3.1)	10 (31.3)
Cleft closure	2 (6.3)		1 (3.1)			1 (3.1)
Closure of pseudo-commissure	3 (9.4)			1 (3.1)		2 (6.3)
Leaflet adaptation	3 (9.4)		1 (3.1)	1 (3.1)		1 (3.1)
Commissural approximation	6 (18.8)			3 (9.4)		3 (9.4)
Edge-to-edge repair	2 (6.3)			1 (3.1)		1 (3.1)
Bicuspidization	1 (3.1)					1 (3.1)
Annuloplasty	5 (15.6)			3 (9.4)	1 (3.1)	1 (3.1)
De-Vega plasty	4 (12.5)			2 (6.3)	1 (3.1)	1 (3.1)
Kay-Wooler plasty	1 (3.1)			1 (3.1)		
Valve closure in pts	2 (6.3)					2 (6.3)
Suture	2 (6.3)					2 (6.3)
LAVV + RAVV surgery in pts	1 (3.1)					1 (3.1)
LAVV cleft closure	1 (3.1)					1 (3.1)
LAVV ring annuloplasty	1 (3.1)					1 (3.1)
RAVV Dacron patch closure						1 (3.1)

Data are expressed as n (%). BCPS = bidirectional cavopulmonary shunt; LAVV = left atrioventricular valve; pts = patients; RAVV = right atrioventricular valve.
*In this patient, Stage II bidirectional cavopulmonary shunt was not performed and atrioventricular valve surgery was performed between stage I and Fontan.

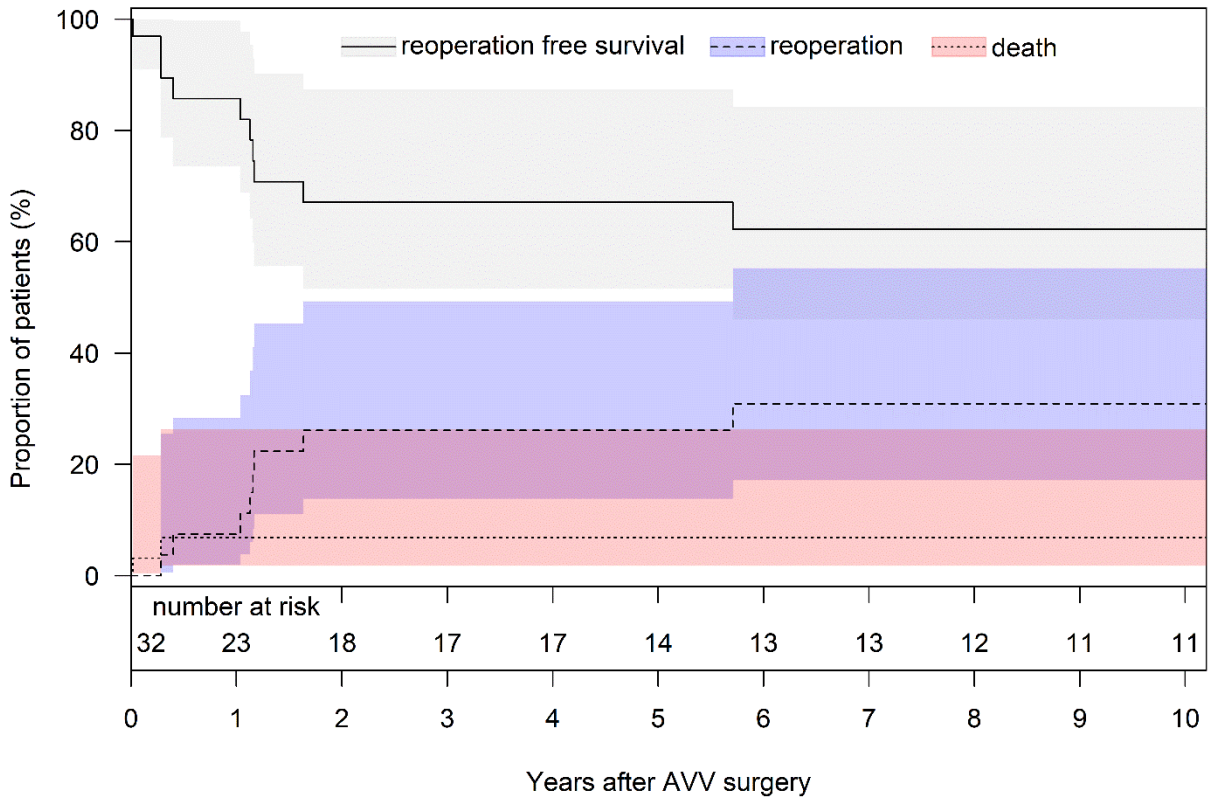
Nach Chirurgie der rechten sowie der linken AV-Klappe zeigte sich eine deutliche Verbesserung der Klappenkompetenz sowohl zum Entlassungszeitpunkt sowie zu dem letzten Nachsorgezeitpunkt (Abbildung 2A+2B).

Abbildung 2: Echokardiographische Untersuchung bei Entlassung und zum letzten Nachsorgezeitpunkt der rechten (2A) und der linken AV-Klappe (2B) [40].



Im Rahmen des mittleren Nachsorgezeitraums von 10 Jahren betrug die Langzeitmortalität 9.7% (n=3) und bei 2 Kindern konnte die rechte AV-Klappe nach Rekonstruktion nicht erhalten werden und musste prothetisch ersetzt werden (Abbildung 1). Die Inzidenz von Reoperationen an der rechten sowie linken AV-Klappe betrug 31% zehn Jahre nach initialer Klappenchirurgie (Abbildung 3). Zehn Jahre nach Chirurgie der rechten und linken AV-Klappe bei Kindern mit univentrikulärem Herz und zwei getrennten AV-Klappen betrug das reoperationsfreie Überleben 62%.

Abbildung 3: Kompetitive Risikoanalyse für Tod und Reoperation an der linken und rechten AV-Klappe. Die graue Kurve zeigt das reoperationsfreie Überleben. Die blaue Kurve stellt die kumulative Inzidenz von Reoperation dar und die rote Kurve die kumulative Inzidenz von Tod ohne Reoperation [40].



Fazit – Studie IV

Chirurgische Eingriffe im Bereich der AV-Klappen bei Kindern mit univentrikulärem Herz und zwei getrennten AV-Klappen sind im Rahmen der univentrikulären Palliation nur bei 16% dieser Kinder notwendig. Bei 7 von 32 Kindern (22%) musste die AV-Klappe verschlossen werden, da eine suffiziente Rekonstruktion der Klappe nicht möglich war. Ein prothetischer Klappenersatz musste initial nicht durchgeführt werden. Trotz der akzeptablen Langzeitmortalität sind diese klappenchirurgischen Eingriffe verknüpft mit einer hohen Reoperationsrate.

Schlussfolgerungen und klinische Auswirkung

Das Gebiet der Atrioventrikularklappenchirurgie im Kindesalter stellt eine hoch anspruchsvolle und spezialisierte Form der Kinderherzchirurgie dar. Aufgrund der großen Fortschritte und Innovationen im Bereich der Kinderherzchirurgie in den letzten Jahrzehnten konnte bei Kindern mit univentrikulärem Herzen und komplexen Atrioventrikularklappenvitien ein deutlich verbessertes Überleben und Rate an Fontan-Komplettierung erreicht werden [24, 36]. Trotz der zunehmenden Entwicklung der katheterbasierten Klappeninterventionen im Erwachsenenbereich ist der Einsatz bei pädiatrischen Patienten nur auf Einzelfälle beschränkt aufgrund der komplexen Anatomie der kongenitalen Fehlbildungen, der kleinen Gefäßdiameter und der eingeschränkten Haltbarkeit der Katheterklappen [41]. Somit bleibt die offene Chirurgie der Atrioventrikularklappe immer noch die Therapie der Wahl im Kindesalter, da diese trotz der kontinuierlichen Veränderung der Klappenmorphologie durch das somatische Wachstum der Kinder in der Mehrzahl der Fälle eine fast kompetente Klappe schafft. Jedoch muss das Risiko von mehrfachen erneuten Eingriffen im Bereich der Atrioventrikularklappen im Hinblick auf ein verbessertes Langzeitergebnis berücksichtigt werden.

In unseren Studien zeigten wir,

- dass bei den Mitralklappenpathologien im Kindesalter zum Großteil angeborene Vitien eine Rolle spielten, vor allem die Spaltbildung im Bereich der Segel. Erworbene Vitien (Funktionell, Endokarditis) spielten eine untergeordnete Rolle.
- dass Mitralklappenchirurgie im Kindesalter sicher durchführbar ist mit einer niedrigen Mortalität. Jedoch mussten 39% der Kinder sechs Jahre nach chirurgischer Rekonstruktion eines angeborenen Mitralklappenvitiums erneut an der Mitralklappe operiert werden.
- dass bei Kindern mit hypoplastischem Linksherzsyndrom ein Prolaps des anterioren Segels sowie eine Restriktion des septalen Segels hauptsächlich für eine relevante Trikuspidalklappeninsuffizienz verantwortlich sind.
- dass bei Restriktion des septalen Trikuspidalklappensegels und Anomalien der Sehnenfäden ein deutlich erhöhtes Risiko für Reoperation und Klappenersatz vorliegt.
- dass die Ergebnisse der Trikuspidalklappenrekonstruktion bei Kindern mit hypoplastischem Linksherzsyndrom vor dem zweiten univentrikulären

Palliationsschritt, der oberen bidirektionalen cavopulmonalen Anastomose, schlecht sind.

- dass bei Kindern mit gemeinsamer Atrioventrikularklappe und funktionell singulärem Ventrikel hauptsächlich Spaltbildungen im Bereich der Klappensegel oder eine Insuffizienz im Bereich der Kommissuren vorliegt.
- dass eine deutliche Reduktion der Insuffizienz der gemeinsamen Atrioventrikularklappe sowohl zum Zeitpunkt der Entlassung als auch beim letzten Nachsorgetermin erreicht werden konnte.
- dass die Chirurgie der gemeinsamen Atrioventrikularklappe bei Patienten mit funktionell singulärem Ventrikel mit einer hohen perioperativen Mortalität und Reoperationsinzidenz assoziiert ist.
- dass bei Kindern mit zwei getrennten Atrioventrikularklappen und univentrikulärem Herz chirurgische Eingriffe im Bereich der Atrioventrikularklappen nur bei einem kleinen Anteil der Kinder im Rahmen der univentrikulären Palliation notwendig sind.
- dass bei 22% der Kinder ein Verschluss der Atrioventrikularklappe durchgeführt werden musste.
- dass die Klappenchirurgie bei diesen Patienten mit einer akzeptablen Langzeitmortalität und einer 31%-igen Reoperationsinzidenz nach zehn Jahren verknüpft ist.

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Anhang I

Mitral Valve Repair in Children Below Age 10 Years: Trouble or Success?

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Background. Mitral valve (MV) repair in children is challenging because of the broad spectrum of lesions and anticipated patient growth. The purpose of the study was to evaluate the outcome of MV repair in children below 10 years of age.

Methods. We reviewed all MV repair procedures performed in children below 10 years of age. Endpoints of the study were survival after MV repair and cumulative incidence of reoperation.

Results. MV repair was performed in 40 patients with congenital MV disease (MVD) and in 10 patients with acquired MVD. Median age at time of repair for congenital MVD was 1.2 years (range, 14 days to 9.8 years) and for acquired MVD 1.9 years (range, 10 days to 9.9 years). Indication for MV repair was mitral regurgitation in 31 congenital MVD patients (77.5%) and in all acquired MVD patients. In patients with congenital MVD operative mortality was 5% and late mortality was 10%. No deaths occurred in patients with acquired MVD. Patients with congenital mitral regurgitation showed a better, yet not significant, 6-year survival than patients with congenital mitral stenosis (85.3% ± 8.2% vs 60% ± 18.2%, $P = .1$). In patients with congenital MVD cumulative incidence of reoperation at 6 years was 38.6% ± 8.3%.

Conclusions. In children below 10 years of age, MV repair is an effective treatment option for MVD. However it often just delays the time to valve replacement.

(Ann Thorac Surg 2020;110:2082-7)

Mitral valve disease (MVD) is rare in children, and the incidence of congenital MVD is about 0.5%.[1] Congenital MVD is often associated with other cardiac malformations such as ventricular septal defect (17%) and subaortic stenosis (12%).[2,3] Because any component of the valvar apparatus may be affected, resulting in stenosis, regurgitation, or combined lesions, decisions on the best surgical strategy are apt to be particularly challenging. However primary reconstruction of the valve seems preferable even though it may simply delay, rather than prevent, mitral valve (MV) replacement as a child grows.[4]

In adults a well-established classification of valvar pathology, addressing etiologic and morphologic aspects of MVD, has led to standardized surgical techniques that show excellent results up to 2 decades later.[5-7] Valvar pathology in the setting of congenital MVD is typically more complex, precluding a standardized approach to MV repair. However some reports do indicate favorable long-term results after MV repair, describing long-term survival rates of 86% to 93% and 79% freedom from reoperation after 10 and 20 years, respectively.[8,9] On the other hand children subjected to MV replacement face a high mortality (14%-24%) and greater long-term need for permanent pacemaker implantation (15%) because of atrioventricular block.[10,11] Other serious disadvantages of MV replacement in a growing child include patient–prosthesis mismatch, requiring serial valve replacements, and obligatory lifelong anticoagulation therapy.[12,13] The aim of our study was to evaluate the durability of MV repair in children below 10 years of age and to show if it is an advisable strategy for these patients.

Patients and Methods

Study Design and Study Population

In this retrospective study we reviewed all patients up to 10 years old undergoing MV repair between February 1975 and December 2017 at the German Heart Center Munich. Patients with complete or partial atrioventricular septal defects and single-ventricle physiology were excluded from analysis. Data for the present study were collected by reviewing medical records, operative notes, and telephone interviews with the referring pediatric cardiologist. Depending on the etiology and underlying diagnosis, patients were divided into 2 groups: patients

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with congenital MVD and patients with acquired MVD, with each group of patients with either prevalent mitral regurgitation (MR) or mitral stenosis (MS).

Follow-up was conducted in our outpatient clinic or by the referring pediatric cardiologists. Operative mortality was defined as described by the Society of Thoracic Surgeons.[14] Endpoints of the study were survival after MV repair and cumulative incidence of reoperation. This study was approved by the Institutional Review Board of the Technical University Munich, and the need for patient consent was waived.

Evaluation of the MV

Evaluation of the MV was performed by transthoracic echocardiography at baseline and discharge. Transthoracic echocardiography was performed according to the American Society of Echocardiography guidelines.[15,16] MR was graded as mild, moderate, moderate to severe, or severe based on qualitative parameters (color-flow jet area and mitral inflow) and semiquantitative or quantitative measures (vena contracta width and regurgitant fraction).[15] MS was graded on the basis of the mean pressure gradient across the valve as mild, <5 mmHg; moderate, ≥5 mmHg but ≤10 mmHg; and severe, >10 mmHg.[16] Left ventricular linear dimensions were assessed in the parasternal long-axis view, using 2-dimensional–targeted M-mode echocardiography.[17] Left ventricular volume and left ventricular ejection fraction were measured in the apical 2-chamber view, using the 2-dimensional modified Simpson's rule.[17] Classification of the predominant MV lesion was done according to Carpentier.[7,18]

Surgical Techniques

All patients were operated through a median sternotomy, with cardiopulmonary bypass and mild hypothermia at 32°C core temperature. Exposure of the MV was gained through a left atriotomy or by incision of the interatrial septum. Injection of saline solution into the left ventricle and careful examination with hooks were performed to assess the coaptation and mobility of the valve leaflets. Interrupted stitches or continuous locked sutures were used for direct closure of leaflet defects or clefts. Different patch materials, namely glutaraldehyde (0.2%)-treated autologous pericardium and decellularized bovine pericardium (CardioCel; Admedus Regen Pty Ltd, Perth, WA, Australia), were applied for leaflet augmentation. Gore-Tex neo-chordae (W.L. Gore & Assoc Inc, Newark, DE) were used for chordal replacement. Assorted annuloplasty rings, ranging from rigid complete to semirigid partial design, were also implanted.

Statistical Analysis

Data were analyzed using SPSS, version 25.0 for Windows (IBM Corp, Armonk, NY) and R (version 3.5.2; R Foundation for Statistical Computing, Vienna, Austria). All continuous variables were non-normally distributed and reported as median with range of minimum and maximum. For time-to-event analysis the mean with SD was reported for follow-up time. Categorical variables were expressed as numbers and percentages. The 2-tailed χ^2 test was used for analysis of categorical data, whereas continuous variables were compared using the Mann-Whitney U test. Kaplan-Meier analysis was applied to calculate estimated survival. The log-rank test was used to compare the survival of patients with congenital MR and MS. Competing risk analysis was used to calculate the cumulative incidence of reoperation. Estimated incidences of survival and reoperation were described at the mean follow-up time. Thus the Kaplan-Meier plots of survival and the competing risk analysis for death and reoperation were truncated at the mean follow-up time. An event-specific proportional risk model was used to calculate the hazard ratio for reoperation. Statistical significance was set at $P < .05$.

Results

Patients With Congenital MVD

Congenital MVD was present in 40 patients with a median age and weight at surgery of 1.2 years (range, 14 days to 9.8 years) and 8.2 kg (range, 2.9-41.9), respectively. Nineteen patients (47.5%) were below 1 year of age. Thirty-one patients (77.5%) showed a prevalent MR, whereas a significant MS was seen in only 9 patients (22.5%). The main reasons for MR were either leaflet clefts in 17 patients (42.5%) or leaflet restrictions due to shortened chordae in 5 patients (12.5%). MS was due to a supravalvar ring (n = 3), papillary muscle–commissural fusion (n = 3), or a parachute valve (n = 3). Further characteristics at baseline and details of MV pathologies are depicted in Tables 1 and 2. Surgical procedures are specified in Table 3.

