

Review

A new arena in cardiac surgery: Pediatric coronary artery bypass surgery

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Abstract: Prior to the 1970s, pediatric coronary artery bypass surgery (PCABS) was seldomly performed due to the lack of compelling surgical indications. The advent of coronary sequelae secondary to Kawasaki disease (KD) and the occurrence of coronary artery complications due to newly developed procedures, such as the arterial switch operation and early repair for intrinsic congenital coronary malformations, necessitated the development of PCABS. Because children grow rapidly and their life expectancy is very long, with increasing exercise capability requirements, the strategy for PCABS should differ from that for bypass surgery in adults. PCABS utilizing unilateral and bilateral internal thoracic arteries (ITA) has become the most reliable surgical method for children because of the distinct structure of ITAs being resistant to KD, growth potential according to the child's somatic growth and long-term patency without wall degeneration. This operation utilizing ITA grafts is now being performed worldwide and is referred to as the "Kitamura operation" for KD coronary sequelae. Notably, the use of vein grafts should be avoided in children. Likewise, this operation can now be successfully performed in infants using a surgical microscope, for congenital coronary disorders. Currently, PCABS with ITAs has been established as a new arena in cardiac surgery, following our initial attempts.

Keywords: pediatric coronary artery bypass surgery, Kawasaki disease, internal thoracic artery, saphenous vein graft, congenital cardiac, arterial switch operation

Introduction

Before the 1970s, pediatric coronary artery bypass surgery (PCABS) was rarely performed due to the lack of compelling surgical indications. The advent of coronary artery sequelae secondary to Kawasaki disease (KD)¹⁾ and the occurrence of coronary artery complications in newly developed procedures for complex congenital heart diseases, including the arterial switch operation²⁾ for complete transpositions of the great arteries or the Taussig–

Bing anomaly requiring a coronary artery transfer and the early correction of intrinsic coronary malformations during the infantile period,^{3)–5)} necessitated the development of PCABS. Particularly in Japan, mortality in children affected by KD was recognized as a social crisis in the 1970s and 1980s.^{6),7)} However, at that time, there were no reports of attempted PCABS, and the prevailing opinion was that surgery would not have been effective for this acute inflammatory condition. We developed a novel method for PCABS involving the use of unilateral or bilateral internal thoracic arteries (ITA), which are quite resistant to KD pathology owing to the distinct arterial wall structure of the ITA compared with other arteries, such as the coronary and peripheral arteries.⁸⁾ We also made use of either a surgical microscope^{9),10)} or powerful magnifying glasses to achieve secure anastomoses for small vessels less than 1 mm in diameter. In 1975, we performed the first surgical cases with autologous vein grafts,¹¹⁾ and in 1983, with ITA grafts^{12),13)} for children with KD. This review article describes

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Abbreviations: CABG: coronary artery bypass grafting; FFR: fractional flow reserve; ITA: internal thoracic artery; KD: Kawasaki disease; LAD: left anterior descending artery; LCX: left circumflex artery; LVEF: left ventricular ejection fraction; PCABS: pediatric coronary artery bypass surgery; RCA: right coronary artery; SVG: saphenous vein graft.

