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ORIGINAL ARTICLE

Stent Implantation for Congenital Heart Diseases in Japan

— Comprehensive Analysis From the Japanese Society of Congenital Interventional Cardiology Registry —

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Background: Stent implantation for vascular stenosis associated with congenital heart diseases is commonly performed as an off-label procedure in Japan because there is no officially approved stent for any congenital heart disease.

Methods and Results: We analyzed data from the Japanese Society of Congenital Interventional Cardiology Registry collected from January 2016 to December 2018. Patients who underwent stent implantation were enrolled in the present analysis. During the study period, there were 470 procedures, 443 sessions, and 391 cases. Of 443 sessions, 427 (96.4%) succeeded procedurally. There were no differences in the procedural success rates among age groups. In all, 416 sessions (367 patients; 94%) resulted in survival to 30 days after catheter intervention. Of 392 admissions, 357 patients (91%) survived to discharge. Only 4 deaths were directly related to stent implantation. Some in-hospital complications were observed during 55 of 443 sessions. Both hospital deaths and serious complications were significantly more frequent in the group with various preoperative risk factors.

Conclusions: Although not officially approved for congenital heart diseases in Japan, stent implantation in congenital heart diseases has been widely and routinely performed for many years with safety and efficacy. The aim of stenting was variable and broad because of many different applications and morphological variations. These data may facilitate approval of such an important device in Japan.

Key Words: Catheter intervention; Congenital heart disease; Registry

The Japanese Society of Congenital Interventional Cardiology (JCIC; formerly the Japanese Society of Pediatric Interventional Cardiology), a general incorporated organization, has collected information, using questionnaires (JPIC questionnaire), of transcatheter interventions for pediatric and congenital heart disease in Japan since 1993, recognizing the importance of real-world efficacy and safety data to spread this innovative procedure in Japan. To collect complete and reliable data, the JCIC Registry was established in 2013, with the questionnaire-based data gradually being replaced by this web-based registry. All participating facilities had completed the transition from questionnaires to the web-based registry in 2016, at which time 4,000 procedures were registered. As of March 2018, 105 centers, including >90% of centers performing transcatheter interventions for pediatric and congenital heart disease, were part of the JCIC Registry.

Editorial p????

To facilitate the development of medical devices for transcatheter interventions for pediatric and congenital heart diseases, not only must the current situation and unmet needs in real-world clinical practice be clarified, but issues and challenges must also be reviewed to develop appropriate devices, based on complete and reliable data. Stenting for vascular stenosis associated with congenital heart diseases is an indispensable procedure in the real-

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world clinical practice of pediatric cardiology, and it is highly recommended in various guidelines. However, it has been commonly performed as an off-label procedure in Japan because there is no officially approved stent for any congenital heart disease. The purpose of the present study was to analyze the current situation of this procedure in Japan based on JCIC Registry data to clarify the unmet needs, procedural success, and complication rates to promote the approval of stenting for congenital heart diseases in Japan.

Methods

The JCIC Registry includes details regarding patients' personal information, procedures, adverse events, and outcomes for each catheter intervention session and is secured under the official confidential system of the National Clinical Database (NCD). We analyzed data in the JCIC Registry collected from January 2016 to December 2018. Patients who underwent stent implantation, except for coronary stenting, were enrolled in the present analysis.

Stent implantations are summarized by the number of procedures, the number of sessions, and the number of patients. For example, when stent implantation was performed in the pulmonary artery and pulmonary vein as part of the first intervention and a single procedure was performed during a second intervention, the number of procedures was 3, the number of sessions was 2, and the number of patients was 1. During the study interval, the total number of procedures was 470, the total number of sessions was 443, and the total number of patients was 391.

Age at stent implantation was divided into 6 categories: ≤28 days old; ≥29 days and <1 year; ≥1 and <3 years; ≥3 and <15 years; ≥15 and <20 years; and ≥20 years. Of the 443 sessions, 92 (20.8%), 116 (26.2%), 62 (11.4%), 128 (28.9%), 20 (4.5%), and 25 (5.6%) stent implantations were performed in each age group, respectively (**Table 1**). The median weight of the treated patients was 7.6 kg (range 0.9–81.7 kg; interquartile range [IQR] 3.2–18.18 kg). The largest number of sessions (70; 15.8%) were for hypoplastic left heart syndrome, followed by single ventricle associated with atrial isomerism (39 sessions; 8.8%). Eighty-four sessions (19.0%) were performed for any type of single ventricle, whereas 66 sessions (14.9%) were performed for tetralogy of Fallot and pulmonary atresia complicated by ventricular septal defect with or without major aortopulmonary collateral arteries. As indicated in **Table 1**, there were 43 sessions (9.7%) for total abnormal pulmonary venous connection with any of these 4 types. There were 135 (30.5%) and 114 (25.7%) sessions for "previous cardiovascular surgery" and "previous catheter intervention", respectively.