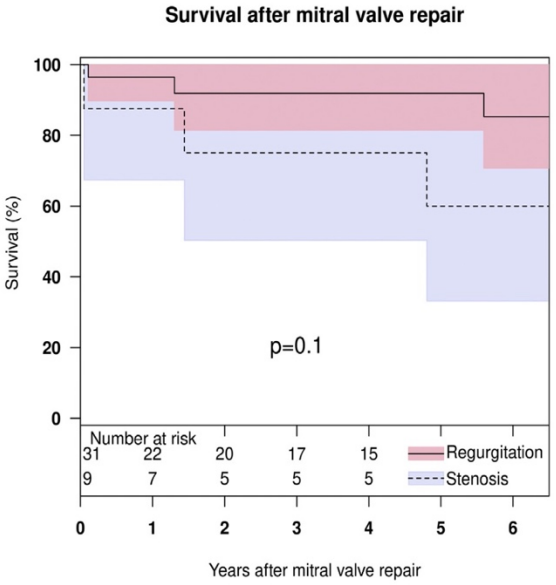

Figure 1. Kaplan-Meier plots of survival of patients with mitral regurgitation (red) or mitral stenosis (blue).

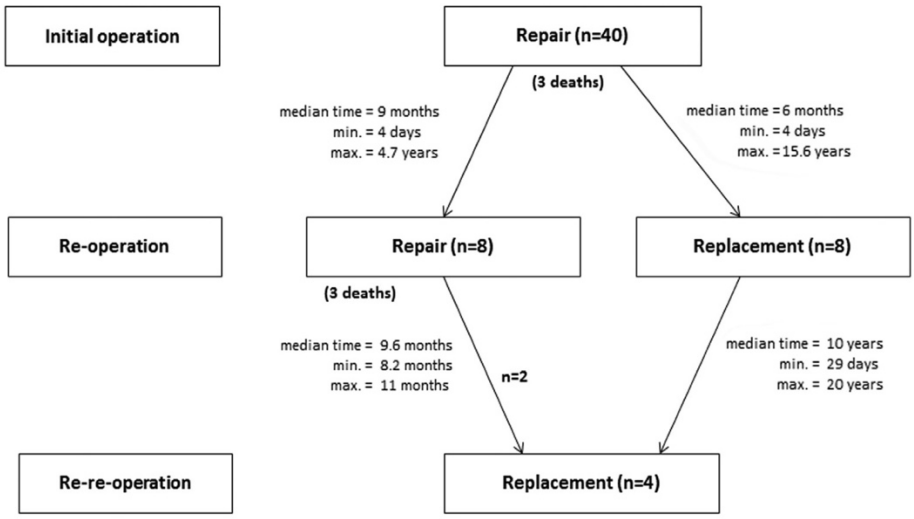

Figure 2. Clinical course and outcomes for patients with congenital mitral valve disease. (max., maximum; min., minimum.)

Autologous pericardium for leaflet augmentation was used in all patients. For ring annuloplasty the following ring prostheses were used: Puig-Massana-Shiley Ring (Shiley Incorporated, Irvine, CA) in 1, Colvin-Galloway Future Ring (Medtronic Inc, Minneapolis, MN) in 2, and Colvin-Galloway Future Band (Medtronic Inc) in 1 patient. Median cardiopulmonary bypass time was 94 minutes (range, 51-295), and median aortic cross-clamp time was 64 minutes (range, 16-177). The end-diastolic volume of the left ventricle decreased from a preoperative median volume of 54.5 mL (range, 11-161) to a postoperative median volume of 36.5 mL (range, 1.6-112; $P = .1$). The left ventricular ejection fraction decreased from a preoperative median ejection fraction of 75% (range, 46%-94%) to a postoperative median ejection fraction of 61.5% (range, 40%-88%; $P = .001$).

Operative mortality was 5% (n = 2). One patient with pulmonary atresia, intact ventricular septum, and severe MR died at age 7.2 months in low cardiac output, 39 days after MV repair, including 4 days after redo MV repair. One patient with congenital aortic stenosis and MS died at age 8.6 months, 18 days after commissurotomy of the aortic and MV due to severe residual aortic valve stenosis.

Late mortality was 10% (n = 4) within a median of 3.1 years (range, 1.3-5.6) after MV repair. Two patients with

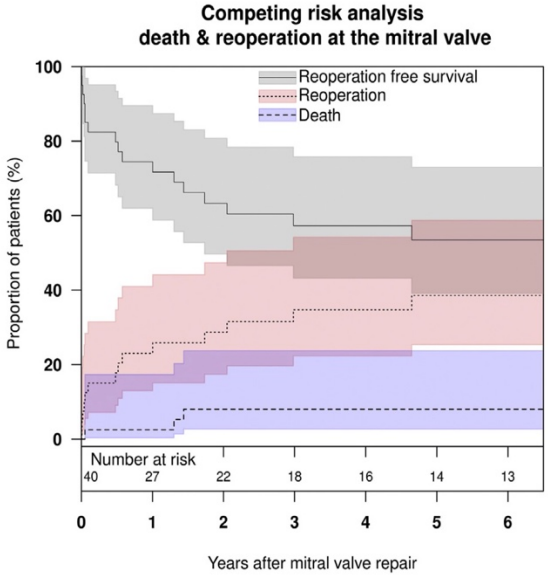

Figure 3. Competing risk analysis for death and reoperation at the mitral valve. Cumulative incidence of reoperation (red) and death with no reoperation (blue). The gray curve shows the patients alive without reoperation.

Table 1. Baseline Characteristics of Patients With Congenital Mitral Valve Disease

Characteristic	Value
Median age, y (range, days-years)	1.2 (14-9.8)
Median weight, kg (range)	8.2 (2.9-41.9)
Male sex	16 (40)
Mitral regurgitation	31 (77.5)
Mitral stenosis	9 (22.5)
Associated cardiac malformations	32 (80)
Ventricular septal defect	11 (27.5)
Aortic stenosis (valvar/subvalvar)	6 (15)
Atrial septal defect II (ostium secundum)	4 (10)
Shone's complex	3 (7.5)
Pulmonary atresia + intact ventricular septum	2 (5)
Tricuspid regurgitation	2 (5)
Transposition of the great vessels	2 (5)
Persistent foramen ovale	1 (2.5)
Patent ductus arteriosus	1 (2.5)

Values are n (%) or median (range).

Table 2. Classification of Congenital Mitral Valve Lesions

Classification	No. of Cases (%)
Mitral valve regurgitation	31 (77.5)
Type I (normal leaflet motion)	21 (52.5)
Annular dilatation	3 (7.5)
Cleft leaflet	17 (42.5)
Leaflet defect	1 (2.5)
Type II (leaflet prolapse)	3 (7.5)
Elongated chordae	3 (7.5)
Type III (restricted leaflet motion)	7 (17.5)
Short chordae	5 (12.5)
Fused commissures	1 (2.5)
Others	1 (2.5)
Mitral valve stenosis	9 (22.5)
Type A (normal papillary muscle)	6 (15)
Supravalvar ring	3 (7.5)
Papillary muscle–commissural fusion	3 (7.5)
Type B (abnormal papillary muscle)	3 (7.5)
Parachute valve	3 (7.5)

additional left ventricular obstruction died of right-sided heart failure more than 8 years after MV repair. In both patients a redo repair had been performed 3 and 4.7 years after MV repair, respectively. One patient died from a viral myocarditis caused by parvovirus B19 more than 1 year after successful MV repair. One patient with MS died of unknown cause 1.4 years after MV repair.

Survival rate at 6 years was 78.6% ± 8%. Patients with congenital MR showed a better, yet not significant, 6-year survival than patients with congenital MS (85.3% ± 8.2% vs 60% ± 18.2%; $P = .1$) (Figure 1).

Mean follow-up time was 6.2 ± 6.9 years, with a median follow-up time of 3.9 years (range, 3 days to 32 years). In

Table 3. Surgical Techniques of Congenital Mitral Valve Repair

Surgical Technique	No. of Cases (%)
Supravalvar repair	3 (7.5)
Resection of a supramitral membrane	3 (7.5)
Valvar repair	32 (80)
Ring annuloplasty	4 (10)
Rigid, complete ring	1 (2.5)
Semirigid, complete ring	2 (5)
Semirigid, partial ring	1 (2.5)
Leaflet procedure	22 (55)
Leaflet/cleft suture	19 (47.5)
Triangular leaflet resection	1 (2.5)
Leaflet augmentation	2 (5)
Alfieri stitch	3 (7.5)
Commissurotomy	3 (7.5)
Subvalvar repair	5 (12.5)
Chordal replacement	1 (2.5)
Papillary muscle splitting	4 (10)

16 patients (40%) a reoperation was performed after initial MV repair. Residual moderate to severe MR was seen in 6 patients, severe MR in 4 patients, moderate MS in 5 patients, and severe MS in 1 patient. In 2 patients reasons for persistent severe MR were functional causes, and in the other 14 patients residual MR or MS was due to morphologic dysfunction of the repaired MV. In 8 patients (50%) a redo repair was performed at a median time of 9 months (range, 4 days to 4.7 years), and 8 patients required a valve replacement at a median time of 6 months (range, 4 days to 15.6 years). During follow-up 4 patients required a MV replacement as re-reoperation. An overview of the clinical course of patients with congenital MVD is shown in Figure 2.

Cumulative incidence of reoperation at 6 years was 38.6% ± 8.3% (Figure 3). In patients with congenital MS risk for reoperation was not significantly higher than for patients with congenital MR (hazard ratio, 1.5; 95% confidence interval, 0.4-2.5; $P = .49$).

Patients With Acquired MVD

Ten patients presented with an acquired MVD, all with prevalent MR. Median age at time of surgery was 1.9 years (range, 10 days to 9.9 years). Reasons for acquired MVD were endocarditis in 5 patients (50%), anomalous left coronary artery originating from the pulmonary artery in 3 patients (20%), and iatrogenic in 2 patients (20%). Iatrogenic MVD included a perforation of the MV after dislocation of a septal occluder and perforation of the anterior MV leaflet during the resection of a left ventricular outflow tract obstruction. Surgical procedures were leaflet suture in 4 patients (40%), cleft suture in 2 patients (20%), and leaflet augmentation in 2 patients (autologous pericardium in 1 patient, CardioCel patch in 1 patient).

Further baseline and operative characteristics of this subgroup are shown in Table 4. No deaths occurred. In 3 patients (30%) a redo repair of the MV because of persistent moderate to severe MR was performed at 3, 30, and 45 days, respectively, after initial MV repair. One patient required a valve replacement 26 days after redo MV repair because of recurrent severe MR.

Comment

The present investigation shows that in children up to 10 years of age, surgical repair of the MV seems beneficial, achieving a survival rate of 79% at 6 years for patients with congenital MVD, whereas patients with congenital MR showed a better, yet not significant, 6-year survival than patients with congenital MS. In patients with congenital MVD cumulative incidence of reoperation at 6 years was 39%.

The most challenging issue in treating pediatric patients with congenital MVD is the range of pathologies affecting leaflets and subvalvar elements of the MV. Systematic classification is thus difficult, as are attempts at surgical standardization, unlike in adults with acquired valvar heart disease. There are excellent, reproducible means of classifying MV pathology in adults[7] contributing to the exceptional outcomes of surgical MV repair

Table 4. Baseline and Operative Data of Patients With Acquired Mitral Valve Disease

Characteristic	Value
Median age, y (range, days-years)	1.9 (10-9.9)
Median weight, kg (range)	10.6 (3.8-30.4)
Male sex	5 (50)
Mitral regurgitation	10 (100)
Endocarditis	5 (50)
Functional	3 (30)
Iatrogenic	2 (20)
Type I leaflet defect	4 (40)
Type I cleft leaflet	2 (20)
Type II elongated chordae	1 (10)
Type II ruptured chordae	1 (10)
Type III fused commissures	1 (10)
Type III others	1 (10)
Associated cardiac malformations	6 (60)
Anomalous left coronary artery originating from the pulmonary artery	3 (50)
Atrial septal defect II (ostium secundum)	2 (33)
Ventricular septal defect	1 (17)
Leaflet suture	4 (40)
Cleft suture	2 (20)
Leaflet augmentation	2 (20)
Chordal replacement	1 (10)
Chordal shortening	1 (10)

Values are n (%) or median (range).

in these patients.[19-21] In a prospective investigation conducted by David and coworkers,[20] the probability of MV reoperation 20 years after initial repair was 5.9% in patients 60 years of age, and freedom from recurrent severe MR was 90.7%. To repair a prolapsed posterior mitral leaflet in adult patients either resection (triangular or quadrangular) or nonresection (chordal replacement) is a viable approach.[22] Lange and colleagues[23] have achieved excellent midterm results through nonresection, which allows the use of larger annuloplasty rings and better physiologic repair, preserving leaflet mobility.

Given these encouraging experiences in adult patients, MV repair has increasingly been applied to children, with good long-term results.[8,9,24,25] However more in-depth analysis is needed to reconcile disparities in outcomes. In our cohort 6-year survival after MV repair was 79%, compared with an 86% survival at 15 years cited by Yakub and colleagues[8] and 93% survival recorded at 20 years by Vida and associates.[9] The median age of our patients with congenital MVD was 1.2 years and for patients with acquired MVD 1.9 years, as opposed to 11 years in the Yakub study and 7 years in Vida's analysis. There was also a higher incidence of associated cardiac defects in our patients, perhaps explaining the difference in survival. We found that patients with congenital MR showed a better, yet not significant, 6-year survival than patients with congenital MS. The frequent association of MS with other left heart obstructive defects may predispose to lethal events.[26]

In children the underlying morphology determines the available surgical options for MV repair. Most MV repairs performed in patients with congenital and acquired MVD were leaflet procedures. Leaflet augmentation was mainly used to treat restrictive leaflets. According to Shomura and coworkers,[27] use of glutaraldehyde-treated autologous pericardium for leaflet augmentation produced good late-term results, with 82% freedom from reoperation at 10 years. In patients with pure dilatation of the mitral annulus, prosthetic annuloplasty rings have proven similarly beneficial for children 11 years of age, with a freedom from reoperation of 79% at 10 years.[8] However the threshold for such implants is higher in smaller children, restricted by their future growth.

The inevitable growth of pediatric patients is both the chief limitation in MV surgery and the principal argument for primary repair instead of valve replacement. Valve replacement at early ages necessitates a multitude of reoperations due to outgrowth of the prosthesis. In terms of freedom from MV reoperation in patients with congenital MVD Vida and colleagues[9] reported a rate of 92% at 10 years, whereas in our study the cumulative incidence of reoperation at 6 years was 39%. This discrepancy can be explained by the higher age at operation and lower incidence of associated cardiac defects in the study by Vida and colleagues. In our study the risk for reoperation in patients with congenital MS was not significantly higher than for patients with congenital MR. This finding was confirmed by Stellin and colleagues[24] and Vida and colleagues.[9]

When comparing patients with congenital MVD and patients with acquired MVD, repair of primary congenital MVD is more complex than repair of acquired MVD reflected in the different reoperation rates and need for valve replacement after initial MV repair. In the present investigation patients with congenital MVD had a higher incidence of MS and left heart obstructive defects such as Shone's complex and severe aortic valve stenosis, resulting in an operative mortality of 5% and a late mortality of 10%. In the retrospective study by Vida and colleagues[9] early and late mortality for patients with congenital MVD was 5% and 9%, respectively, confirming our mortality rates in congenital MVD patients. In the group of patients with acquired MVD no deaths were seen, which underlines the lesser complexity of these patients. It is also important to stress that in our patients acquired MVD was mostly due to endocarditis or functional reasons, resulting in prevalent MR in contrast to most published investigations in which acquired MVD was due to rheumatic causes.[8,28] In patients with rheumatic etiology MV repair is usually more challenging and complex,[13] making a comparison with our subgroup of patients with acquired MVD difficult.

Limitations of this study include its single-center, nonrandomized, and retrospective design. The number of available patients was also rather small for such a long study period, and morphology of the MV was heterogeneous. Finally inconsistencies in preoperative, operative, and postoperative management may have affected our outcome parameters in a way not covered by our analysis.

In conclusion the durability of MV repair in children below the age of 10 years depends on the etiology of the MVD and the underlying morphology. Although MV replacement is not always inevitable in the long term, a repair of the valve should still be the goal of treatment in such patients, even if it just delays the time to replacement.

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Anhang II

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Tricuspid valve repair in children with hypoplastic left heart syndrome: impact of timing and mechanism on outcome

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Key question

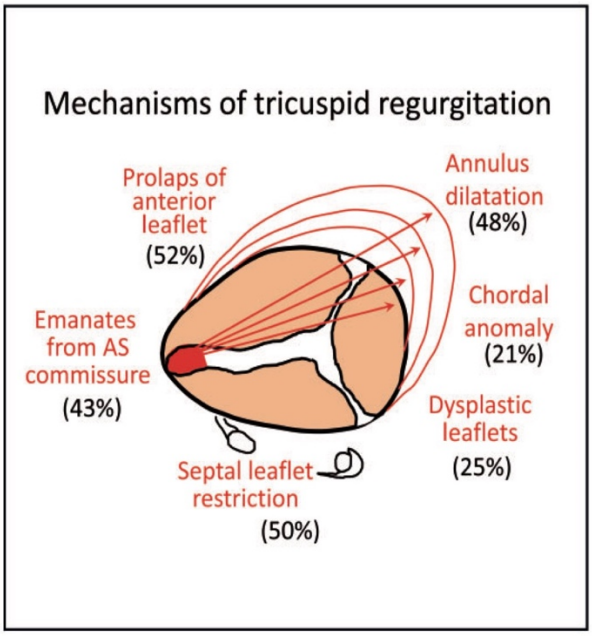
What are the significant risk factors affecting outcome after tricuspid valve repair in children with hypoplastic left heart syndrome?