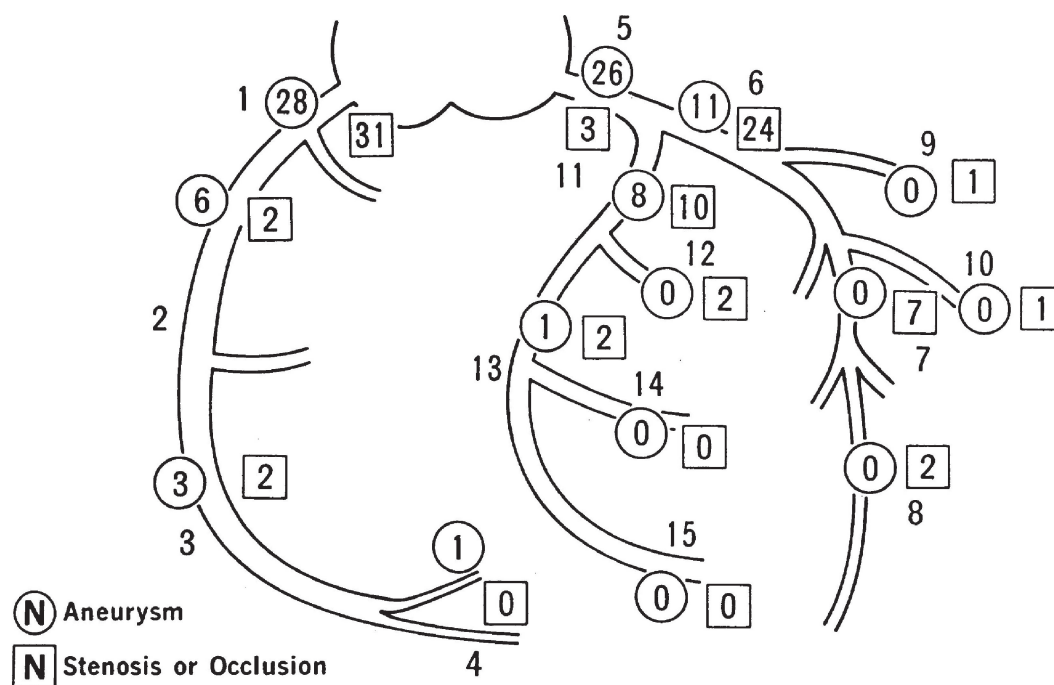


Fig. 1. Distribution of coronary artery lesions in 43 children with KD evaluated by selective coronary arteriography. The numbers in circles, squares, and without boxes show those of aneurysms, stenoses or obstructions, and the coronary segment number, respectively. Lesions tended to concentrate in the proximal segments of the left and right coronary arteries. This fact indicated the feasibility of surgical treatment for KD coronary lesions. This figure was reproduced with modifications based on the original literature.¹⁶⁾

the development and recent global popularization of PCABS.

Identifying surgical indications in children with KD

In 1975, Kato *et al.*⁷⁾ first reported that significant coronary artery lesions persisted in children after the convalescence stage of acute KD. In such children, acute myocardial infarction was associated with mortality rates as high as 22.0%, 62.5%, and 83.3% after the first, second, and third myocardial infarction episodes, respectively,¹⁴⁾ thus demonstrating the need for more effective treatments including a new surgical approach. In reports published in the late 1970s, coronary artery imaging depended on aortic root injection of a contrast medium, which provided limited details of coronary artery pathology. Selective coronary arteriography was not performed in children because there were no compelling indications, coupled with concerns regarding possibly higher complication rates for small children. However, selective angiography was considered essential for determining potential targets for surgical treatment.

We began to perform selective coronary arteriography in small children, using a 4F or 5F handmade catheter shaped like Judkins coronary catheters.^{11),15)} These had size and curve adjustments fashioned by superimposing the catheters on the lateral chest radiographic films of the pediatric subject. Although a variety of coronary lesions were identified among individuals with KD, obstructive lesions most commonly involved the entry or exit portions of coronary aneurysms, which were most often located on the proximal coronary arteries, particularly in the left coronary system, *i.e.*, the left main trunk and the proximal left anterior descending artery (LAD). On the other hand, right coronary artery (RCA) lesions tended to involve more distal areas before, and sometimes beyond the bifurcation.¹⁶⁾ The distribution of KD coronary artery lesions is shown in Fig. 1. The formation of both inter- and intra-coronary collateral vessels was greater in children than in adults;¹⁶⁾ therefore, ischemic symptoms were less prominent in children. Left ventricular function varied from the normal to the cardiomyopathic, according to the presence

of myocardial infarction and/or diffuse myocardial fibrosis after acute myocarditis due to KD.^{16),17)} These findings undermined the initial belief that surgical indications were quite rare in children with KD.¹⁸⁾ Surgical coronary revascularization was soon accepted to have a role in KD management and was included in the treatment guidelines for KD in Japan.¹⁹⁾