Methodology

Target lesions for stent implantation were classified into 5 lesions: pulmonary artery, systemic artery, systemic artery, pulmonary vein, atrial septum, and ductus arteriosus. Risk factors for stent-related complications were duct-dependent circulation, pulmonary hypertension, a dependence on mechanical ventilation, inotropes, or mechanical circulatory support, and intra-aortic balloon pumping. The procedural success rate was calculated by subtracting the number of unfinished sessions from the number of total sessions and then dividing the difference by the number of total sessions. Because the JCIC registry does not include data on hemodynamic and morphological changes following stent implantation, effectiveness and feasibility of stenting were assessed in terms of: (1) procedural success rate (whether catheter intervention was achieved as it was planned); (2) 30-day survival after catheter intervention; and (3) survival to discharge.

Statistical Analysis

Descriptive statistics were used to summarize stent implantation status, as well as the efficacy and safety of stent implantation. The results are presented as frequency tables, cross-tabulation tables, bar graphs, or scatter plots, as appropriate. Statistical hypothesis testing used the Wilcoxon rank sum test for continuous variables and Fisher's exact test for categorical variables. All tests were 2-tailed and significance was set at $P<0.05$. Efficacy was summarized descriptively according to target lesion and underlying congenital heart disease. Safety was also summarized descriptively by age, weight, target lesion, and preprocedural risk factors. Age, target lesion, and risk factors before stent implantation were compared between patients who died from serious complications and those who did not.

Ethics Approval

Registration to the JCIC Registry was approved by the local ethics committee of each attending hospital by an opt-out rule. The use of the registry data was approved by the Committee for Academic Use of the Registry Data in the JCIC Society (B-001), and by the Institutional Review Board of Shizuoka Children's Hospital (75).

Results

Target Lesions

The most common target of stent implantation was the pulmonary artery (in up to 156 procedures; 33.2%), followed by the pulmonary veins (93 procedures; 19.8%), and ductus arteriosus (67 procedures; 14.3%). According to age group analysis, most stent implantations for ductus arteriosus (66 procedures; 98.5%) were performed in infants <1 year of age, with approximately half (34 procedures) performed in neonates (≤28 days old). There were 64 procedures (68.8%) for pulmonary vein stenting during infancy in (**Table 2**).

Types of Stents

Stents were classified into 7 categories: balloon-expandable bare metal stent (BMS); balloon-expandable covered stent; self-expandable BMS; coronary BMS; coronary drug-eluting stent (DES); coronary covered stent; and coronary bioabsorbable vascular scaffold. Balloon-expandable BMSs were most commonly implanted (362 cases; 77.0% of all 470 procedures). Four types of stent for coronary arteries were implanted in 87 procedures, where 40 procedures were performed using coronary BMSs and 44 procedures performed using coronary DES. Furthermore, 66 procedures implanting a coronary stent were performed in infants <1 year of age, and 27 procedures (31.0%) were performed in newborns aged ≤28 days or younger (**Table 2**).

Stent Selection According to Target Lesions

Of the 156 stents implanted in the pulmonary artery, balloon expandable BMSs were used in 142 (91.0%) of cases.