Key finding(s)

Early need for tricuspid valve repair, septal leaflet restriction and chordal anomalies are significant predictors of worse outcomes.

Take-home message

Refinement of repair techniques in early infancy, especially for septal leaflet restriction and chordal anomalies, is mandatory to improve outcomes.



Abstract

OBJECTIVES: Our aim was to evaluate the results of tricuspid valve repair (TVr) in patients with hypoplastic left heart syndrome during staged reconstruction, focussing on the timing of the repair and the mechanisms of tricuspid regurgitation (TR).

METHODS: Records of 44 children with hypoplastic left heart syndrome who underwent a total of 62 tricuspid valve (TV) procedures during staged reconstruction were retrospectively analysed.

RESULTS: TVr was performed before stage II in 4 (9%) patients, at stage II in 23 (52%) patients, between stages II and III in 3 (7%) patients and at stage III in 14 (32%) patients. The median age at the first TV procedure was 5 months. At surgery, TR emanated commonly from the

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anteroseptal commissure in 21 (48%) patients. Anterior leaflet prolapse was observed most frequently ($n = 23$; 52%), followed by septal leaflet restriction ($n = 22$; 50%), dilated annulus ($n = 21$; 48%) and cleft anterior leaflet ($n = 9$; 21%). Surgical techniques included commissuroplasty in 27 (61.4%) patients, leaflet adaptation in 20 (44%) patients, partial annuloplasty in 11 (25%) patients, chordal reconstruction in 10 (23%) patients and cleft closure in 10 (23%) patients. Among all 44 patients, 27 (61%) patients had preoperative grade III TR and 17 (39%) patients had grade IV; postoperatively, there were no patients with grade IV, 25 patients with grade III (57%), 10 patients with grade II (23%) and 6 patients with grade I (14%). Fifteen patients required redo TV surgeries. Reoperation-free survival was 52% at 5 years. Lower weight at initial TVr predicted mortality [hazard ratio (HR) 0.7, $P = 0.044$] and reoperation (HR 0.8, $P = 0.015$). TVr before stage II was a risk for both reoperation (HR 5.5, $P = 0.042$) and TV replacement (HR 36.9, $P = 0.013$). Among morphological factors, septal leaflet restriction was a risk for reoperation (HR 4.7, $P = 0.017$) and anterior (HR 4.7, $P = 0.037$) and posterior (HR 7.3, $P = 0.015$) leaflet chordal anomaly for TV replacement.

CONCLUSIONS: Anterior leaflet prolapse and septal leaflet restriction are the main mechanisms of TR in hypoplastic left heart syndrome. Early-onset TR before stage II predicts worse outcome. Refinements to repair techniques in early infancy, especially for septal leaflet restrictions and chordal anomalies, are mandatory to improve outcomes.

Keywords: Hypoplastic left heart syndrome • Tricuspid regurgitation • Tricuspid valve repair

ABBREVIATIONS

AA	Aortic atresia
AoS	Aortic stenosis
HLHS	Hypoplastic left heart syndrome
HR	Hazard ratio
IQR	Interquartile ranges
MA	Mitral atresia
MS	Mitral stenosis
RV	Right ventricle
RVFAC	Right ventricular fractional area change
TR	Tricuspid regurgitation
TV	Tricuspid valve
TVr	Tricuspid valve repair
TVR	Tricuspid valve replacement

INTRODUCTION

Tricuspid regurgitation (TR) is reported in up to 25% of children with hypoplastic left heart syndrome (HLHS) and remains an important risk for successful staged palliation [1–3]. The pathophysiology of TR is complex and multifactorial, including morphological abnormalities of the tricuspid valve (TV) and functional causes such as tricuspid annular dilatation and right ventricular (RV) dysfunction [4–10]. Changes in the geometry of the RV and TV apparatus according to age have also been implicated in the development of TR [11, 12].

As for the timing of surgical intervention, significant TR may emerge at various points. Significant TR at birth may require TV repair (TVr) concomitant with Norwood procedure [13, 14]; TR that develops after the Norwood procedure may require isolated TVr before or at the stage II procedure [10, 14]. TR may develop even after volume unloading by stage II palliation [15], and some children need TVr before or concomitant with the Fontan procedure [10, 14].

Previous studies have shown that TVr ameliorates TR and contributes to improved outcomes in HLHS [10, 13–18]. Various techniques for TVr have been reported [14–20]. However, no standard guideline exists regarding indication, timing and surgical approach. TVr may be necessary at various points during the staged palliation, but explicit recommendations on when to repair the TV in this specific patient population are still lacking, while the durability of TVr is limited and the results of TVr are far from satisfactory. Few studies offer a systematic evaluation of the exact mechanisms of TR with the objective of tailoring the surgical technique to the specific abnormality.

The aim of our study was to evaluate the mechanisms of TR in children with HLHS using intraoperative findings at initial TVr, to evaluate the results of TVr during staged reconstruction and to analyse the risk factors influencing survival, redo TV surgery and TV replacement (TVR) with attention to the aetiology of TR.

MATERIALS AND METHODS

Ethical statement

The Institutional Review Board of the Technical University of Munich approved the study.

Patients

We reviewed the medical records of all 249 consecutive patients with classic HLHS who underwent a Norwood procedure at the German Heart Center Munich between 1999 and 2018, and patients who underwent TVr during staged reconstruction were included in this study. Medical records including in-hospital and outpatient notes and echocardiography data were reviewed. Mechanisms of TR at the initial repair were enumerated based on operative records.

Indication and timing of tricuspid valve repair

Moderate TR was either addressed in a separate procedure or added to a planned surgery, and severe TR was addressed in a separate procedure between the staged procedures. Indications for TVr were based on transthoracic echocardiography findings and confirmed by intraoperative transoesophageal echocardiography. Usually, severe recurrent TR was treated as soon as it was detected, whereas moderate recurrent TR was addressed at the next stage of palliation.

Operative techniques

TV repair was performed under standard cardiopulmonary bypass with cardioplegic cardiac arrest, and the mechanism of TR

Table 1: Baseline characteristics of patients

Variables	
Total number of patients	44
Total number of TV procedures	62
Primary diagnosis	
Aortic atresia, *n* (%)	29 (65.9)
Mitral atresia, *n* (%)	17 (38.6)
Diameter of ascending aorta (mm), median (IQR)	3.0 (2.0–3.8)
Pre-Norwood echocardiography	
TR, median (IQR)	1.0 (0.8–2.0)
TAPSE, median (IQR)	12 (10–12)
Reduced RV function, *n* (%)	2 (4.5)
Premature birth, *n* (%)	3 (6.8)
Associatied extracardiac anomaly, *n* (%)	6 (13.6)
Norwood operation	
Age at Norwood (days), median (IQR)	9 (7–11)
Weight at Norwood (kg), median (IQR)	3.2 (2.9–3.6)
Operation time (min), median (IQR)	274 (236–304)
CPB time (min), median (IQR)	143 (110–163)
AXC time (min), median (IQR)	50 (41–59)
BT shunt, *n* (%)	24 (54.5)
RV–PA conduit, *n* (%)	20 (45.5)
Time of initial TV procedure, *n* (%)	
Before stage II (BCPS)	4 (9.1)
Stage II	23 (52.3)
Between stages II and III	3 (6.8)
Stage III (Fontan)	14 (31.8)
Age at first TV procedure (months), median (IQR)	5 (3–19)

AXC: aortic cross-clamp; BCPS: bidirectional cavopulmonary shunt; BT: Blalock-Taussig; CPB: cardiopulmonary bypass; IQR: interquartile range; PA: pulmonary artery; RV: right ventricle; TAPSE: tricuspid annular plane systolic excursion; TR: tricuspid regurgitation; TV: tricuspid valve.

was assessed by saline injection in the RV. Attention was paid to the annular dimension, commissural leak and prolapse, restriction, cleft or perforation of the leaflets, as well as abnormalities of the subvalvular apparatus. We did not perform papillary muscle approximation. Details of surgical techniques were described in our previous study [6]. In case of severe residual regurgitation or irreparable leaflet abnormalities, TVR was performed using a standard bi-leaflet mechanical valve. Intraoperative transoesophageal echocardiography was performed routinely. The repair was revised if residual regurgitation was moderate or severe.

Echocardiography

An experienced echo cardiographer reviewed the archived echocardiography data from pre-Norwood, pre-initial TVr and post-repair imaging and assessed the RV function quantitatively by calculating the RV fractional area change (RVFAC) [10]. TV function was assessed by the degree of TR, the size of the TV annulus, vena contracta (VC) and tricuspid annular plane systolic excursion, as described in our previous study [21]. The degree of TR was determined by the width and length of the insufficiency jet.

Follow-up data

The patients maintained outpatient follow-up with paediatric cardiologists, and follow-up times were defined per patient as the time from initial TVr to last follow-up. For patients who died, censoring occurred at the time of death. The data were regularly tracked using our institutional single ventricle patient database system.

Identification of factors affecting mortality and redo tricuspid valve operation

Risk factors for death, redo operation and TVR following the initial repair were identified using Cox regression models. Independent variables included morphological and functional characteristics listed in Supplementary Material, Table S1.

Statistical analysis

Categorical variables are presented as absolute numbers and percentages. A χ^2 test was used for categorical data. Continuous variables are expressed as means ± standard deviations or medians with interquartile ranges (IQR), if appropriate. An independent sample *t*-test was used to compare normally distributed variables. The Mann–Whitney test was used for variables that were not normally distributed. Overall survival was determined by using the Kaplan–Meier method. A competitive risk analysis for reoperation and death was performed. The results were reported as cumulative incidences. Risk factors influencing survival, reoperation and TVR were identified using a Cox regression method. Data analysis was performed using Statistical Package for the Social Sciences (SPSS), version 25.0 for Windows (IBM, Ehningen, Germany) and R-statistical software (state package and CMPRSK package).

RESULTS

Patient characteristics and timing of initial tricuspid valve repair

Among 249 patients with classic HLHS who underwent Norwood procedures, 44 (17.7%) patients underwent a total of 62 TV procedures during staged reconstruction. Their baseline characteristics, Norwood procedure-related data and timing of initial TV repair are presented in Table 1.

Mechanisms of tricuspid regurgitation

Mechanisms of TR according to surgical findings at the initial TV procedure and those at each palliation stage are shown in Table 2. Most commonly, TR emanated along the anteroseptal (AS) commissure ($n = 21$, 43%). Anterior leaflet prolapse was identified in 23 patients (52%) and posed the most common pathology of TR (Fig. 1). The second most common cause was septal leaflet restriction, which was observed in 22 (50%) patients.

Surgical procedures

Details of the initial TVr and detailed description of the surgical techniques for each palliative stage are found in Table 3. The most common surgical technique was approximation of the AS commissure ($n = 27$; 61%), followed by leaflet adaptation in 20 (46%) patients and approximation of the SP commissure in 11 (25%) patients. Eleven (25%) patients had annuloplasty. TV repair

Table 2: Mechanisms of tricuspid regurgitation at initial tricuspid valve repair

Variables	*N* (%)				
Stage		Norwood or post	At BCPS	Post BCPS	Fontan
Number of patients	44	4 (9.1)	23 (52.3)	3 (6.8)	14 (31.8)
Site of regurgitation					
Central	16 (36.4)	2 (50)	6 (26.1)	3 (100)	5 (35, 7)
AS commissure	21 (42.7)		14 (60.9)	1 (33.3)	6 (42.9)
AP commissure	9 (20.5)	1 (25)	6 (26.1)		2 (14.3)
SP commissure	8 (18.2)	1 (25)	4 (17.4)		3 (21.4)
Primary pathology					
Annulus dilation	21 (47.7)	1 (25)	9 (39.1)	3 (11)	8 (57.1)
Leaflet prolapse	27 (61.4)	3 (75)	14 (60.9)	1 (33.3)	9 (64.3)
Anterior	23 (52.3)	2 (50)	14 (60.9)		7 (50.0)
Septal	3 (6.8)		1 (4.3)		2 (14.3)
Posterior	5 (11.4)	1 (25)	1 (4.3)	1 (33.3)	2 (14.3)
Restrictive leaflet	24 (54.5)	2 (50)	17 (73.9)	1 (33.3)	5 (35.3)
Anterior					
Septal	22 (50.0)	1 (25)	17 (73.9)	1 (33.3)	3 (21.4)
Posterior	7 (15.9)	1 (25)	1 (17.4)		2 (14.3)
Cleft	10 (22.8)				
Anterior	9 (20.5)	1 (25)	6 (26.1)		2 (14.3)
Septal					
Posterior	1 (2.3)		1 (4.2)		
Dysplastic leaflet	11 (25.0)		5 (21.7)	1 (33.3)	6 (42.9)
Anterior	8 (18.2)		3 (13)		5 (35.7)
Septal	9 (20.5)		3 (13)	1 (33.3)	6 (42.9)
Posterior	10 (22.7)		4 (17.4)		6 (42.9)
Chordal anomalies	9 (20.5)		5 (21.7)	1 (33.3)	3 (21.4)
Anterior	4 (9.1)		1 (4.3)	1 (33.3)	2 (14.3)
Septal	4 (9.1)		3 (13)		1 (7.1)
Posterior	2 (4.5)		1 (4.3)	1 (33.3)	
Co-mechanisms	35 (79.5)	3 (75)	18 (78.3)	2 (66.7)	12 (85.7)

AP: anteroposterior; AS: anteroseptal; BCPS: bidirectional cavopulmonary shunt; SP: septal-posterior.

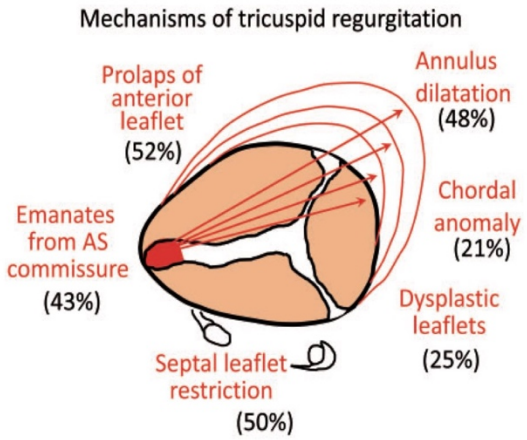

Figure 1: Mechanisms of tricuspid regurgitation in children with hypoplastic left heart syndrome.

was converted to TVR during the initial TV operation in 3 patients (Supplementary Material, Fig. S1).

Echocardiography

Echocardiographic data are shown in Table 4. Moderate TR was seen in 27 (61%) patients at the initial TV surgery, and severe TR was seen in 17 (39%) patients. No patient had severe TR after the initial TV surgery. TV annulus *Z*-score decreased after repair significantly ($P = 0.039$). RVFAC was not improved after TV surgery ($P = 0.61$).

Outcomes after initial tricuspid valve surgery

Two patients died in hospital (5%). The first was a 13-day-old girl who died with low cardiac output on the fourth postoperative day after TV repair with Norwood. The second was a 6-month-old boy who underwent isolated TV repair prior to BCPS and died with heart failure on postoperative day 19.

The median follow-up period after the initial TVr was 4.8 years (IQR 2.3–6.7). There were 9 late deaths during a median follow-up of 7.7 months (IQR 4.3–19) after the initial TV surgery. The 5-year survival rate after the initial TV surgery was 73.4% (Supplementary Material, Fig. S2). Notably, the overall survival after Norwood was not significantly different ($P = 0.297$) between the 44 children who had TV surgery and the remaining 205 patients who did not (Supplementary Material, Fig. S3).

There were 15 patients who required redo TV surgeries at a median interval of 1.7 years (IQR 0.6–2.2) after the initial repair (Supplementary Material, Fig. S1). The median age at the second TV procedure was 2.1 years (IQR 1.6–2.7). Eight patients had redo repairs, 6 patients had TVR and 1 patient needed a re-replacement of a prosthetic valve. The reoperation-free survival was 52.1% at 5 years (Fig. 2). The cumulative incidence of reoperations was 36.1% at 5 years.

Table 3: Initial surgical technique

Variables	*N* (%)	Norwood or post	At BCPS	Post-BCPS	At Fontan
Initial repair technique		4 (9.1)	23 (52.3)	3 (6.8)	14 (31.8)
Valve reconstruction					
Leaflet adaptation	20 (45.5)	1 (25)	13 (56.5)		6 (42.9)
Cleft closure	10 (22.8)	1 (25)	7 (30.4)		2 (14.3)
Alfieri stitch	7 (15.9)	1 (25)	3 (13)		3 (21.4)
Bicuspidization	4 (9.1)		1 (3.3)	1 (33.3)	2 (14.3)
Pericard patch augumentation	5 (11.4)		5 (21.9)		
Commisural approximation					
AS commussure	27 (61.4)	1 (25)	14 (60.9)	2 (66.7)	10 (71.4)
AP commissure	9 (20.5)	2 (50)	4 (17.4)	1 (33.3)	2 (14.3)
SP commissure	11 (25.0)	1 (25)	8 (34.8)		2 (14.3)
Chordae reconstruction	10 (22.7)		6 (26.1)	1 (33.3)	4 (28.6)
Annuloplasty	11 (25.0)		6 (26.1)	1 (33.3)	4 (28.6)
DeVega	4 (9.1)		1 (4.3)	1 (33.3)	2 (14.3)
Partial annuloplasty	7 (15.9)		5 (21.5)		2 (14.3)

AP: anteroposterior; AS: anteroseptal; BCPS: bidirectional cavopulmonary shunt; SP: septal-posterior.