Surgery and graft selection in PCABS

The first PCABS for KD was performed on a 4-year-old boy who had an antero-septal myocardial infarction after acute KD in 1975 and was published in 1976.¹¹⁾ Selective coronary arteriography showed total occlusion of both the LAD and the RCA, with a reduced left ventricular ejection fraction (LVEF) of 0.45. At the time of operation, an autologous saphenous vein graft (SVG) was harvested from the thigh, and 2 aortocoronary bypass grafts were implanted. Postoperative angiograms revealed excellent graft patency with an improved LVEF of 0.61. Unfortunately, both grafts became totally occluded within 2 years; the child only survived because of the presence of intercoronary collateral vessels that developed from the left circumflex artery (LCX) to the LAD and the bridging intracoronary collaterals from the proximal RCA to the distal RCA. The LVEF again deteriorated. Hence, the PCABS utilizing autologous SVG in children ultimately proved unsuccessful within a couple of years postoperatively. A 26-year-old young man probably with KD who had an anterior myocardial infarct due to a left main-LAD aneurysm with severe stenosis at the LAD origin also underwent 2 aortocoronary vein graft bypasses²⁰⁾ (published in 1975). Ten years later, left ventricular function had deteriorated to the extent that heart transplantation was indicated, and both vein grafts were found to be occluded. Because patients with KD are often small children or very young adults, the ideal conduit must have a patency that would last for their lifetime. Although a SVG was exclusively used as the conduit during the early development stage of PCABS for KD coronary lesions both in Japan^{18),21),22)} and in the U.S.A.,²³⁾ long-term patency of SVGs proved unsatisfactory, particularly in small children. As a result, a better graft material was sought. In 1983, Mains *et al.*²⁴⁾ reported the use of the left subclavian artery as a coronary bypass conduit; however, this operation had strong limitations, such as loss of the main blood supply for the left arm of a child and a very limited graft length.

Another important but unresolved question was how grafts would respond to the somatic growth of children. We decided to use a pedicled ITA, which was a small-caliber artery but was expected to grow when used in children. We performed the first PCABS using ITA grafts in 1983 and reported the results in 1985.¹²⁾ The fact that the ITA is rarely affected by KD is an important aspect of this surgical approach. KD affects mostly muscular arteries,⁸⁾ and the ITA has less muscle and more elastic fibers than other arteries, such as the coronary and peripheral arteries. This may be the reason why the ITA is least affected by KD. In addition, we demonstrated the safety of the bilateral use of the ITA,¹³⁾ without any visible compromise in thoracic growth. Subsequently, we have promoted ITA grafting as the best option for children requiring PCABS. Takeuchi *et al.*²⁵⁾ reported the successful use of a pedicled gastroepiploic artery as a graft in a child with KD coronary lesions; we also adopted the use of this arterial graft for the distal RCA only, in addition to bilateral ITAs for the proximal RCA and the left coronary arteries (Fig. 2).^{13),26),27)}

The ITA of small children is a short, thin-walled artery with a diameter of 1 mm or less, reflecting the small size of a child's thorax relative to their large head. It requires meticulous and precise dissection and anastomosis using high-magnification surgical glasses or a microscope, and use of 8-0 or 9-0 small needles and sutures.^{9),10)} Although a surgical microscope is not commonly used for adult patients, it may be an important tool in PCABS. Indeed, the use of a surgical microscope for PCABS with ITA grafts, which we started in 1994,⁹⁾ has been recently revived for infants or small children, with a high anastomotic success rate^{28),29)} (Fig. 3).

Growth responses of grafts in children and clinical effects of PCABS

Using mathematical analyses of bidirectionally imaged grafts, we demonstrated for the first time that the ITA graft has the potential to grow longitudinally and circumferentially in tune with the child's somatic growth^{30),31)} (Figs. 4–8). The fact that bilateral use of the ITA¹³⁾ does not result in any adverse effects on the thoracic development of children was also demonstrated by long-term follow-up of the patients until adulthood.²⁷⁾ The right and left ITAs have completely the same wall structure and demonstrated similar graft qualities in terms of graft patency, growth potential, and very low late degeneration. All of these excellent ITA graft