Table 1. Background Characteristics of the Stent Sessions

	No. sessions (%)
Age group	
≤28 days	92 (20.8)
≥29 days−<1 year	116 (26.2)
≥1−<3 years	62 (14.0)
≥3−<15 years	128 (28.9)
≥15−<20 years	20 (4.5)
≥20 years	25 (5.6)
Fundamental diagnosis of congenital heart disease	
Aortic stenosis, subvalvular	1 (0.2)
Aortic stenosis, supravalvular	3 (0.7)
Aortic stenosis, valvular	8 (1.8)
Coarctation of aorta (±VSD)	31 (7.0)
Interrupted aortic arch+VSD	13 (3.0)
Interrupted aortic arch+aortopulmonary window	2 (0.5)
VSD (perimembranous)	1 (0.2)
ASD, secundum	1 (0.2)
AVC (AVSD), complete AVSD	12 (2.7)
TOF, pulmonary stenosis	27 (6.1)
TOF, Absent pulmonary valve	5 (1.1)
TOF, AVC (AVSD)	1 (0.2)
Pulmonary atresia	3 (0.7)
Pulmonary atresia, IVS	8 (1.8)
Pulmonary atresia, VSD (including TOF, PA)	17 (3.8)
Pulmonary atresia, VSD-MAPCA (pseudotruncus)	16 (3.6)
Pulmonary stenosis, valvular	1 (0.2)
Pulmonary artery stenosis (hypoplasia), main (trunk)	1 (0.2)
Pulmonary artery stenosis, branch, peripheral (at or beyond the hilar bifurcation)	2 (0.5)
Pulmonary artery, discontinuous	4 (0.9)
Pulmonary artery origin from ascending aorta (hemitruncus)	2 (0.5)
DORV, VSD type	6 (1.4)
DORV, TOF type	6 (1.4)
DORV, TGA type	11 (2.5)
DORV, remote VSD (uncommitted VSD)	2 (0.5)
DORV+AVSD (AVC)	5 (1.1)
Truncus arteriosus	8 (1.8)
Truncus arteriosus+interrupted aortic arch	1 (0.2)
TGA, IVS	9 (2.0)
TGA, VSD	3 (0.7)
TGA, VSD-LVOTO	5 (1.1)
Congenitally corrected TGA, VSD	2 (0.5)
Hypoplastic left heart syndrome	70 (15.8)
Hypoplastic LV	11 (2.5)
Hypoplastic RV	3 (0.7)
Mitral stenosis	3 (0.7)
Single ventricle, atrial isomerism	39 (8.8)
Single ventricle, DILV	3 (0.7)
Single ventricle, DIRV	4 (0.9)
Single ventricle, tricuspid atresia	7 (1.6)
Single ventricle, mitral atresia	6 (1.4)
Single ventricle, unbalanced AVC	9 (2.0)
Single ventricle+total anomalous pulmonary venous connection	14 (3.2)
Single ventricle, other	2 (0.5)
Total anomalous pulmonary venous connection, supracardiac type	23 (5.2)
Total anomalous pulmonary venous connection, cardiac type	3 (0.7)
Total anomalous pulmonary venous connection, infracardiac type	10 (2.3)
Total anomalous pulmonary venous connection, mixed type	7 (1.6)
Partial anomalous pulmonary venous connection	1 (0.2)
Pulmonary venous stenosis	2 (0.5)
Pulmonary vascular obstructive disease	1 (0.2)
Systemic venous obstruction	1 (0.2)
Tricuspid valve, other	1 (0.2)
Miscellaneous, other	4 (0.9)
Normal heart	2 (0.5)

The number of sessions was counted as 1, even if more than 1 procedure was performed at the same time in the same session. ASD, atrial septal defect; AVC, atrioventricular canal; AVSD, atrioventricular septal defect; DILV, double inlet left ventricle; DIRV, double inlet right ventricle; DORV, double outlet right ventricle; IVS, intact ventricular septum; LV, left ventricle; LVOTO, left ventricular outflow obstruction; MAPCA, major aortopulmonary collateral artery; PA, pulmonary atresia; RV, right ventricle; TGA, transposition of great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