Table 4: Changes in tricuspid valve dimensions, area and vena contracta

Variables	Pre-Norwood	Pre-TV surgery	Post-TV surgery	*P*-value*
TR grade				
None	8	0	3	0.022
Trivial	20	0	6	
Mild	9	0	10	
Moderate	5	27	25	
Severe	2	17	0	
TV dimension				
TV annulus (mm)	14.09 ± 0.49	23.05 ± 5.33	23.76 ± 4.56	0.651
TV annulus *Z*-score	0.63 ± 1.08	2.29 ± 1.05	1.79 ± 1.10	0.039
Vena contracta (mm)	2.58 ± 1.69	4.95 ± 1.63	4.48 ± 1.86	0.362
RV function				
RVESA (cm^2)	2.83 ± 0.84	7.29 ± 3.24	8.04 ± 3.57	0.296
RVEDA (cm^2)	4.80 ± 1.17	11.44 ± 4.39	12.82 ± 4.43	0.168
RVFAC (%)	40.65 ± 9.44	35.93 ± 12.27	37.41 ± 11.63	0.606
TAPSE (mm)	11.16 ± 2.15	11.11 ± 2.77	10.33 ± 2.40	0.066
TAPSE *Z*-score	1.77 ± 1.84	-1.88 ± 2.01	-4.10 ± 2.00	<0.001

*Between pre- and post-TV surgery.

RV: right ventricle; RVEDA: right ventricle end-diastolic area RVESA: right ventricle end-systolic area; RVFAC: right ventriclular fractional area change; TAPSE: tricuspid annular plane systolic excursion; TR: tricuspid regurgitation; TV: tricuspid valve.

Risk factor analysis

Results of the risk factor analysis by Cox regression model are shown in Table 5. As for mortality, lower weight at the initial TV procedure was identified as an independent risk factor. As for reoperation, the univariate model identified septal leaflet restriction as a significant morphological factor. On multivariate analysis, TV surgery before stage II and lower weight at TV surgery were significant risks. As for TVR, anterior and posterior leaflet chordal anomalies were significantly associated with a higher risk on univariate analysis and pre-stage II operation was a significant risk on multivariate analysis. Detailed results of risk factor analyses for mortality, TV reoperation and TVR are shown in Supplementary Material, Tables S1–S3.

Because pre-stage II TV surgery was such a strong factor for each outcome, a subgroup analysis was performed using 40 patients who underwent initial TV surgery at stage II procedure or later. The results are shown in Supplementary Material, Table S4. In this subgroup, age at the initial TV surgery was not a risk for mortality or TVR. Instead, cardiopulmonary bypass time during Norwood was identified as a risk for mortality and regurgitation from the AS commissure emerged as a new risk for reoperation.

Influence of anatomical subtype and shunt type on the incidence of tricuspid valve operation

Influence of anatomical subtype of aortic atresia/stenosis (AA/AoS) and mitral atresia/stenosis (MA/MS) on incidence of TV operation was analysed (Supplementary Material, Table S5). Four anatomical subtypes did not influence the incidence of TV operation: AA/MA ($P = 0.230$), AA/MS ($P = 0.280$), AoS/MS ($P = 0.193$)

and AoS/MA ($P = 0.162$). Incidence of TV operation was higher in AA patients (22.3%) than in AoS patients (12.6%, $P = 0.045$) but similar in MA (18.9%) and MS (17.0%) patients ($P = 0.705$). The shunt type did not influence the incidence of TV operation ($P = 0.143$).

DISCUSSION

In the present study, TR commonly emanates from the AS commissure and the common mechanisms were anterior leaflet prolapse and septal leaflet restriction. Risk factor analysis identified early repair with lower weight at the initial TV surgery as an independent risks for mortality and morbidity. Among morphological factors, septal leaflet restriction was a predictor of TV reoperation and chordal anomalies predicted TVR.

Impact of timing of initial tricuspid valve intervention

Younger age at the initial TV surgery was identified as a significant risk factor. In particular, initial TV repair before stage II palliation was identified as a high risk for mortality [hazard ratio (HR) 6.1], reoperation (HR 6.8) and TVR (HR 51.8). Sano *et al.* [3] reported that moderate or greater TR at stage I palliation was

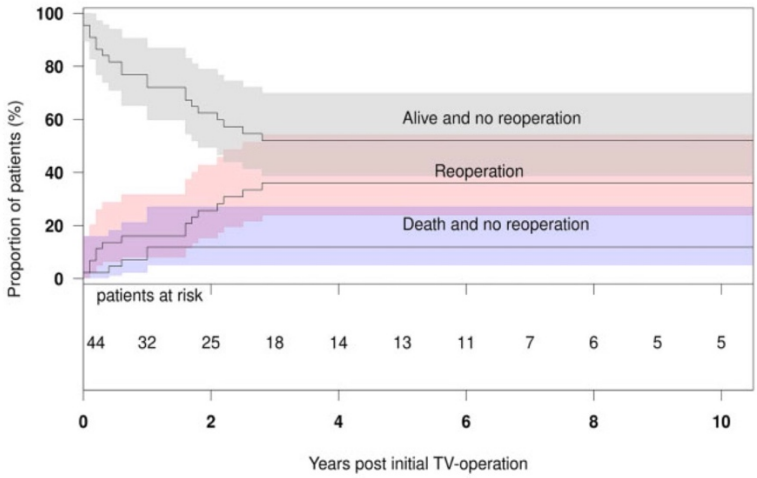

Figure 2: Outcome after TV repair in children with hypoplastic left heart syndrome: Cumulative incidence of reoperation (red) and death with no prior reoperation (purple). The grey curve shows the patients who are alive without reoperation. TV: tricuspid valve.

Table 5: Risk analysis for adverse outcome following tricuspid valve repair

	Univariate model			Multivariate model		
Variables	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Mortality						
Pre-stage II (BCPS)	6.092	1.587–23.381	0.008			
Age at initial TV procedure	0.874	0.749–1.019	0.085			
Weight at initial TV procedure	0.738	0.550–0.992	0.044	0.738	0.550–0.992	0.044
Reoperation						
TR pre-Norwood	1.490	0.941–2.360	0.089			
TAPSE pre-Norwood	0.731	0.508–1.051	0.091			
Z-score TAPSE pre-Norwood	0.694	0.454/1.060	0.091			
Pre-stage II (BCPS)	6.813	1.286–36.086	0.024	5.510	1.063–29.620	0.042
At stage II	3.043	0.962–9.625	0.058			
TR at initial TV procedure	2.393	0.860–6.663	0.095			
Age at initial TV procedure	0.912	0.840–0.990	0.027			
Weight at initial TV procedure	0.768	0.626–0.944	0.012	0.769	0.623–0.950	0.015
Restrictive septal leaflet	4.723	1.326–16.814	0.017			
Pericard patch augumentation	3.558	1.120–11.304	0.031			
TV replacement						
TR pre-Norwood	2.163	1.178–3.924	0.013			
Pre-stage II (BCPS)	51.762	5.104–524.94	0.001	36.917	2.165–629.63	0.013
Anterior leaflet chordal anomalies	4.382	1.095–17.541	0.037			
Posterior leaflet chordal anomalies	7.371	1.473–36.877	0.015			

BCPS: bidirectional cavopulmonary shunt; CI: confidence interval; HR: Hazard ratio; TAPSE: tricuspid annular plane systolic excursion; TR: tricuspid regurgitation; TV: tricuspid valve.

associated with worse outcome, and Sugiura *et al.* [19] also showed that the survival of patients with HLHS who develop moderate or greater TR around the time of the first palliative surgery is worse. Our results are quite consistent with these studies. Significant TR at first presentation remains a very challenging problem with very poor prognosis. These small infants may have intrinsic valve abnormalities, and very fragile valve tissue would render successful repair notoriously difficult. Meza *et al.* [22] have recommended that prompt referral for heart transplantation may offer a greater chance at long-term survival in post-Norwood patients with significant valve pathology. Patients who underwent TV surgery concomitant with stage II palliation or later had better survival. However, younger age is still a risk for reoperation, indicating that early-emerging TR is technically difficult to manage.

Mechanisms of tricuspid regurgitation in hypoplastic left heart syndrome

In this study, TR emanated mainly from the AS commissure, which supports the findings of Bautista-Hernandez *et al.* [10] and Nii *et al.* [11]. The most common structural abnormalities in our patients were prolapsed anterior leaflet and septal leaflet restriction. This result is also consistent with the previous reports; Bharucha *et al.* [9] found anterior leaflet abnormality in 97%, septal leaflet abnormality in 91% and posterior leaflet abnormality in 66% in 32 patients with HLHS. Bautista-Hernandez *et al.* [10] found that 69% of patients with HLHS had leaflet prolapse and 63% had leaflet restriction. Takahashi *et al.* [12] used 2- and 3-dimensional echocardiography in 35 patients with HLHS and confirmed the link between TR and leaflet tethering or prolapse. These previous reports and our findings emphasize that TR in HLHS is not merely functional but is caused by a structural abnormality of the valve. Our analysis identified septal leaflet restriction as a significant risk factor for TV reoperation. Sugiura *et al.* [19] described commissural gaps in addition to leaflet prolapse among morphological abnormalities of the TV. Thus, failure of leaflet adaptation due to prolapsed anterior leaflet or restricted septal leaflet is the most commonly described mechanisms of TR.

Secondary to these commonly described leaflet alterations, Bharucha *et al.* [9] have noted that dilation of the TV annulus is detectable at surgery in certain patients. The Norwood procedure will result in a shunt-dependent in-parallel circulation. The RV is exposed to considerable volume overload until the time of stage II palliation and the TV is more susceptible to pressure or volume overload. Kasnar-Samprec *et al.* [21] reported on 18 of 90 consecutive patients with HLHS and significant TR before stage II, and all patients had a dilated annulus, 61% had prolapsed anterior leaflet, and septal leaflet tethering was present in 67%. Unloading by BCPS promoted RV remodelling but failed to improve TR. Nii *et al.* [11] reported on TV annulus function in 26 patients with HLHS and found that annular dilatation and area change correlated with TR. Takahashi *et al.* [12] evaluated 35 patients with HLHS and observed an enlarged TV area in the HLHS group compared with a control group. Annular dilatation was more commonly associated with late-onset TR in our group and was found in 25% before stage II, 39% at stage II and 57% at Fontan. Therefore, there may be mechanisms of annular dilation besides shunt-dependent volume loading, including age-related geometrical changes in the RV and TV annulus. The possible mechanisms of TR are shown in Supplementary Material, Fig. S4.

It is well known that RV dysfunction is closely related to TR; Alsoufi *et al.* [14] showed that RV dysfunction is progressive after TV repair in patients with HLHS and is a major determinant of survival. Ohye *et al.* [16] analysed the results of 28 patients with HLHS and significant TR after stage I and reported that successful TV repair was predictive of preserved TV and RV function. We evaluated the RV function quantitatively by calculating RVFAC and tricuspid annular plane systolic excursion. RVFAC was not identified as a predictor of worse outcome, but tricuspid annular plane systolic excursion at Norwood operation was a risk for reoperation.

Repair techniques and durability of tricuspid valve repair

Tsang *et al.* [17] have published an overview of various surgical techniques for TV repair in HLHS. The most common surgical techniques were partial annuloplasty and commissuroplasty. An edge-to-edge repair is also applicable to the TV by suturing the free edges of the septal and anterior leaflets. If the septal leaflet is tethered by abnormally short chordae, chordae replacement is a potentially ideal solution. However, in our series, chordal anomalies were identified as favouring TVR rather than synthetic chordae. For a severely restricted septal leaflet, a downsizing annuloplasty combined with mobilization of chordae, and leaflet extension with a pericardial patch, is the preferred strategy.

The durability of the initial TV repair is limited. Honjo *et al.* [5] reported that survival without re-repair was 51%, and Alsoufi *et al.* showed that 10-year survival without reoperation was 61%. Our results are consistent with these outcomes.

Limitations

This study was limited by its retrospective and single-centre design. Mechanisms of TR were inferred from the operation records, and bias among surgeons can be expected. Because of the small size of some subgroups, results should be interpreted cautiously because only large effects could be identified. Finally, surgical and medical management may have changed during the study period, probably influencing the long-term outcomes.

CONCLUSIONS

TV repair is most commonly performed as a concomitant procedure during stage II palliation. Most often TR emanates from the AS commissure. Anterior leaflet prolapse and restriction of the septal leaflet are the main mechanisms of TR. Early onset of significant TR before stage II palliation was a significant risk for worse outcomes. Among morphological variables, restricted septal leaflet was identified as a risk for TV reoperation and chordal anomalies are a risk for TVR. Surgical management of septal leaflet restriction and anterior leaflet prolapse, often resulting from the remodelling of the right ventricle, might be the most important issue. Surgical management of early-onset TR is another important subject of concern.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

Conflict of interest: none declared.

Author contributions

Masamichi Ono: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Writing—original draft; Writing—review & editing; **Benedikt Mayr:** Data curation; Writing—original draft; **Melchior Burri:** Validation; Visualization; **Nicole Piber:** Data curation; Investigation; Project administration; **Christoph Röhlig:** Data curation; Formal analysis; **Martina Strbad**: Data curation; **Julie Cleuziou:** Investigation; Methodology; Project administration; **Alfred Hager:** Conceptualization; Methodology; Supervision; Validation; **Jürgen Hörer:** Conceptualization; Investigation; Project administration; Supervision; Validation; **Rüdiger Lange:** Conceptualization; Supervision.

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Anhang III

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Common atrioventricular valve surgery in children with functional single ventricle

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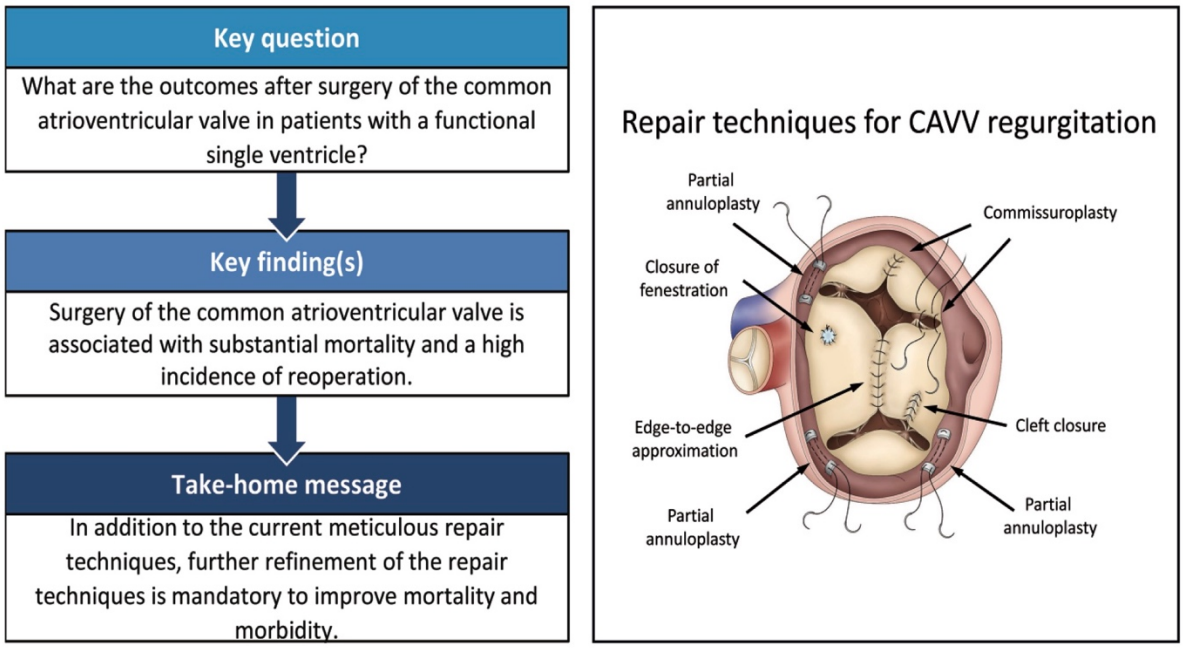

Abstract

OBJECTIVES: A common atrioventricular valve (CAVV) is considered to be a risk factor for early and late deaths in patients with functional single ventricle (FSV). CAVV surgery in patients with FSV is challenging and there is limited knowledge of the outcomes of CAVV repair with univentricular physiology.

Presented at the 34th Annual Meeting of the European Association for Cardio-Thoracic Surgery, Barcelona, Spain, 8–10 October 2020.

METHODS: We reviewed all CAVV surgical procedures in patients with FSV who underwent univentricular palliation. End points of the study were survival after CAVV surgery and cumulative incidence of reoperation.

RESULTS: Between 1984 and 2019, 66 children with CAVV and FSV underwent single-ventricle palliation, of whom 45.5% (30/66) required CAVV surgery. Indication for surgery was moderate CAVV regurgitation in 40% (12/30) and severe CAVV regurgitation in 60% (18/30). CAVV repair was performed in 93.3% (28/30) and CAVV replacement in 6.7% (2/30). The median age and weight at surgery were 0.9 years (interquartile range 0.3–1.8) and 6.5 kg (interquartile range 3.9–8.7), respectively. Operative and late mortality were 23.3% and 8.7%, respectively. Survival and cumulative incidence of reoperation at 4 years after CAVV surgery were 68.9% [standard deviation (SD): 8.7] and 35.8% (SD: 9.1), respectively. Fontan completion was achieved in 60% (18/30). Survival at 4 years after birth was 69.7% (SD: 8.5) in 30 patients with CAVV surgery, whereas it was 83% (SD: 6.3) in 36 patients without CAVV surgery ($P = 0.32$).

CONCLUSIONS: CAVV surgery in patients with FSV is associated with substantial mortality and a high incidence of reoperation.