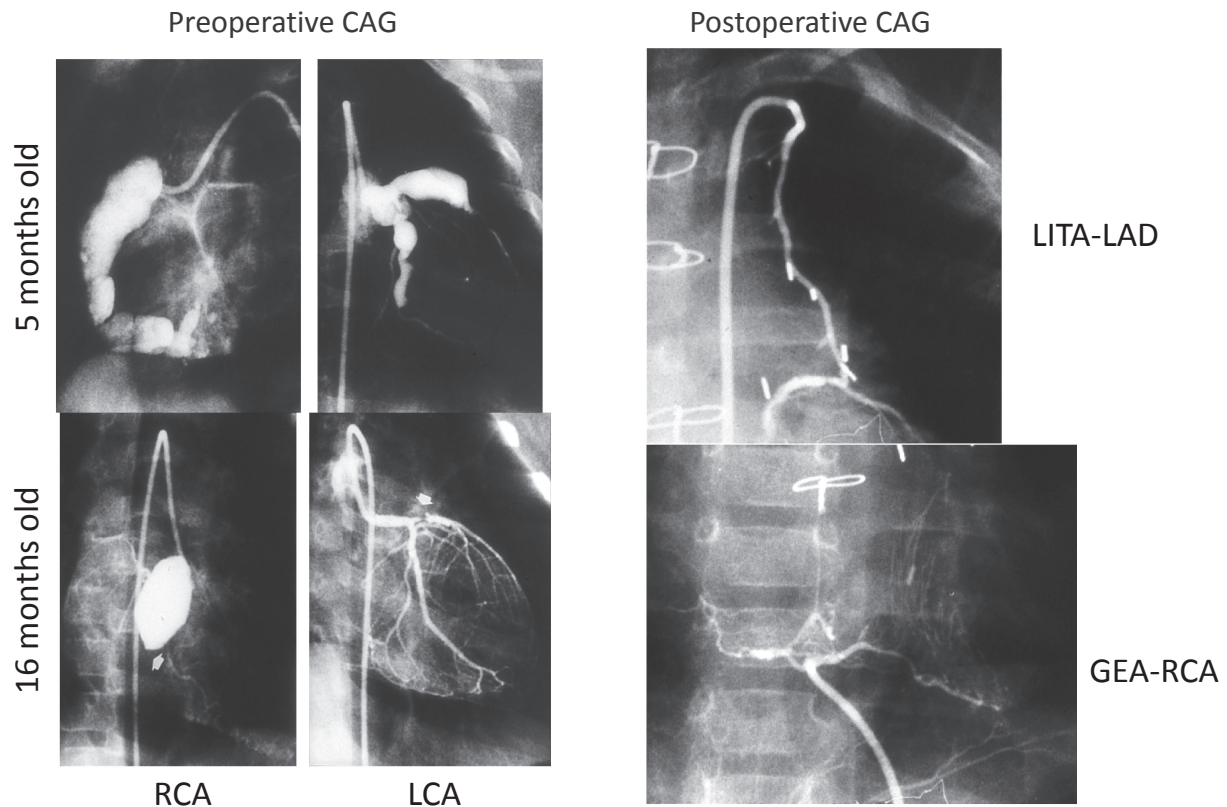


Fig. 2. Preoperative and post-PCABS angiograms in a 1-year-old boy with severe KD coronary lesions. At 5 months old, huge coronary artery aneurysms both in the right and left coronary arteries, and at 16 months old, the RCA was totally obstructed and a 95% stenosis was found at the origin of the LAD artery. At operation, the left ITA was anastomosed to the LAD and the gastroepiploic artery (GEA) to the distal RCA using a surgical microscope.

qualities in children have been clearly demonstrated in a 30-year follow-up study involving more than 100 children.^{27),32),33)} Use of the right or left ITA depended on the anatomical location of the target coronary artery.

In contrast, the autologous SVG, which was used in the initial stages of development of PCABS,^{11),16),18)} has proven to be inadequate as a graft in children because of the lack of longitudinal growth potential, significantly worse early- and long-term patency compared with ITA use, particularly in small children younger than 10 years,^{27),30),31),34)} and early vein graft degeneration (intimal hyperplasia) eventually leading to immature atherosclerosis at 10 to 20 years after surgery during childhood.^{27),35)} A total of 95% of children operated on with at least 1 ITA graft were alive at 30 years postoperatively, while more than 84% could work well and had integrated into society without specific limitations, and female subjects could safely sustain pregnancy and deliver a baby.^{27),33)}

Long-term patency and graft morphology in growing children

When long-term graft patency in PCABS was investigated, ITA patency was far superior to that of SVG for both the LAD and non-LAD coronary arteries^{27),36)–39)} (Figs. 9, 10). In addition, the patencies of ITA grafts for KD have shown no significant differences between the LAD and non-LAD as target coronary arteries,²⁷⁾ and between younger (<10 years old) and older children (≥ 10 years old)²⁷⁾ (Fig. 11). ITA grafts that were patent at 1 year after surgery remained so for up to 25 years,^{27),40)} and I believe they will remain that way for the entire lifetime of the patients. ITA string sign followed by occlusion did occur in a few patients within a year after surgery, but in 20–25% of such ITAs, recanalization occurred within several years thereafter.^{41)–43)} In contrast, the SVG became occluded not only early on, within 1 year postoperatively, but also much later postoperatively due to intimal