Table 2. Age Distribution According to Target Lesions and Stent Types

	Age distribution (n)						Total (%)
	≤28 days	≥29 days–<1 year	≥1–<3 years	≥3–<15 years	≥15–<20 years	≥20 years	
Target lesions							
Pulmonary artery	3	28	28	80	7	10	156 (33.2)
Pulmonary vein	29	35	18	9	0	2	93 (19.8)
Ductus arteriosus	34	32	0	1	0	0	67 (14.3)
Shunt/conduit (other than Rastelli conduit)	1	12	10	7	1	3	34 (7.2)
Systemic vein	5	6	8	6	2	5	32 (6.8)
Intracardiac septum/ fenestration	3	5	3	17	2	1	31 (6.6)
Systemic artery	1	5	0	8	10	3	27 (5.7)
Rastelli conduit	0	1	2	0	0	0	3 (0.6)
MAPCA	0	0	1	2	0	0	3 (0.6)
Others/unknown	16	3	1	3	0	1	24 (5.1)
Stent type							
Balloon-expandable (BMS)	58	82	60	118	22	22	362 (77.0)
Balloon-expandable (covered)	1	2	1	2	0	0	6 (1.3)
Self-expandable (BMS)	6	4	0	3	0	2	15 (3.2)
Coronary (BMS)	13	18	5	3	0	1	40 (8.5)
Coronary (DES)	14	21	4	5	0	0	44 (9.4)
Coronary (covered)	0	0	0	2	0	0	2 (0.4)
Coronary (BVS)	0	0	1	0	0	0	1 (0.2)

BMS, bare metal stent; BVS, bioabsorbable vascular scaffold; DES, drug-eluting stent; MAPCA, major aortopulmonary collateral artery.

Table 3. Stent Selection According to Target Lesions

Target lesions	Balloon-expandable (n)		Coronary (n)				Self-expandable (BMS; n)	Total (%)
	BMS	Covered	DES	BMS	Covered	BVS		
Pulmonary artery	142	2	2	8	2	0	0	156 (33.2)
Pulmonary vein	58	2	2	6	25	0	0	93 (19.8)
Ductus arteriosus	52	1	6	5	3	0	0	67 (14.3)
Shunt/conduit (other than Rastelli conduit)	20	0	1	10	2	0	1	34 (7.2)
Systemic vein	25	0	3	0	4	0	0	32 (6.8)
Intracardiac septum/fenestration	25	0	0	4	2	0	0	31 (6.6)
Systemic artery	25	1	0	1	0	0	0	27 (5.7)
Rastelli conduit	3	0	0	0	0	0	0	3 (0.6)
MAPCA	0	0	0	1	1	1	0	3 (0.6)
Others/Unknown	12	0	1	5	5	1	0	24 (5.1)

Abbreviations as in Table 2.

For pulmonary vein stenting, 58 procedures (62.3%) were performed using balloon-expandable BMSs and 31 procedures (33.3%) were performed using stents for coronary arteries. Among the stents for coronary arteries used in pulmonary veins, 25 procedures (26.9%) were performed using coronary DESs (**Table 3**).

Stent Implantation for Ductus Arteriosus

Among the stents implanted for ductus arteriosus, 47 procedures (70.1%) were performed for duct-dependent systemic circulation, including 4 procedures for aortic stenosis, 7 procedures for coarctation of the aorta, 11 procedures for an interrupted aortic arch, and 25 procedures for hypoplastic left heart syndrome and its variants. There were 6 diagnoses (9.0%) of duct-dependent pulmonary circulation in total, 1 each of tetralogy of Fallot, pulmonary atresia, pulmonary stenosis, abnormal origin of the right pulmonary artery from the ascending aorta, and 2 of complete transposition of the great arteries complicated by ventricular septal defect and left ventricular outflow stenosis. We could not determine the purpose of duct stenting in the other fundamental diagnoses. The Registry data over the 3-year period of the study clearly indicate the most common purpose of duct stenting was for duct-dependent systemic circulation (**Table 4**).

Number of Stent Implantations in Each Institute

In 2018, 105 institutes were affiliated with the JCIC Registry in Japan, although there have been small fluctuations from year to year. For the 3-year period from 2016 to 2018, there were 94 hospitals registered for stent implantation. Of these 94 institutes, 63 (67.0%) performed fewer than 5 sessions of stent implantation during the 3-year study period, 21 (23.4%) performed ≥5 and <10 sessions, 5 (5.3%)

Table 4. Classification of the Fundamental Diagnosis at Stent Implantation for Ductus Arteriosus

Fundamental diagnosis	No. procedures (%)
Aortic stenosis, valvular	4 (6.0)
Coarctation of aorta (±VSD)	7 (10.4)
Interrupted aortic arch + VSD	9 (13.4)
Interrupted aortic arch + aortopulmonary window	2 (3.0)
AVC (AVSD), complete AVSD	3 (4.5)
TOF, pulmonary stenosis	1 (1.5)
Pulmonary atresia	1 (1.5)
Pulmonary stenosis, valvular	1 (1.5)
Pulmonary artery, discontinuous	2 (3.0)
Pulmonary artery origin from ascending aorta (hemitruncus)	1 (1.5)
DORV, VSD type	2 (3.0)
DORV, TGA type	1 (1.5)
TGA, VSD-LVOTO	2 (3.0)
Hypoplastic left heart syndrome	21 (31.3)
Hypoplastic LV	4 (6.0)
Single ventricle, heterotaxia syndrome	2 (3.0)
Single ventricle, mitral atresia	3 (4.5)
Total anomalous pulmonary venous connection, supracardiac	1 (1.5)
Total	67 (100.0)

Abbreviations as in Table 1.