Keywords: Single-ventricle physiology • Common atrioventricular valve • Valve repair

ABBREVIATIONS

BCPS	Bidirectional cavopulmonary shunt
CAVSD	Complete atrioventricular septal defect
CAVV	Common atrioventricular valve
CAVVR	CAVV regurgitation
ECMO	Extracorporeal membrane oxygenation
FSV	Functional single ventricle
IQR	Interquartile range
SD	Standard deviation
UVH	Univentricular heart

INTRODUCTION

Common atrioventricular valve (CAVV) is a single-orifice atrioventricular valve associated with complete atrioventricular septal defect (CAVSD) or univentricular heart (UVH) [1]. This immature and undivided atrioventricular valve has been considered a risk factor for early and late deaths in patients with functional single ventricle (FSV) [2, 3]. FSV is defined as a heart not amenable to biventricular repair, as the 2 ventricles are unable to sustain separate pulmonary and systemic circulations in sequence [4]. CAVV in patients with FSV is often unbalanced, and these children require univentricular palliation, which is associated with substantial mortality and morbidity [5, 6]. CAVV regurgitation (CAVVR) is a challenging issue due to its multifactorial and anatomic complexity influencing mortality and survival after Fontan completion [1, 7]. In patients with unbalanced atrioventricular septal defect, the incidence of CAVVR is 15–30%. In these patients, surgical intervention on the CAVVR is an independent predictor of mortality [7–9]. In addition, CAVVR represents a known risk factor for death in all patients with univentricular palliation [10–12]. Thus, patients with CAVVR are less likely to reach Fontan completion and have an increased risk of Fontan failure [6, 13, 14]. Outcomes after CAVV repair have improved [6, 15], but they are still unsatisfactory when compared to patients with FSV without CAVVR [16]. Indication and timing for CAVV repair are still controversial. Buratto *et al.* [6] performed the majority of CAVV repairs during bidirectional cavopulmonary shunt (BCPS) construction. In contrast, He *et al.* [15] performed most CAVV repairs concomitant with total cavopulmonary connection. Different CAVV repair techniques in FSV have been described [2, 6, 7, 15], and they should aim for functional, not physiological correction. In addition, the durability of CAVV repair is limited with a high probability of recurrence [17]. Consequently, patients with CAVV and FSV often require multiple valve repair procedures. The aim of our study was to evaluate the underlying mechanisms of CAVVR in children with FSV and to review our results of CAVV repair during univentricular palliation.

MATERIALS AND METHODS

The Institutional Review Board of the Technical University of Munich approved the study (ID: 65/20 S-KH, date: 18 February 2020) and the need for informed patient consent was waived. We reviewed the medical records of patients with CAVV and FSV who underwent univentricular palliation at the German Heart Center Munich between February 1984 and February 2019. CAVV with FSV was present in patients with either CAVSD (balanced and unbalanced) or UVH. Unbalanced CAVSD was defined as not suitable for biventricular repair due to a hypoplastic left or right ventricle. Reasons for univentricular palliation in patients with balanced CAVSD were either CAVV straddling or additional cardiac malformations such as double-outlet right ventricle. Medical records including in-hospital and outpatient notes and echocardiography data were retrospectively collected and reviewed. Operative mortality was defined according to the STS [18].

Common atrioventricular valve anatomy and function

CAVV and ventricular morphology, as well as structural abnormalities of the CAVV, were determined from echocardiographic reports. After CAVV surgery, mechanisms of CAVVR were based on the surgical reports. The extent of CAVVR was classified as 0 (none), 1 (mild), 2 (moderate) or 3 (severe). Significant regurgitation of the CAVV was considered to be present when CAVVR was moderate or greater.

Indication and timing of common atrioventricular valve surgery

Indication for CAVV surgery was seen if CAVVR was significant on preoperative transthoracic echocardiography findings and confirmed by intraoperative transoesophageal echocardiography. CAVV replacement was only performed if extensive valve

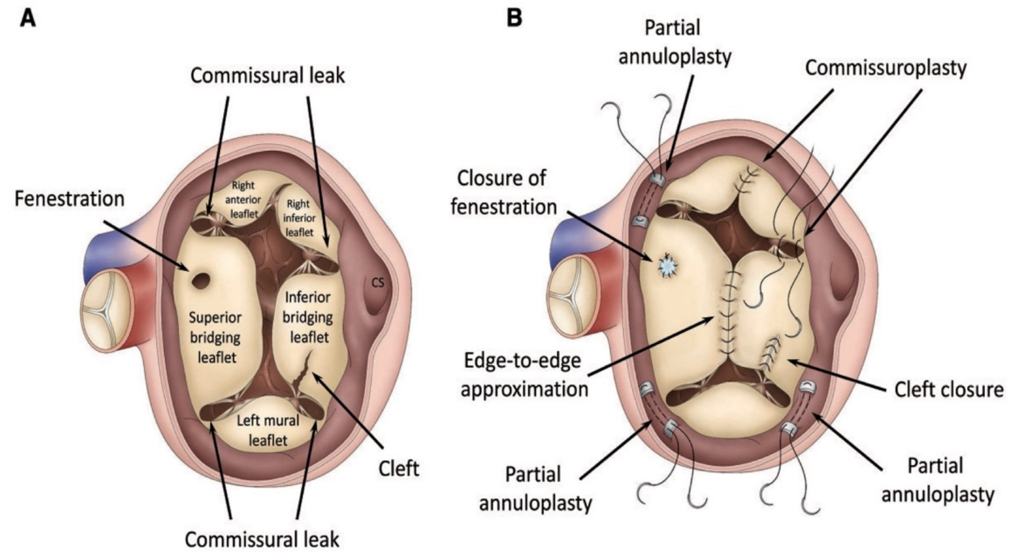

Figure 1: Mechanisms (**A**) and repair techniques (**B**) of common atrioventricular valve regurgitation. CS: coronary sinus.

dysplasia was initially evident or if CAVV redo repair was not technically possible with no prospect of achieving a less than severe regurgitant CAVV. Moderate or greater CAVVR was addressed at the time of staged palliation, and severe symptomatic CAVVR as separate surgery between the palliative steps. For patients with moderate CAVVR post-repair a wait-and-see approach with strict echocardiographic check-up was adopted. If no worsening of CAVVR was seen, redo CAVV operation was performed concomitant with the next palliation stage. If sudden worsening of the regurgitation, as well as new onset of clinical symptoms were seen, a prompt redo CAVV operation was performed, even between the classic palliative steps.

Operative techniques

CAVV surgery was performed under standard cardiopulmonary bypass with cardioplegic cardiac arrest. Surgical techniques were individualized according to the valve pathology. Intraoperatively, saline was injected into the ventricle to confirm the mechanism of CAVVR. Attention was paid to the annular dimension, commissural leak, prolapse or restriction of the leaflets, and leaflet and subvalvular abnormalities. Partial and semi-circular annuloplasties were performed. For partial annuloplasty a 5-0 or 6-0 Prolene horizontal mattress suture was placed along the commissure where the predominant regurgitant jet was detected. Another technique used for partial annuloplasty was the Kay–Wooler plasty. Semi-circular annuloplasty was performed using the De Vega technique. Commissuroplasty was achieved with edge-to-edge approximation of the leaflet tissue using 6–0 or 7–0 Prolene sutures. In patients with poor coaptation of 2 opposing leaflets, suturing of the free-floating segments of the opposing leaflets created double orifices, and edge-to-edge repair was performed. Gore-Tex neo-chordae (W.L. Gore & Assoc Inc., Newark, DE, USA) were used for chordal replacement. Interrupted stitches or continuous locked sutures were used for direct closure of clefts. For the closure of leaflet fenestration autologous pericardium fixed in glutaraldehyde (0.6%) for 10 min was used. If the valve leaflets were dysplastic with irreparable leaflet abnormalities, CAVV replacement was performed using a standard bileaflet mechanical valve. Intraoperative transoesophageal echocardiography was performed routinely. Details on mechanisms of the regurgitation of the CAVV and repair techniques are depicted in Fig. 1.

Follow-up data

Patients were regularly followed by paediatric cardiologists in an outpatient setting. Mortality, cause of death and morbidity were tracked using our institutional single-ventricle patient database system. The severity of CAVVR was regularly evaluated with transthoracic echocardiography.

Statistical analysis

Data were analysed using Statistical Package for the Social Sciences (SPSS), version 25.0 for Windows (IBM Corp., Armonk, NY, USA) and R (version 3.5.2; R Foundation for Statistical Computing, Vienna, Austria). All continuous variables were non-normally distributed and reported as median with interquartile range (IQR). For the time-to-event analysis, the mean with standard deviation (SD) was reported for follow-up time. Categorical variables were expressed as numbers and percentages. Two-tailed χ^2 test was used for the analysis of categorical data. Kaplan–Meier analysis was applied to calculate the estimated survival. Log-rank test was used to compare survival between groups. Competing risk analysis was used to calculate the cumulative incidence of reoperation. Cumulative incidence of reoperation was described at the mean follow-up time after CAVV surgery. Statistical significance was set at P-value <0.05.

RESULTS

Patients with common atrioventricular valve surgery

Patient characteristics. In 66 children with CAVV and FSV, single-ventricle palliation was performed during the study period,

Table 1: Baseline characteristics of patients

Total	30
Age (years)	0.9 (0.3–1.8)
Weight (kg)	6.5 (3.9–8.7)
Male gender	16 (53)
Primary diagnosis	
Unbalanced CAVSD	25 (83.3)
Right ventricular dominance	23 (76.7)
Left ventricular dominance	2 (6.7)
Balanced CAVSD	3 (10)
Univentricular heart	2 (6.7)
Associated cardiac defects	
Heterotaxy	12 (40)
DORV	8 (26.7)
PS	8 (26.7)
TAPVD	8 (26.7)
Heterotaxy and TAPVD	7 (23.3)
Chromosomal anomalies	3 (10)
Preoperative CAVV regurgitation	
Moderate	12 (40)
Severe	18 (60)
CAVV straddling	3 (10)
Timing of CAVV surgery	
At stage I	6 (20)
Between stage I and II	3 (10)
At stage II	12 (40)
Between stage II and Fontan	1 (3.3)
At Fontan	8 (26.7)
Initial stage I palliation	
MBTS	4 (13.3)
Central shunt	4 (13.3)
PA banding	11 (36.7)
Norwood	4 (13.3)
RV–PA conduit	1 (3.3)
No stage I palliation	6 (20)

Values are expressed as *n* (%) or median (interquartile range).

CAVSD: complete atrioventricular septal defect; CAVV: common atrioventricular valve; DORV: double-outlet right ventricle; MBTS: modified Blalock–Taussig shunt; PA: pulmonary artery; PS: pulmonary stenosis; RV–PA conduit: right ventricle to pulmonary artery conduit; TAPVD: total anomalous pulmonary venous drainage.

with 45.5% (30/66) requiring CAVV surgery. Indication for CAVV surgery was moderate CAVVR in 12 patients (40%) and severe CAVVR in 18 patients (60%). The median age and weight at initial CAVV surgery were 0.9 years (IQR 0.3–1.8) and 6.5 kg (IQR 3.9–8.7), respectively. Sixteen patients (53.3%) were below 1 year of age. The primary diagnoses were unbalanced CAVSD in 25 patients (83.3%), balanced CAVSD in 3 patients (10%) and UVH in 2 patients (6.7%). Commonly associated cardiac malformations were heterotaxy in 12 patients (40%) and double-outlet right ventricle in 8 patients (26.7%). CAVV surgery was performed before BCPS (stage II) in 9 patients (30%), concomitant with BCPS in 12 (40%), between BCPS and total cavopulmonary connection (Fontan) in 1 (3.3%) and concomitant with Fontan in 8 (26.7%). Further baseline demographics are shown in Table 1. The main pathologies of CAVVR were leaflet clefts (8/30, 26.6%), commissural regurgitation (7/30, 23.3%), lack of coaptation (6/30, 20%) and annular dilatation (5/30, 16.6%). Further details of CAVV pathologies are depicted in Table 2.

Surgical procedures. CAVV repair was performed in 28 patients (93.3%) and primary CAVV replacement was required in 2 patients (6.7%). Mechanical valve replacement was required

Table 2: Pathologies of the common atrioventricular valve at initial repair

Leaflet cleft	8 (26.7)
BL right inferior	2 (6.7)
BL left superior + inferior	2 (6.7)
BL right superior + inferior	1 (3.3)
BL right superior + anterior	1 (3.3)
Location undetermined	2 (6.7)
Commissural regurgitation	7 (23.3)
BL right superior + inferior	2 (6.7)
BL left superior + inferior	2 (6.7)
BL right superior + anterior	1 (3.3)
BL superior	1 (3.3)
BL left mural	1 (3.3)
Lack of coaptation	6 (20)
Annular dilatation	5 (16.7)
Circular	2 (6.7)
Right inferior	1 (3.3)
Left inferior	1 (3.3)
Location undetermined	1 (3.3)
Leaflet fenestration BL superior	1 (3.3)
Leaflet prolapse BL inferior	1 (3.3)

Data are expressed as *n* (%).

BL: bridging leaflet.

Table 3: Details of surgical procedures on the CAVV

Techniques for first CAVV surgery	
CAVV repair	28 (93.3)
Cleft closure	8 (28.6)
Commissuroplasty	7 (25)
Edge-to-edge repair	6 (21.4)
Annuloplasty	5 (17.9)
De Vega plasty	2 (7.1)
Partial plasty	2 (7.1)
Kay–Wooler plasty	1 (3.6)
Fenestration closure	1 (3.6)
Chordal replacement	1 (3.6)
CAVV replacement	2 (6.7)
Techniques for second CAVV surgery	
CAVV redo repair	11 (36.7)
Cleft closure	4 (13.3)
Partial annuloplasty	3 (10)
Commissuroplasty	2 (6.7)
Edge-to-edge repair	1 (3.3)
Fenestration closure	1 (3.3)
CAVV redo replacement	2 (6.7)
Techniques for third CAVV surgery	
Partial annuloplasty	1 (3.3)
CAVV re-redo replacement	3 (10)

Data are expressed as *n* (%).

CAVV: common atrioventricular valve.

due to extensive valve dysplasia in both patients. The most common surgical techniques were cleft closure (8/28, 28.6%), followed by commissuroplasty (7/28, 25%) and edge-to-edge repair (6/28, 21.4%). In 5 patients (17.9%), annuloplasty alone was performed. For the closure of leaflet fenestration, autologous pericardium was used in 1 patient (3.6%). The median cardiopulmonary bypass time was 117.5 min (IQR 95–165.8) and the median aortic cross-clamp time was 49.5 min (IQR 34–86.3). Details of the surgical procedures are specified in Table 3.

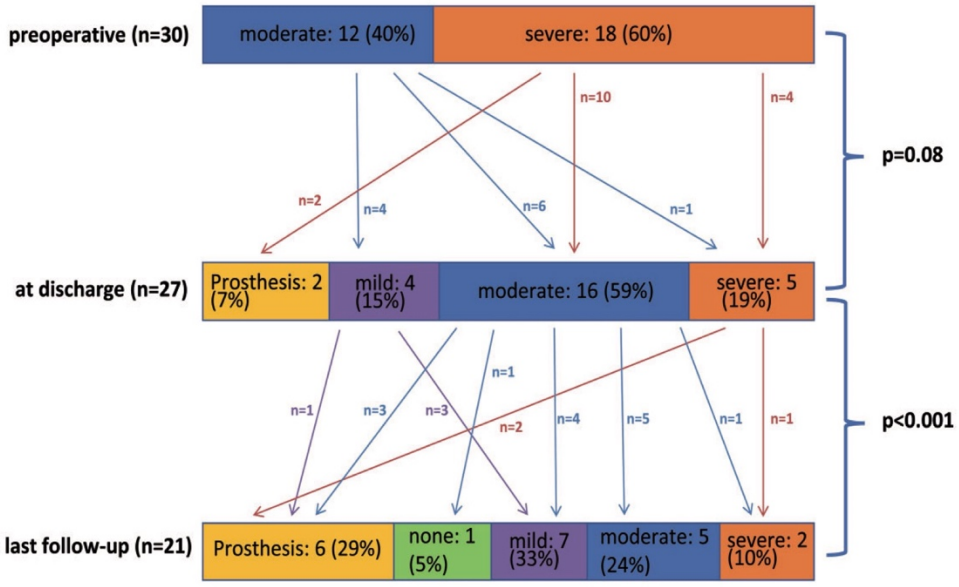

Figure 2: Echocardiographic evaluation and course of the regurgitation of the common atrioventricular valve.

In-hospital outcomes. Operative mortality was 23.3% (7/30). Death was cardiac related in 5 patients (16.6%) and non-cardiac related in 2 patients (6.7%). The first patient was a 7-day-old girl in whom a CAVV edge-to-edge repair had been performed concomitant with the Norwood procedure using a modified Blalock-Taussig shunt. The patient died due to low cardiac output 6.2 months after initial repair. Her postoperative course had been complicated by the need for a redo repair due to recurrent severe CAVVR 3.7 months after initial surgery and requirement for temporary extracorporeal membrane oxygenation (ECMO) support. The second was a 1.8-year-old boy with unbalanced CAVSD and severe pulmonary hypertension who received a commissuroplasty in combination with the Norwood procedure using a central aorto-pulmonary shunt who died intraoperatively due to low cardiac output. The third patient was a 7-day-old girl who died on the fifth postoperative day after closure of a fenestration of the superior bridging leaflet due to heart failure in the intensive care unit. The fourth patient was a 3.5-month-old girl who died 1 day after CAVV repair in combination with BCPS due to heart failure despite postoperative ECMO support. Persistent hypoxia due to severe stenosis of the left pulmonary artery despite stent implantation and ECMO support was the cause of mortality in the fifth patient who was a 1.2-year-old girl who died 8 days after CAVV repair and BCPS. In the sixth and seventh patients, cause of death was sepsis: 4 days after CAVV replacement and 23 days after CAVV repair.

Echocardiographic data at discharge were available in 27 patients (90%). After CAVV repair, mild CAVVR was recorded in 4 patients (14.8%), moderate CAVVR in 16 (59.3%) and severe CAVVR in 5 (18.5%) (Fig. 2). CAVVR was reduced ($P = 0.08$) and improvement of CAVVR was seen in 14 patients. No improvement of CAVVR was detected in 14 patients including 3 in-hospital deaths.

Three patients required in-hospital redo repairs because of severe recurrent CAVVR at 9, 60 and 113 days after initial repair. In 1 patient with severe persistent CAVVR, an in-hospital redo valve replacement was performed on the 18th postoperative day after initial CAVV repair. Four patients (13%) developed complete heart block after CAVV surgery and epicardial pacemaker implantation was performed in all 4 patients.

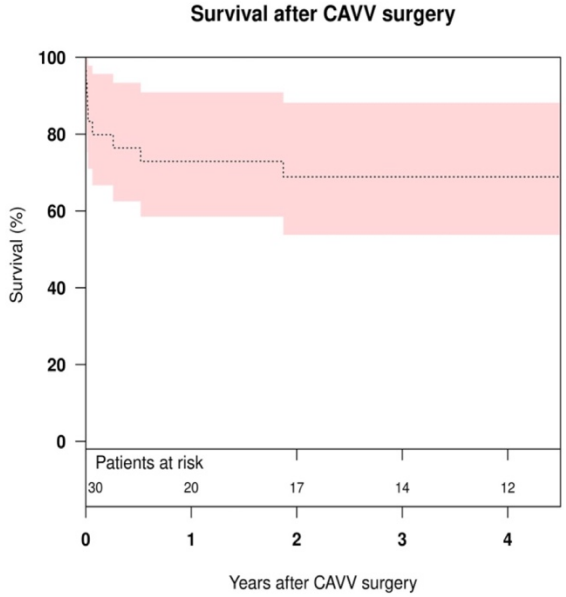

Figure 3: Kaplan–Meier plots of survival of patients with surgery of the CAVV. CAVV: common atrioventricular valve.

Follow-up outcomes. The mean follow-up time after CAVV surgery was 4.2 years (SD: 4.6) (median 2.7 years; IQR 0.2–6.3). Late mortality was 8.7% (2/23). In both patients, the cause of death was cardiac related. The first patient was a 1.7-year-old girl who died 3.1 months after CAVV repair and BCPS due to heart failure. In that patient a redo repair was performed 60 days after initial repair due to recurrent severe CAVVR. The second patient was a 6.7-month-old girl who died due to heart failure 1.9 years after CAVV replacement with a mechanical valve. Four-year survival after CAVV surgery was 68.9% (SD: 8.7) (Fig. 3) and in 18 of

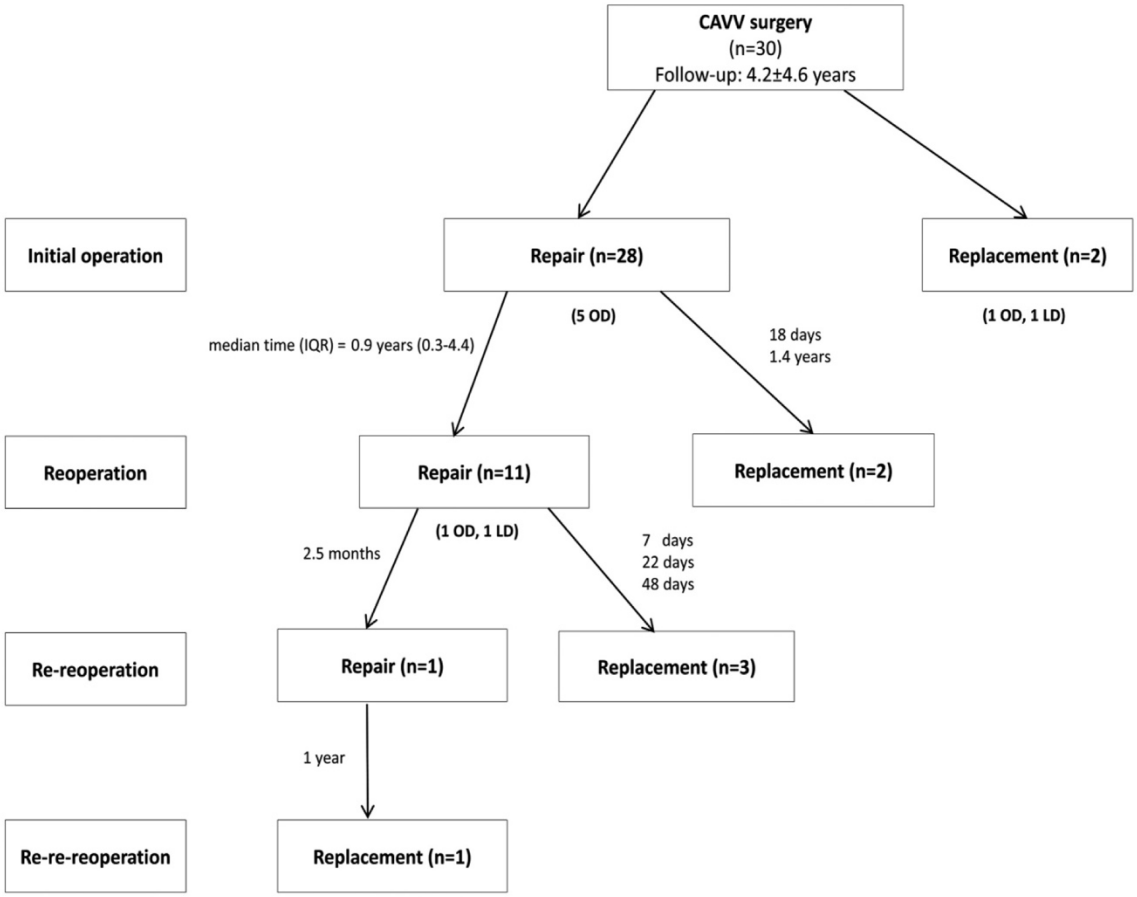

Figure 4: Clinical course and outcomes for patients with surgery of the CAVV. CAVV: common atrioventricular valve; IQR: interquartile range; LD: late death; OD: operative death.

these patients (60%) completion of Fontan circulation was achieved. However, there was no significant difference in 4-year survival between patients after CAVV surgery with and without heterotaxy and total anomalous pulmonary venous drainage [68.6% (SD: 18.6) vs 68.8% (SD: 9.8), respectively; $P = 0.81$] (Supplementary Material, Fig. S1). Patients with improvement of CAVVR showed a better 4-year survival than patients without CAVVR improvement [92.9% (SD: 6.9) vs 57.1% (SD: 13.2); $P = 0.03$] (Supplementary Material, Fig. S2). As for reoperation, there were 11 patients who required redo CAVV repair at a median interval of 0.9 years (IQR 0.3–4.4) and 2 patients whose CAVV was replaced with a mechanical valve 18 days and 1.4 years after initial CAVV repair. The median age at CAVV reoperation was 1.9 years (IQR 0.9–4.4). Four patients required a second operation. In 1 patient, a redo repair was performed 2.5 months after redo repair and valve replacement was required in 3 patients at 7, 22 and 48 days after redo repair. In the 1 patient with a redo repair, the CAVV was successfully replaced in combination with the Fontan procedure 1 year after the second operation due to persistent moderate CAVVR. An overview of the clinical course after CAVV surgery in patients with FSV is shown in Fig. 4. Details on the CAVV pathologies at redo repair are listed in Supplementary Material, Table S1. The reoperation-free survival 4 years after CAVV surgery was 40.4% (SD: 9.3), and the cumulative incidence of reoperation at 4 years was 35.8% (SD: 9.1) (Fig. 5).

At the last follow-up, echocardiographic information was available for 21 patients (70%) and CAVVR had significantly improved compared to discharge ($P < 0.001$) (Fig. 2). No CAVVR was seen in 1 patient (4.8%), mild in 7 patients (33.3%), moderate in 5 patients (23.8%) and severe in 2 patients (10%). The 6 patients with mechanical valve prosthesis in CAVV position showed no pathological findings (29%).

Patients without common atrioventricular valve surgery

In 36 patients with CAVV and FSV, no CAVV surgery was performed. Main diagnoses included unbalanced CAVSD in 23 patients (64%), UVH in 8 (22%), balanced CAVSD in 3 (8%) and others in 2 (6%). At the time of initial referral, echocardiography showed that CAVVR was severe in 1 patient (3%), moderate in 11 (31%) and mild in 15 (42%). In 9 patients (25%), no CAVVR was seen. The mean follow-up time after birth was 7.3 years (SD: 6.8) (median 4.9 years; IQR 1.2–13.3). There was no statistically significant difference in 4-year survival after birth between patients without and with CAVV surgery [83% (SD: 6.3) vs 69.7% (SD: 8.5), respectively; $P = 0.32$] (Supplementary Material, Fig. S3).

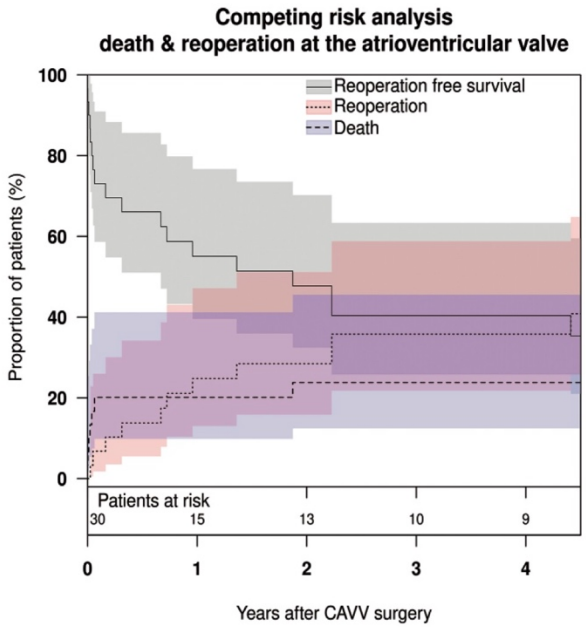

Figure 5: Competing risk analysis for death and reoperation at the CAVV. Cumulative incidence of reoperation (red) and death with no reoperation (blue). The grey curve shows the patients being alive without reoperation. CAVV: common atrioventricular valve.

DISCUSSION

In the present investigation, 46% of children with CAVV and FSV required surgery of the CAVV during staged palliation and surgical intervention was most commonly performed as a concomitant procedure during BCPS. Significant regurgitation of the CAVV was mainly due to clefts of the superior and/or inferior bridging leaflets. Four years after CAVV surgery survival was 69%, however, associated with a 36% incidence of reoperation at 4 years after the initial CAVV surgery.

CAVV in patients with FSV has been reported to be a considerable risk factor for early and late death due to the high tendency of these valves to leak and fail [3, 6, 12]. According to Buratto *et al.* [6] significant regurgitation of the CAVV with the need for surgery is associated with an early mortality of 18% and a 10-year survival of 66%. These results are consistent with ours. Another retrospective study of 38 Fontan patients who underwent CAVV repair between 1995 and 2012 reported a 5-year survival rate of 70%, also supporting our results [2]. He *et al.* [15] recently reported more promising results of CAVV repair using the bivalvation technique in patients with FSV, demonstrating an early mortality of 5% and a 10-year survival of 77%. An important difference of the study by He *et al.* is that the mean age of their study population was 10 years greater than ours, which could have contributed to the improved mortality as well as long-term survival rate.

Our institutional policy is to preserve the CAVV as long as possible, but the optimal timing for CAVV surgery in patients with FSV is currently unclear. In our study, surgical CAVV intervention was most commonly performed during BCPS. In line with other studies, repair of a significant CAVVR during BCPS can prevent volume overload, thus minimizing the risk of ventricular geometric changes and functional deterioration [2, 6, 7]. If CAVVR is mainly due to functional reasons such as annular dilatation, reduction of ventricular overload through BCPS can minimize CAVVR and in these cases CAVV repair should be limited to patients with dysplastic valve leaflets [9]. However, we have previously demonstrated that atrioventricular valve repair should be done as a sole operation before the Fontan procedure as the additional procedure of valve repair may prolong the bypass and aortic cross-clamp time leading to a higher incidence of postoperative complications and increased mortality [1]. Performing CAVV repair as a separate procedure before Fontan completion also yields the possibility to work on the valve at the time of Fontan procedure to improve suboptimal repairs and to prevent the breakdown of systemic ventricular function at the time of Fontan completion. Some groups have performed CAVV repair concomitantly with the Fontan procedure as CAVVR was due to anatomic abnormalities of the leaflets or subvalvular apparatus and not due to functional reasons [15, 19]. Thus, the number of cumulative operations is minimized, but no clear data exist to support one approach over the other [20].

Additional to the intrinsic abnormalities of the CAVV leaflets, ventricular imbalance and other cardiac malformations such as heterotaxy and total anomalous pulmonary venous drainage are often seen in such patients. These associated anomalies make a sufficient CAVV repair more complicated [21]. However, we did not see a significant difference in the 4-year survival between patients after CAVV surgery with and without heterotaxy and total anomalous pulmonary venous drainage. Several CAVV repair techniques have been reported such as the modified Alfieri technique, the bivalvation valvuloplasty technique and the two-strip technique [2, 15, 22, 23]. The bivalvation valvuloplasty technique was first introduced as a CAVV repair technique in the mid-1990s [24] and He *et al.* [15] could show that this technique is feasible with a 10-year survival rate of 77% and freedom from CAVV failure of 63%. The modified Alfieri technique described by Misumi *et al.* [2] involves a central bridging band annuloplasty, which is placed across the superior–inferior bridging leaflets with the use of a Gore-Tex (Gore-Tex, W.L. Gore and Associates Inc., Flagstaff, AZ, USA) strip fixed at the annulus above the valve plane. Thus, the central superior–inferior annular dimension is reduced to improving coaptation of the bridging leaflets. A modification of this technique is the two-strip technique, which is characterized by additional septation of the CAVV using either 0.625% glutaraldehyde-treated autologous pericardium or a Gore-Tex strip offering support for the central region of the bridging leaflets [22, 23]. Usage of a Gore-Tex strip was also advocated by Buratto *et al.* [6] as apposition of the bridging leaflets and annular stabilization is provided. However, there was no significant difference in 4-year survival after birth between patients with and without CAVV surgery. This can be explained by the fact that we performed CAVV surgery in 40% of patients during BCPS and these patients were survivors of stage I palliation. In the group of patients without CAVV surgery, operative mortality at stage I palliation was 16%.

Despite advances in CAVV repair techniques, multiple valve repair procedures are frequently required as these frail valves have a high tendency to fail [17]. In our study, cumulative incidence of reoperation at 4 years after CAVV surgery was 36%, which is slightly higher than the cumulative incidence of reoperation at 4 years of 25% reported by Buratto *et al.* [6]. This discrepancy can be explained by the lower mean age at operation in our study associated with more friable leaflet tissue to work with. King *et al.* [25] described more promising results with a cumulative incidence of atrioventricular valve intervention at 4 years of 13% and

a 4-year freedom from atrioventricular valve repair failure of 50%. Wong *et al.* [10] described a freedom from valve reoperation of 69% at 5 years after CAVV repair in FSV patients. With the use of the bivalvation technique, He *et al.* [15] reported a 10-year rate of freedom from valve repair failure of 82%.

After multiple valve repair procedures, the valve morphology would become more complex and the patients were more likely to have residual CAVVR [15, 26]. Our strategy for redo CAVV operations is consistent with the fact that severe residual regurgitation of the CAVV is associated with a considerable higher risk of mortality and reoperation [6, 27]. The risk of leaving residual CAVVR must be thoroughly contemplated against the risks associated with CAVV replacement. Mahle *et al.* [28] could show that systemic atrioventricular valve replacement was associated with a 44% rate of complete heart block as well as an early mortality of 29%. Despite these risks, Jang *et al.* [29] demonstrated, in a cohort of 33 patients with FSV who underwent valve surgery, that atrioventricular valve replacement was associated with a significantly lower rate of reoperation when compared to valve repair (67% vs 45% at 5 years). Thus, we advise to replace the CAVV with a mechanical prosthesis only if massive valve dysplasia is initially evident or if a redo CAVV repair may not be technically possible and moderate CAVVR cannot be achieved. However, a benefit of CAVV replacement could be that these children can have a relatively large prosthesis implanted [6].

Limitations

This study was limited by its retrospective nature and single-centre design. Main limitation of this study is the small sample size and thus differences between subgroups may not be detected. Mechanisms of CAVV anomalies were inferred from the operation records, and bias among surgeons can be expected. Inconsistencies in preoperative, operative and postoperative management during the 35-year study period may have affected our outcome parameters.

CONCLUSION

Significant regurgitation of the CAVV in patients with FSV undergoing univentricular palliation is common and requires surgical repair at various palliation points. CAVV surgery improves regurgitation but rarely achieves a competent valve. CAVV surgery in this highly specific patient population is associated with substantial operative mortality and a high incidence of reoperation. Due to the complicated anatomy of CAVV, further understanding of the mechanisms of regurgitation and corresponding repair techniques is mandatory to improve outcomes.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Author contributions

Benedikt Mayr: Data curation; Investigation; Methodology; Project administration; Writing–original draft; Writing–review & editing. **Melchior Burri:** Formal analysis; Methodology. **Martina Strbad:** Data curation; Investigation. **Julie Cleuziou:** Supervision; Validation; Writing–review & editing. **Alfred Hager:** Investigation; Resources. **Peter Ewert:** Supervision; Visualization. **Jürgen Hörer:** Project administration; Supervision; Validation; Visualization. **Rüdiger Lange:** Project administration; Supervision; Validation; Visualization; Writing–review & editing. **Masamichi Ono:** Conceptualization; Project administration; Supervision; Validation; Writing–review & editing.