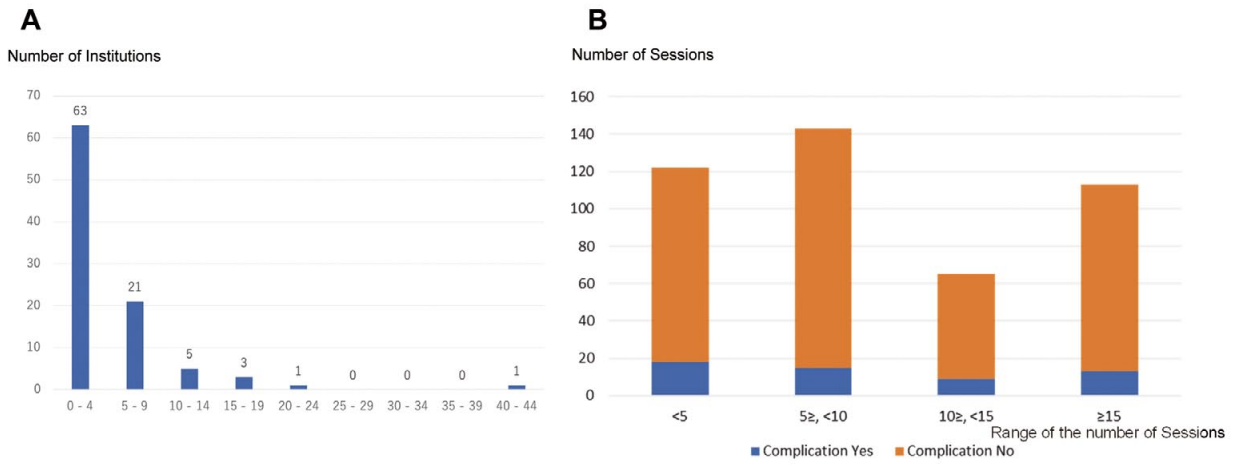

Figure. (**A**) Distribution of the number of stent sessions in each institute. (**B**) The number of complications according to the number of sessions at each institute.

performed 10–15 sessions, and 5 (5.3%) performed >15 sessions. Consequently, most of the Japanese institutes performed <10 sessions per year, with only ≤10 conducting 10 sessions or more (**Figure A**).

Procedural Success Rate of Stent Implantation

Out of 443 sessions, 427 (96.4%) succeeded procedurally. There were no differences in the procedural success rate among age groups or among lesions where >20 sessions were performed (**Table 5**).

Safety of Stent Implantation

For the 443 stenting sessions conducted during 419 hospitalizations, 35 (8.4%) patients died. Among these, only 4 deaths were directly related to stent implantation. These patients were more likely to have had a high-risk background at stent implantation. Compared with those who survived to discharge after stenting, those who died during hospitalization were younger (median age 25 days [IQR 1–131 days] vs. 895 days [IQR 136–3,494 days]; P<0.0001), more likely underwent interventions to the pulmonary vein (41% vs. 16%; P=0.005), had more advanced heart failure (New York Heart Association [NYHA] Class III/IV 71% vs. 26%; P<0.0001), and had preprocedural risk factors, such as duct-dependent circulation (34% vs. 18%; P=0.04), pulmonary hypertension (54% vs. 17%; P<0.0001), and a

Table 5. Success Rate of Stenting for Each Target Lesion

Lesions	No. successful	No. unsuccessful	Success rate (%)
Pulmonary artery	150	6	96.2
Pulmonary vein	89	4	95.7
Ductus arteriosus	64	3	95.5
Shunt or conduit	33	1	97.1
Systemic vein	32	0	100
Atrial septal defect or fenestration	29	2	93.5
Systemic artery	27	0	100
Major aortopulmonary collateral artery	3	0	100
Rastelli conduit	2	1	66.7
Others	24	0	100