Reviewer information

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Anhang IV

Cardiology in the Young

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Original Article

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Atrioventricular valve surgery in patients with univentricular heart and two separate atrioventricular valves

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Abstract

Objectives: Atrioventricular valve regurgitation in patients with univentricular heart is a well-known risk factor for adverse outcomes and atrioventricular valve repair remains a particular surgical challenge. *Methods:* We reviewed all surgical atrioventricular valve procedures in patients with univentricular heart and two separate atrioventricular valves who underwent surgical palliation. Endpoints of the study were reoperation-free survival and cumulative incidence of reoperation. *Results:* Between 1994 and 2021, 202 patients with univentricular heart and two separate atrioventricular valve morphology underwent surgical palliation, with 15.8% (32/202) requiring atrioventricular valve surgery. Primary diagnoses were double inlet left ventricle (n = 14, 43.8%), double outlet right ventricle (n = 7, 21.9%), and congenitally corrected transposition of the great arteries (n = 7, 21.9%). Median weight at valve surgery was 10.6 kg (interquartile range, 7.9–18.9). Isolated left or right atrioventricular valve surgery was required in nine (28.1%) and 22 patients (68.8%), respectively. Concomitant left and right atrioventricular valve surgery was performed in one patient (3.1%). Closure of the left valve was conducted in four patients (12.5%) and closure of the right valve in three (9.4%). Operative and late mortality were 3.1% and 9.7%, respectively. Reoperation-free survival and cumulative incidence of reoperation at 10 years after surgery were 62.3% (standard error of the mean: 6.9) and 30.9% (standard error of the mean: 9.6), respectively. *Conclusions:* In patients with univentricular heart and two separate atrioventricular valves, surgical intervention on these valves is required in a minority of patients and is associated with low mortality but high incidence of reoperation.

Introduction

Moderate or severe atrioventricular valve regurgitation in patients with univentricular heart is not uncommon and represents a well-known risk factor for increased long-term morbidity and mortality.[1–4] The risk of failure of Fontan circulation is significantly increased in the majority of these patients leading to death or heart transplantation.[5] Yet, most of the published research about atrioventricular valve regurgitation in surgical palliation of univentricular heart is centred either on patients with a common atrioventricular valve or on patients with hypoplastic left heart syndrome with a single tricuspid valve.[6] However, patients with two separate atrioventricular valves and univentricular heart undergoing surgically staged palliation are prone to valve failure with a cumulative incidence of atrioventricular valve failure of 26% at 25 years of age.[1] Atrioventricular valve repair in this specific subset of univentricular heart patients is challenging, and freedom from reoperation has been reported as 57% at 5 years after initial atrioventricular valve repair.[7] Another option for valve repair in patients with univentricular heart and two separate atrioventricular valves is closure of the diminutive atrioventricular valve. Closure of the diminutive valve should be performed in case of significant regurgitation or stenosis with concomitant valve dysplasia. Another prerequisite for this surgical technique is that the other atrioventricular valve is of appropriate size. King and colleagues could demonstrate in a cohort of 36 patients with univentricular heart and atrioventricular valve closure that valve closure is associated with no operative mortality and freedom from reintervention at 18 years post-valve closure of 83%.[6] Our group could show that early valve

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closure is an effective surgical alternative with no incidence of atrioventricular valve reoperations in 17 patients with two separate atrioventricular valves and single-ventricle physiology.[8] However, caution should be taken in atrioventricular valve closure as it is linked with a 17% risk of patch dehiscence and a 14% risk of heart block.[6] Despite these risks and in contrast to the limited durability of atrioventricular valve repair in patients with univentricular heart and two separate atrioventricular valves undergoing surgical palliation, valve closure may represent an effective surgical tool for the management of atrioventricular valve regurgitation. Yet, data on the outcome of atrioventricular valve surgery in patients with univentricular heart and two separate atrioventricular valves are still limited. The aim of our study was to examine our experience with atrioventricular valve repair and closure in children with univentricular heart and two separate atrioventricular valves.

Materials and method

Ethical statement

This study was approved by the Institutional Review Board of the Technical University of Munich (approved number of 2022-303-SKH on 27 June, 2022). Because of the retrospective nature of the study, the need for individual patient consent was waived.

Patients

We reviewed the medical records of patients with univentricular heart and two separate atrioventricular valves who underwent staged surgical palliation at the German Heart Center Munich between May 1994 and November 2021. Univentricular heart and two separate atrioventricular valves were present in patients with double inlet left ventricle, double inlet right ventricle, double outlet right ventricle, and congenitally corrected transposition of the great arteries. Patients with a common atrioventricular valve were excluded from this study. Medical records including in-hospital and outpatient notes and echocardiography data were retrospectively collected and reviewed. Operative mortality was defined according to the Society of Thoracic Surgeons.[9]

Atrioventricular valve anatomy and function

Atrioventricular valve and ventricular morphology were determined from echocardiographic reports and were confirmed by intraoperative inspection. Based on morphologic criteria, the atrioventricular valve was defined either as a left or right atrioventricular valve. After atrioventricular valve surgery, mechanisms of regurgitation and stenosis were based on the surgical reports. The extent of regurgitation was classified as 0 (none), 1 (trivial), 2 (mild), 3 (moderate), or 4 (severe). Significant regurgitation was considered to be present when regurgitation was moderate or severe.

Operative techniques

Atrioventricular valve surgery was performed under standard cardiopulmonary bypass with cardioplegic cardiac arrest. Surgical techniques were individualised according to the valve pathology. Intraoperatively, saline was injected into the ventricle to confirm the mechanism of regurgitation. Attention was paid to the annular dimension, commissural leak, prolapse or restriction of the leaflets, and leaflet and subvalvular abnormalities. Partial and semi-circular annuloplasties were performed. For partial annuloplasty, a 5-0 or 6-0 Prolene horizontal mattress suture was placed along the commissure where the predominant regurgitant jet was detected. Another technique used for partial annuloplasty was the Kay-Wooler plasty. Semi-circular annuloplasty was performed using the De Vega technique. Semi-rigid partial annuloplasty ring (Edwards Lifesciences, Inc., Irvine, CA, USA) was also implanted. Commissuroplasty was achieved with edge-to-edge approximation of the leaflet tissue using 6-0 or 7-0 Prolene sutures. In patients with poor coaptation of two opposing leaflets, edge-to-edge repair was performed. Interrupted stitches or continuous locked sutures were used for direct closure of clefts and fenestrations. In case of significant regurgitation or stenosis of the diminutive atrioventricular valve, closure of the valve was achieved either with a patch or by direct suture. Patch materials used included Gore-Tex (W. L. Gore & Associates, Inc., Flagstaff, AZ, USA) and Dacron (DuPont, Midland, MI, USA). In case of severe residual regurgitation or irreparable leaflet abnormalities, valve replacement was performed. Implanted valve prostheses were the mechanical ATS valve (ATS Medical, Inc., Minneapolis, Minn, USA) and the porcine Medtronic Intact valve (Medtronic, Inc., Minneapolis, Minn, USA). Intraoperative transesophageal echocardiography was performed routinely.

Follow-up data

Patients were regularly followed by paediatric cardiologists in an outpatient setting. Mortality, cause of death, and morbidity were tracked using our institutional single-ventricle patient database system. The severity of atrioventricular valve regurgitation was regularly evaluated with transthoracic echocardiography. Listwise deletion was used for missing data.

Statistical analysis

Continuous variables are expressed as mean with standard deviation or median with interquartile range. Distribution of continuous variables was tested with the Kolmogorov–Smirnov test, histograms as well as P–P plots for graphical testing. For time-to-event analysis, the mean with standard deviation was reported for follow-up time. Categorical variables are presented as absolute numbers and percentages. Kaplan-Meier analysis was applied to calculate estimated survival. Log-rank test was used to compare survival between groups. Competing risk analysis was used to calculate the cumulative incidence of reoperation. Cumulative incidence of reoperation with standard error of the mean was described at the mean follow-up time after atrioventricular valve surgery. Statistical significance was set at $p < 0.05$. Data were analysed using Statistical Package for the Social Sciences, version 28.0 for Windows (IBM, Ehningen, Germany) and R-statistical software (version 3.5.2; R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics and timing of initial atrioventricular valve surgery

In 202 children with univentricular heart and two separate atrioventricular valve morphology, single-ventricle palliation was performed during the study period, with 15.8% (32/202) requiring atrioventricular valve surgery. Main indications for surgery of the left atrioventricular valve were moderate or greater regurgitation in nine patients (28.1%), and severe stenosis in one patient (3.1%).

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Indications for surgery of the right atrioventricular valve were severe and moderate regurgitation in six (18.8%) and 17 patients (53.1%), respectively. Median age and weight at initial atrioventricular valve surgery were 1.9 years (interquartile range, 0.9–5.7) and 10.6 kg (interquartile range, 7.9–18.9), respectively. Nine patients (28.1%) were below 1 year of age. The primary diagnoses were double inlet left ventricle (n = 14, 43.8%), double outlet right ventricle (n = 7, 21.9%), congenitally corrected transposition of the great arteries (n = 7, 21.9%), and Shone Complex (n = 2, 6.3%). Frequently associated cardiac malformations were coarctation of the aorta in nine patients (28.1%) and subvalvular pulmonary stenosis in eight patients (25%). Atrioventricular valve surgery was performed at Fontan completion in 17 patients (53.1%), concomitant with bidirectional cavopulmonary shunt in 11 (34.4%), at Norwood procedure in one (3.1%), and during interstage in three (9.4%). Further baseline demographics are depicted in Table 1.

Mechanisms of atrioventricular valve regurgitation and stenosis

Mechanisms of atrioventricular valve regurgitation and stenosis according to surgical findings at the initial surgical procedure are shown in Table 2. Leaflet cleft was identified in four patients (12.5) and posed the most common pathology of left atrioventricular valve regurgitation. The second most common cause was leaflet prolapse, which was observed in three patients (9.4%). Stenosis of the left atrioventricular valve was due to extensive valve dysplasia in one patient (3.1%). Main mechanisms of right atrioventricular valve regurgitation were leaflet prolapse and commissural regurgitation in eight (25%) and six patients (18.8%), respectively.

Surgical procedures

Details of the initial atrioventricular valve surgery and detailed description of the surgical techniques for each palliative stage are specified in Table 3. Surgery of the left atrioventricular valve was performed in nine patients (28.1%) with valve repair in five patients (15.6%) and valve closure in four patients (12.5%). Main techniques for repair of the left atrioventricular valve were either closure of clefts or leaflet adaptation in two patients (6.3%) each. Closure of the left atrioventricular valve was performed with the use of a Gore-Tex patch in two patients (6.3%) and with direct suture in two patients (6.3%). Surgery of the right atrioventricular valve was conducted in 22 patients (68.8%) with valve repair in 20 patients (62.5%) and valve closure in two patients (6.3%). The most common technique for repair of the right atrioventricular valve was commissural approximation in six patients (18.8%), followed by annuloplasty in five patients (15.6%). Closure of the right atrioventricular valve was achieved by suture in two patients (6.3%). Concomitant right atrioventricular valve Dacron patch closure and repair of the left atrioventricular valve was performed in one patient (3.1%) during Fontan completion. The median cardiopulmonary bypass time was 100.5 minutes (interquartile range, 78.3–136) and the median aortic cross-clamp time was 40.5 minutes (interquartile range, 27–60.8).

In-hospital outcomes

Operative mortality was 3.1% (1/32). Cause of death was basal ganglia infarction in a 3.4-year-old girl who died on the day of concomitant right atrioventricular valve repair and Fontan completion. Echocardiographic data at discharge were available

Table 1. Baseline characteristics of patients at initial atrioventricular valve surgery

Total	32
Age, years	1.9 (0.9–5.7)
Weight, kg	10.6 (7.9–18.9)
Female sex	18 (56.3)
Primary diagnosis	
DILV	14 (43.8)
DORV	7 (21.9)
CCTGA	7 (21.9)
Shone Complex	2 (6.3)
Other	2 (6.3)
Left ventricular dominance	19 (59.4)
Right ventricular dominance	13 (40.6)
Associated cardiac defects	
CoA	9 (28.1)
PS subvalvular	8 (25)
LPSVC	6 (18.8)
Pulmonary atresia	3 (9.4)
Dextrocardia	3 (9.4)
TAPVD	1 (3.1)
Preoperative AVVR	
Moderate	23 (71.9)
RAVV	17 (53.1)
LAVV	6 (18.8)
Severe	9 (28.1)
RAVV	6 (18.8)
LAVV	3 (9.4)
Preoperative severe LAVVS	1 (3.1)
RAVV straddling	4 (12.5)
LAVV straddling	3 (9.4)
Timing of initial AVV surgery	
At stage I	
LAVV	1 (3.1)
At BCPS	
RAVV	8 (25)
LAVV	3 (9.4)
At Fontan	
RAVV	12 (37.5)
LAVV	4 (12.5)
LAVV + RAVV	1 (3.1)
Between stage I and BCPS	
LAVV	2 (6.3)
Between stage I and Fontan*	
RAVV	1 (3.1)

(*Continued*)

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Table 1. (*Continued*)

Total	32
Initial stage I palliation	
Main PA banding	8 (26.7)
Central shunt	7 (21.9)
Norwood	5 (15.6)
MBTS	3 (9.4)
DKS + Central Shunt	1 (3.1)
DKS + MBTS	1 (3.1)
Aortic valve Repair + CoA Resection	1 (3.1)
No stage I palliation	6 (18.8)

Values are expressed as n (%) or median (interquartile range). AVV = atrioventricular valve; AVVR = atrioventricular valve regurgitation; BCPS = bidirectional cavopulmonary shunt; CCTGA = congenitally corrected transposition of the great arteries; CoA = coarctation of the aorta; DILV = double inlet left ventricle; DKS = Damus-Kaye-Stansel anastomosis; DORV = double outlet right ventricle; kg = kilogram; LAVV = left atrioventricular valve; LAVVS = left atrioventricular valve stenosis; LPSVC = persistent left superior vena cava; MBTS = modified Blalock-Taussig shunt; PA = pulmonary artery; PS = pulmonary stenosis; RAVV = right atrioventricular valve; TAPVD = total anomalous pulmonary venous drainage; VSD = ventricular septal defect.
*In this patient, Stage II bidirectional cavopulmonary shunt was not performed.

Table 2. Atrioventricular valve pathology at initial surgery

Left atrioventricular valve regurgitation	9 (28.1)
Cleft	4 (12.5)
Anterior leaflet	2 (6.3)
Posterior leaflet	1 (3.1)
Anterior + posterior leaflet	1 (3.1)
Leaflet prolapse	3 (9.4)
Anterior leaflet	2 (6.3)
Posterior leaflet	1 (3.1)
Valve dysplasia	3 (9.4)
Annular dilatation	1 (3.1)
Leaflet fenestration anterior + posterior	1 (3.1)
Left atrioventricular valve stenosis	1 (3.1)
Valve dysplasia	1 (3.1)
Right atrioventricular valve regurgitation	23 (71.9)
Leaflet prolapse	8 (25)
Posterior	4 (12.5)
Anterior	3 (9.4)
Septal	1 (3.1)
Commissural regurgitation	6 (18.8)
Anteroseptal	4 (12.5)
Posteroseptal	2 (6.3)
Pseudo-commissure leaflet	5 (15.6)
Anterior	1 (3.1)
Posterior	1 (3.1)
Septal	1 (3.1)
Anteroseptal	1 (3.1)
Posteroseptal	1 (3.1)
Annular dilatation	5 (15.6)
Valve dysplasia	3 (9.4)
Lack of coaptation	2 (6.3)
Cleft septal leaflet	1 (3.1)
Cleft anterior leaflet	1 (3.1)

Data are expressed as n (%).

in 31 patients (96.9%). After right atrioventricular valve repair, mild or less valve regurgitation was recorded in 16 patients (50%) and moderate valve regurgitation in four (12.5%) (Fig. 1A). After closure of the right atrioventricular valve with suture, moderate valve regurgitation was seen in one patient (3.2%). After repair of the left atrioventricular valve, moderate valve regurgitation was seen in two patients (6.5%), and mild regurgitation in one (3.2%) (Fig. 1B). After closure of the left atrioventricular valve with suture, mild valve regurgitation was diagnosed in one patient (3.2%). After concomitant closure of the right atrioventricular valve and repair of the left valve, no atrioventricular valve regurgitation was detected in the echocardiogram at discharge. Two patients required redo repair of the right atrioventricular valve during Fontan completion because of recurrent moderate regurgitation at 13.6 and 12.5 months after initial repair. In one patient (3.1%), epicardial ventricular pacemaker implantation was necessary due to second-degree atrioventricular block 9 days after DeVega annuloplasty.

Follow-up outcomes

The mean follow-up time after atrioventricular valve surgery was 10.3 years (standard deviation: 8.3) (median 9.7; interquartile range, 1.5–18.6). Late mortality was 9.7% (3/31). Death was cardiac-related in two patients (6.5%) and non-cardiac-related in one patient (3.2%). The first patient was a 2-year-old boy who underwent cleft closure of the anterior left atrioventricular valve leaflet and bidirectional cavopulmonary shunt at 9 months of age and died subsequently due to heart failure. The second patient was a 4-year-old girl who died from heart failure 3.4 months after closure of the left atrioventricular valve with a Gore-Tex patch in combination with Fontan completion. In the third patient, cause of death was protein-losing enteropathy 10.5 years after closure of the left atrioventricular valve with a Gore-Tex patch. Ten-year survival after atrioventricular valve surgery was 89.4% (standard deviation: 5.8) (Supplemental Fig. 1), and in all patients, completion of Fontan circulation was achieved. However, patients with surgery of the right atrioventricular valve showed a significant better 10-year survival than patients with surgery of the left atrioventricular valve (95.5% [standard deviation: 4.4] vs. 71.4% [standard deviation: 17.1], respectively; $p = 0.02$) (Supplemental Fig. 2).

As for reoperations during follow-up, there were eight patients who required redo atrioventricular valve surgery at a median interval of 1.2 years (interquartile range, 0.6–4.7) after initial atrioventricular valve surgery. Redo surgery of the left atrioventricular valve included repair (n = 1) due to recurrent moderate

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Table 3. Details of initial surgical techniques on the atrioventricular valves

Variable	N (%)	Stage I	Stage I - BCPS	BCPS	Stage I – Fontan*	Fontan
LAVV surgery in pts	9 (28.1)	1 (3.1)	1 (3.1)	3 (9.4)		4 (12.5)
Valve repair in pts	5 (15.6)			3 (9.4)		2 (6.3)
Cleft closure	2 (6.3)			1 (3.1)		1 (3.1)
Closure of fenestration	1 (3.1)					1 (3.1)
Leaflet adaptation	2 (6.3)			1 (3.1)		1 (3.1)
Edge-to-edge repair	1 (3.1)			1 (3.1)		
Valve closure in pts	4 (12.5)	1 (3.1)	1 (3.1)			2 (6.3)
Suture	2 (6.3)	1 (3.1)				1 (3.1)
Gore-Tex patch	2 (6.3)		1 (3.1)			1 (3.1)
RAVV surgery in pts	22 (68.8)		1 (3.1)	8 (25)	1 (3.1)	12 (37.5)
Valve repair in pts	20 (62.5)		1 (3.1)	8 (25)	1 (3.1)	10 (31.3)
Cleft closure	2 (6.3)		1 (3.1)			1 (3.1)
Closure of pseudo-commissure	3 (9.4)			1 (3.1)		2 (6.3)
Leaflet adaptation	3 (9.4)		1 (3.1)	1 (3.1)		1 (3.1)
Commissural approximation	6 (18.8)			3 (9.4)		3 (9.4)
Edge-to-edge repair	2 (6.3)			1 (3.1)		1 (3.1)
Bicuspidization	1 (3.1)					1 (3.1)
Annuloplasty	5 (15.6)			3 (9.4)	1 (3.1)	1 (3.1)
De-Vega plasty	4 (12.5)			2 (6.3)	1 (3.1)	1 (3.1)
Kay-Wooler plasty	1 (3.1)			1 (3.1)		
Valve closure in pts	2 (6.3)					2 (6.3)
Suture	2 (6.3)					2 (6.3)
LAVV + RAVV surgery in pts	1 (3.1)					1 (3.1)
LAVV cleft closure	1 (3.1)					1 (3.1)
LAVV ring annuloplasty	1 (3.1)					1 (3.1)
RAVV Dacron patch closure						1 (3.1)

Data are expressed as n (%). BCPS = bidirectional cavopulmonary shunt; LAVV = left atrioventricular valve; pts = patients; RAVV = right atrioventricular valve.
*In this patient, Stage II bidirectional cavopulmonary shunt was not performed and atrioventricular valve surgery was performed between stage I and Fontan.

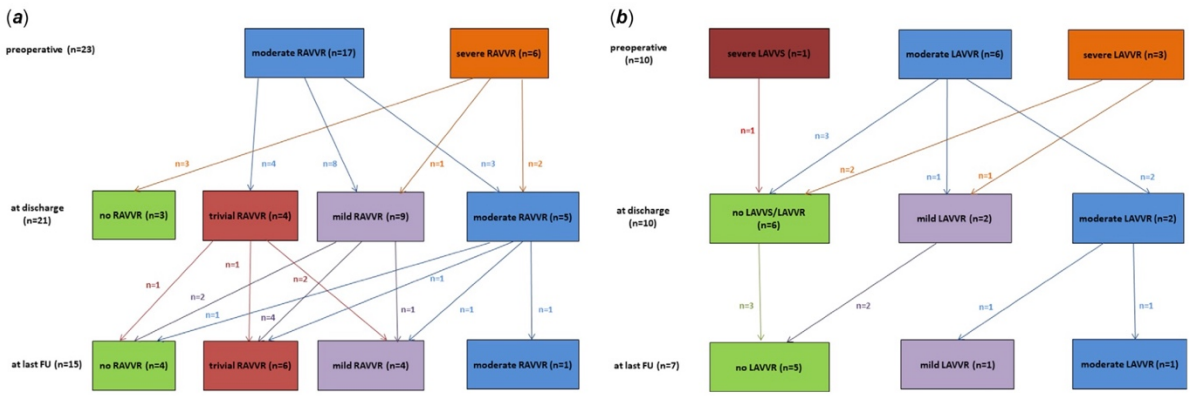

Figure 1. Echocardiographic evaluation and course of right (A) and left (B) atrioventricular valve pathology. FU = follow-up; LAVVR = left atrioventricular valve regurgitation; LAVVS = left atrioventricular valve stenosis; RAVVR = right atrioventricular valve regurgitation.

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Table 4. Details of redo operations on the atrioventricular valves

Variable	N (%)	BCPS	BCPS-Fontan	Stage I-Fontan*	Fontan	Post Fontan
LAVV surgery in pts	2 (20)				1 (10)	1 (10)
Valve repair in pts	1 (10)				1 (10)	
Cleft closure	1 (10)				1 (10)	
Partial annuloplasty	1 (10)				1 (10)	
Edge-to-edge repair	1 (10)				1 (10)	
Valve closure in pts	1 (10)					1 (10)
Suture	1 (10)					1 (10)
RAVV surgery in pts	6 (60)		1 (10)	1 (10)	3 (30)	1 (10)
Valve repair in pts	2 (20)				2 (20)	
Commissural approximation	2 (20)				2 (20)	
Valve closure in pts	2 (20)				1 (10)	1 (10)
Suture	1 (10)				1 (10)	
Gore-Tex patch	1 (10)					1 (10)
Valve replacement in pts	2 (20)		1 (10)	1 (10)		
Porcine Medtronic Intact valve	1 (10)		1 (10)			
Mechanical ATS valve	1 (10)			1 (10)		
LAVV + RAVV surgery in pts	2 (20)	1 (10)			1 (10)	
RAVV Edge-to-edge repair	1 (10)	1 (10)				
RAVV Partial annuloplasty	1 (10)	1 (10)				
RAVV Kay-Wooler plasty	1 (10)				1 (10)	
RAVV Commissural approximation	1 (10)				1 (10)	
LAVV Gore-Tex patch closure	2 (20)	1 (10)			1 (10)	

Data are expressed as n (%). BCPS = bidirectional cavopulmonary shunt; LAVV = left atrioventricular valve; pts: patients; RAVV = right atrioventricular valve.
*In this patient, Stage II bidirectional cavopulmonary shunt was not performed and atrioventricular valve surgery was performed between stage I and Fontan.

valve regurgitation and valve suture closure (n = 1) due to severe left atrioventricular valve regurgitation. Indications for redo surgery of the right atrioventricular valve were moderate valve regurgitation (n = 2) and consisted of valve closure (Suture = 1, Gore-Tex patch = 1). One patient developed severe regurgitation of the right atrioventricular valve due to a significant restriction of the septal leaflet 1.2 years after bicuspidization of the anterior and posterior right atrioventricular valve leaflet and the valve had to be replaced with a 31 mm large porcine Medtronic Intact valve prosthesis. In another patient, replacement of the right atrioventricular valve with a 27 mm large mechanical ATS valve prosthesis was necessary due to suture line dehiscence with severe regurgitation 5 months after DeVega annuloplasty. Details of the surgical redo procedures of the atrioventricular valves are depicted in Table 4. An overview of the clinical course after atrioventricular valve surgery in patients with two separate atrioventricular valves and univentricular heart is shown in Figure 2. The reoperation-free survival 10 years after atrioventricular valve surgery was 62.3% (standard error of the mean: 6.9), and the cumulative incidence of reoperation at 10 years was 30.9% (standard error of the mean: 9.6), respectively (Fig. 3). Details on the atrioventricular valve pathologies at redo surgery are listed in Supplementary Material, Table S1.

In one patient (3.1%), epicardial dual chamber pacemaker implantation was necessary during concomitant redo repair of the right atrioventricular valve and Gore-Tex patch closure of the left atrioventricular valve. In another patient, upgrade to a dual chamber pacemaker during suture closure of the right atrioventricular valve was performed. Indication for pacemaker implantation was complete atrioventricular block in both patients.

At the last follow-up, echocardiographic results were available for 22 patients (68.8%). No severe regurgitation of the left or right atrioventricular valve was seen. Moderate regurgitation of the left atrioventricular valve was visible in one patient (4.5%) and moderate regurgitation of the right atrioventricular valve was diagnosed in one patient (4.5%). Mild and less regurgitation of the left atrioventricular valve was seen in six patients (27.3%) and mild or less regurgitation of the right atrioventricular valve was found in 14 patients (63.6%) (Fig. 1A, 1B).

Discussion

In the present investigation, 16% of children with two separate atrioventricular valves and univentricular heart required surgery of the atrioventricular valves during staged palliation and surgical intervention was most commonly performed as a concomitant procedure during Fontan completion. Atrioventricular valve closure was performed in 22% of children. Significant regurgitation of the left atrioventricular valve was mainly due to clefts of the anterior leaflet and posterior and anterior leaflet prolapse of the right atrioventricular valve were the main pathologies for regurgitation of the right atrioventricular valve. Ten years after

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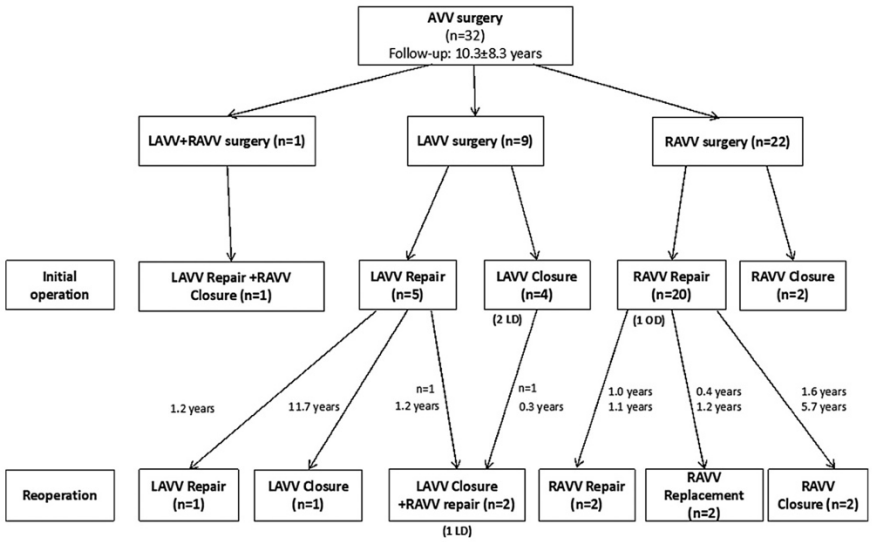

Figure 2. Clinical course and outcomes for patients with surgery of the atrioventricular valves. AVV = atrioventricular valve; LAVV = left atrioventricular valve; LD = late death; OD = operative death; RAVV = right atrioventricular valve.

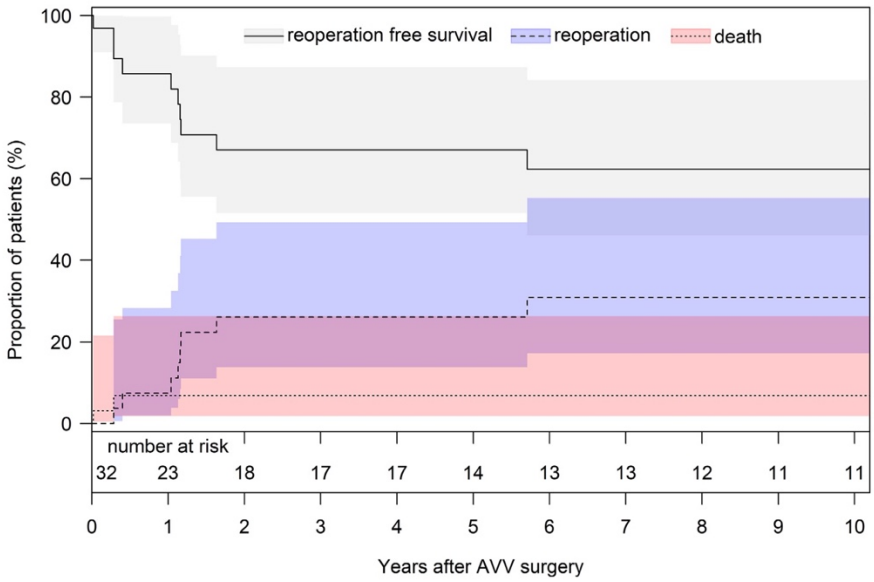

Figure 3. Competing risk analysis for death and reoperation at the atrioventricular valves. Cumulative incidence of reoperation (blue) and death with no reoperation (red). The grey curve shows the patients being alive without reoperation. AVV = atrioventricular valve.

atrioventricular valve surgery survival was 62%, however, associated with a 31% incidence of reoperation at 10 years after the initial valve surgery.

Despite improvements in treatment strategies, surgery, and management of patients with two separate atrioventricular valves and univentricular heart, significant atrioventricular valve regurgitation and stenosis remain a surgical challenge in this highly specific patient population.[1,7] Atrioventricular valve morphology is complex and often associated with valve dysplasia in these patients. Most published studies about atrioventricular valve repair in single-ventricle patients focus on patients with a common atrioventricular valve or on patients with hypoplastic left heart syndrome and a single tricuspid valve.[10–12] Patients with two separate atrioventricular valve morphology such as double inlet left ventricle or double outlet right ventricle represent only a small subgroup of univentricular heart patients with atrioventricular valve surgery and significant atrioventricular valve regurgitation is more frequently associated in patients with a systemic tricuspid or a common atrioventricular valve.[8] In the retrospective study by Nakata and colleagues, atrioventricular valve repair in 29 consecutive patients with double outlet right ventricle and right atrial isomerism was associated with 5-year freedom from reoperation rate of 57%.[7] Survival at 5 years after atrioventricular valve repair was 70% and body weight less than 4 kg was identified

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as an independent risk factor for mortality.[7] In patients with double outlet right ventricle and hypoplastic left ventricle, coincidence of total anomalous pulmonary venous drainage has been shown to be an independent risk factor for mortality.[13] According to Lim and colleagues, significant valve regurgitation in patients with two atrioventricular valve morphology and functional single ventricle is associated with an early mortality of 2.6% and late mortality of 18.4% after atrioventricular valve surgery.[14] Difference in late mortality to the present investigation is due to the higher rate of atrioventricular valve replacement in the study by Lim and colleagues.

Our institutional policy is to preserve the atrioventricular valve as long as possible, but the optimal timing for atrioventricular valve surgery in patients with univentricular heart and two separate atrioventricular valves is currently unclear. In our study, surgical intervention on the left and right atrioventricular valves was most commonly performed during Fontan completion. However, atrioventricular valve surgery can also be performed as a sole operation before the Fontan procedure as the additional procedure of valve surgery may prolong the bypass and aortic cross-clamp time leading to a higher incidence of postoperative complications and increased mortality.[8] Atrioventricular valve surgery as a separate procedure before Fontan completion also yields the possibility to work on the valve at the time of Fontan procedure to improve suboptimal repairs and to prevent the breakdown of systemic ventricular function at the time of Fontan completion.[12] If one of the valves is not amenable to repair and severe regurgitation or stenosis is present, prompt atrioventricular valve closure should be performed, even between the classic palliative steps.

Despite advances in the treatment of double inlet left ventricle and double outlet right ventricle with univentricular palliation, redo atrioventricular valve procedures are frequently required as these frail valves have a high tendency to fail. In our study, the cumulative incidence of reoperation at 10 years after atrioventricular valve surgery was 31% with valve replacement in only 6.3% of children. In the retrospective study by Ono and colleagues, 32% of single-ventricle patients required atrioventricular valve reoperations with a slightly higher rate of valve replacement (8.7%).[8] However, atrioventricular valve replacement in single-ventricle patients is associated with a 25–44% rate of complete heart block as well as an early mortality of 29%.[15,16] Another option in patients with two separate atrioventricular valves and univentricular heart is valve closure. Atrioventricular valve closure, either with patch or suture, is associated with low operative mortality and an 18-year freedom from reintervention rate of 83%.[6] In the present investigation, valve closure was performed in 22% of children (7/32), mainly (5/7) during Fontan completion. In one child (1/7), redo closure of the left atrioventricular valve was performed due to suture dehiscence 3.6 months after valve suture closure. In our study, no patch dehiscence (Gore-Tex or Dacron) occurred. In the retrospective study by King and colleagues, atrioventricular valve closure in Fontan circulation was associated with an incidence of patch dehiscence of 17%.[6] In the present investigation, epicardial pacemaker implantation was required in two patients due to postoperative complete heart block after redo atrioventricular valve closure in both patients. After atrioventricular valve closure, King and colleagues reported a 14% risk of heart block.[6] According to Nunez and colleagues, atrioventricular valve closure using suture may be able to decrease the risk of alterations to the heart conduction system with lower need for pacemaker implantation.[17] However, published data on outcomes of atrioventricular valve closure, either with patch or suture, are limited making further comparison with our data difficult.

This study was limited by its retrospective nature and single-centre design. Main limitation of this study is the small sample size and thus differences between subgroups may not be detected. Mechanisms of atrioventricular valve anomalies were inferred from the operation records, and bias among surgeons can be expected. Inconsistencies in preoperative, operative, and postoperative management during the 27-year study period may have affected our outcome parameters.

Surgical atrioventricular valve intervention in patients with two separate atrioventricular valves and univentricular heart is required in 16% of patients during and after the staged Fontan completion and can be performed at various palliation points. Atrioventricular valve closure was performed in 22% and was mainly performed during Fontan completion. No atrioventricular valve replacement was necessary at the initial surgery. Atrioventricular valve surgery in this highly specific patient cohort is associated with low operative and late mortality. However, a high incidence of reoperation was observed due to the complex atrioventricular valve anatomy in these patients. Therefore, thoughtful considerations are needed to evaluate how the atrioventricular valve reintervention affects the long-term results of Fontan circulation in patients with two separate atrioventricular valve morphology and univentricular heart.

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