Table 6. Severity of In-Hospital Complications

Severity	Session solely for stenting (n)	Session with multiple procedures including stenting (n)
None	14	6
Transient/not life threatening	11	6
Transient/life threatening if not treated	8*	1*
Life threatening	4*	1*
Resulted in subsequent death	3*	1*
Total	40	15

*Serious adverse events.

dependence on mechanical ventilation (77% vs. 15%; P<0.0001), inotropes (63% vs. 12%; P<0.0001), or mechanical circulatory support (17% vs. 1.8%; P<0.001). In addition, patients who died during hospitalization also underwent emergency stent implantation more frequently (71% vs. 24%; P<0.0001).

In-hospital complications were observed in 55 of 443 sessions. Serious adverse events (SAEs), that is "life threatening if not treated", "life threatening", and "resulted in subsequent death", were reported in 18 sessions (32.7% of sessions with complications, 4.1% of all stenting sessions; **Table 6**). Compared with patients without an SAE (in 425 sessions), those with an SAE (in 18 sessions) were younger (median age 47 days [IQR 25–248 days] vs. 524 days [IQR 66–2,749 days]; P=0.003), had more advanced heart failure (NYHA Class III/IV 63% vs. 35%; P=0.03), and had preprocedural risk factors, such as duct-dependent circulation (44% vs. 21%; P=0.03), pulmonary hypertension (44% vs. 21%; P=0.004), and a dependence on mechanical ventilation (67% vs. 23%; P=0.0002), inotropes (61% vs. 18%; P<0.0001), or mechanical circulatory support (17% vs. 3.1%; P=0.02).

Patients were discharged alive in 357 of 419 hospitalizations (85%). None of those who survived to discharge died within 30 days after the stent procedure. Only 3 complications (2 stent embolization, 1 sepsis) were observed after discharge.

Frequencies of in-hospital complications were higher in those <1 year of age than in those >1 year of age (P<0.001; **Table 7**), whereas those with complications had significantly lower body weight at the time of stent implantation (8.5±12 kg vs. 15±17 kg; P=0.0001). The complication rates for each factor were as follows: duct-dependent circulation, 20% (18/90); pulmonary hypertension, 19% (19/99); dependence on mechanical ventilation, 23% (25/110); dependence on inotropes, 23% (20/87); and dependence on mechanical circulatory support and on aortic balloon pumping 25% (4/16). Meanwhile, the incidence of complications was 20% if any of these preprocedural risk factors was present, which was significantly higher than for patients without any preprocedural risk factors (P<0.0001; **Table 7**). Although statistically not significant, ductus arteriosus, atrial septum, and shunt/conduit had high frequencies of in-hospital complications (19.4%, 13.3%, and 20.6%, respectively; **Table 7**).

The number of stent implantations in each institute was not related to the incidence of in-hospital complications (**Figure B**).

Discussion

Current Status of Stent Implantation

The procedural success rate of stenting for diverse underling heart diseases, as well as target lesions, was as high as 93.5–100%, except for stenting in the right ventricular outflow tract, where the number of patients was extremely small. These results are comparable to those of previous registry data from the US and the Japanese National Survey.[1,2] The age-specific procedural success rates were also high (94.5–100%) for all ages, with no significant differences among age groups. These data show the universal effectiveness of stenting regardless of the target lesion, or of the age at the time of the procedure. Stenting is highly recommended[3–5] when the stent can be expanded to an adult size. In this study, 208 sessions were performed in patients <1 year old; 132 sessions were for ductus arteriosus, aortopulmonary shunt, conduit in the right ventricular outflow tract, and intra-atrial septum. Although we do not have data on detailed specifications of these stents, we suppose that most lacked the potential to achieve adult size. Consequently,

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Table 7. Incidence of In-Hospital Complications by Age Group, Preprocedural Risk Factors, and Implantation Site

	In-hospital complications		Incidence (%)
	Yes (n)	No (n)	
Age group			
≤28 days	16	76	17.4
≥29 days–<1 year	22	94	19
≥1–<3 years	6	56	9.7
≥3–<15 years	8	120	6.3
≥15–<20 years	0	20	0
≥20 years	3	22	12
Total	55	388	12.4
Preprocedural risk factors			
Any	39	156	20
None	16	232	6.5
Total	55	388	12.4
Implantation site			
Pulmonary artery	12	137	8.1
Pulmonary vein	10	70	12.5
Ductus arteriosus	13	54	19.4
Systemic vein	2	29	6.5
Atrial septum	4	26	13.3
Shunt or conduit (other than Rastelli conduit)	7	27	20.6
Systemic artery	1	25	3.8
MAPCA	1	2	33.3
Rastelli conduit	1	2	33.3
Others/unknown	4	20	16.7
Total	55	392*	12.3

*Multiple site stent placements are included. MAPCA, major aortopulmonary collateral artery.

these stents could be implanted as a palliative measure as part of a cooperative surgical strategy, where they would need to be enlarged surgically or removed during a future planned operation.

The type and the severity of adverse events were similar to previous registry data from the US.[6] Both hospital deaths (8.4% of all hospitalizations) and serious complications (4.1% of all stenting) were significantly more frequent in the group with preoperative risk factors, such as duct-dependent circulation, pulmonary hypertension, and a dependency of mechanical ventilation, inotropes, and circulation assist devices. However, serious complications were not associated with the target lesion or with emergency procedures. Age-specific complication rates was clearly high in small infants, whereas the lesion-specific rates were higher in stenting for pulmonary vein, ductus arteriosus, and communication/fenestration of the atrial septum than for the other target lesions. These results are comparable to previous registry data from the US.[6] The risk of adverse events was not related to the experience of each institute in this study. We suppose the experience of the operator, but not that of the institute, may be more important in determine such risk for the generally low volume of stenting in Japan; however, we could not clarify this point. Consequently, high complication rates in some target lesions, despite similar efficacy among the procedures, may be caused not by the target lesion itself, but by the critical condition of the patient, which requires palliative stenting at a young age and is complicated by risk factors.

Challenge to Developing a Stent for Pediatric and Congenital Heart Diseases

In the real-world clinical data used in this study, there was a wide variation in both target lesions and in the age and constitution of the patients. Even for the pulmonary artery, which was the most common target in this study, there were only 156 sessions in 3 years. Although we did not collect data on the name and specification of each coronary and balloon-expandable stent, several types of stent were used for a wide variety of target lesions, as well as for patients with different ages and constitutions. Consequently, such a wide variation in both patient profiles and the stents used makes it difficult to evaluate the clinical utility of a specific stent for a specific lesion. Furthermore, among the 100 facilities in the JCIC Registry, only 2 centers performed 20–40 sessions in the 3-year study period, with most centers conducting fewer than 5 sessions. Taking these data into account, we believe that a clinical trial to evaluate the efficacy of stent implantation for each target lesion would be unrealistic.

The other challenge would be deciding the primary endpoint in the study. Death, onset of acute coronary syndrome, and target lesion revascularization are established endpoints to evaluate the efficacy and safety of coronary stents. Meanwhile, reintervention is always necessary following palliative stenting because it is a part of a staged strategy. In such a situation, the final outcome (e.g., death and survival rate) depends on the next stage surgery after stenting. Reintervention is also regarded as a scheduled procedure to deal with size mismatch following physical

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growth; however, indications for such reintervention are not established. Extremely long-term follow-up is necessary to evaluate life expectancy associated with stenting for young children. Acute hemodynamic changes also may not be a primary endpoint when the underlining diseases are not uniform.

Study Limitations

To collect comprehensive data, the JCIC Registry focuses on simple items; for example, we collect procedural success rates and adverse events for each catheter intervention, although we do not collect data on indication or hemodynamic and/or morphological effectiveness. This may limit the interpretation of the clinical usefulness of stenting in this study.

Conclusions

Although being not officially approved for congenital heart diseases in Japan, stent implantation in congenital heart diseases has been widely and routinely performed for many years with safety and efficacy. The aim of stenting was variable and broad because of the many different applications and morphological variations. Consequently, we definitely need to have appropriate pediatric-approved stents in Japan. To facilitate the approval of such an important device, we should take action with the regulatory bodies based on such clinical data.

Sources of Funding

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Disclosures

All authors do not have any conflicts of interest to declare.

IRB Information

The use of the registry data was approved by the Committee for Academic Use of the Registry Data in the JCIC Society (B-001) and by the Shizuoka Children's Hospital (75).

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