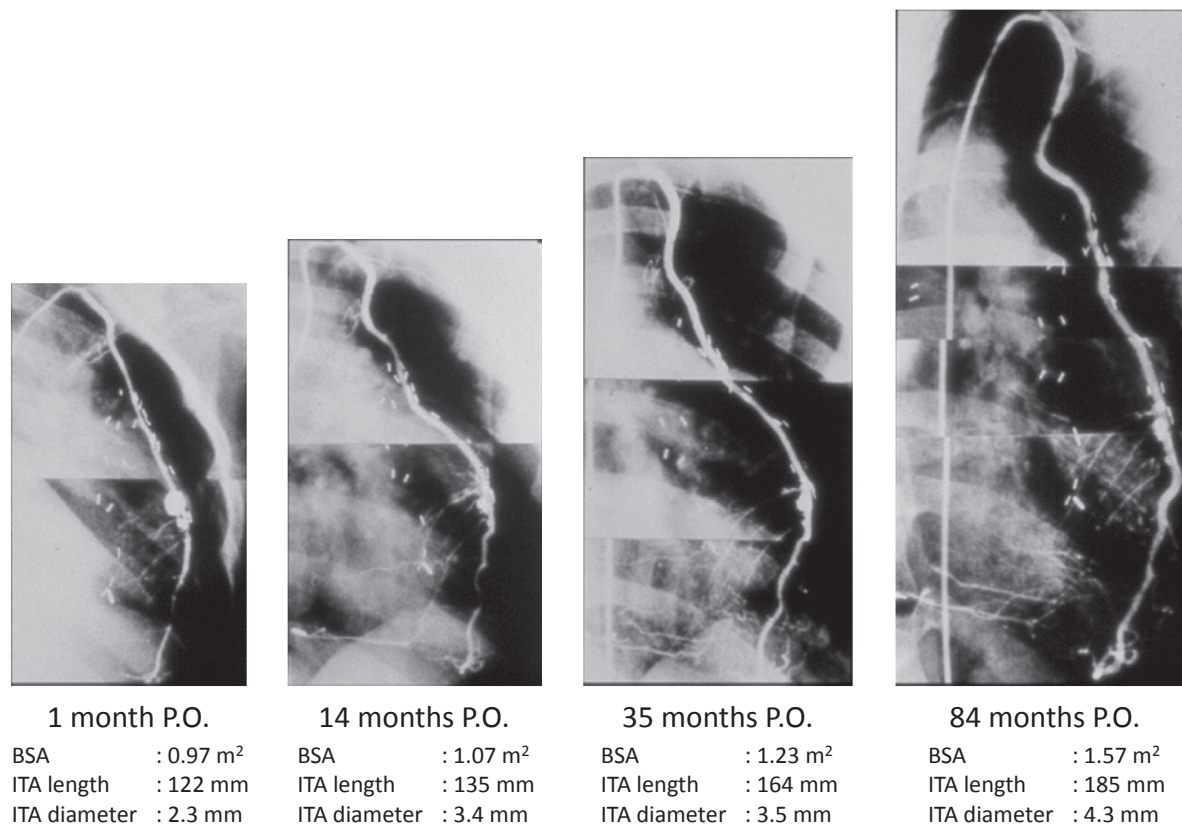
Fig. 3. We started utilizing a surgical microscope for PCABS in small children and reported its utility in 1994⁹⁾ and 1998.¹⁰⁾ The utilization of a surgical microscope has expanded the indications of PCABS in neonates and infants. The use of $\times 8$ – $\times 10$ magnification and 8-0 or 9-0 sutures is common and practical.

fibroproliferation that eventually resulted in atherosclerosis.^{27),33),35),44)}

Late postoperative angiographic graft morphology was quite different between the SVG and ITA grafts. The wall configuration of the ITA graft was smooth, with no luminal stenosis or dilatation, and it matched well in size with that of the recipient coronary artery at 20 years after the operation.^{27),33)} In addition, ITA grafts length grew in proportion to the patient's body growth^{30),31)} ($r = 0.845$, $P < 0.001$). In contrast, SVGs had poor response to body growth, was usually dilated with local narrowing, and was sometimes aneurysmal, with prominent irregularities of the wall contour.^{30),31),35)} Patients in their twenties showed fibroproliferative thickening and atherosclerotic changes of the vein graft with mural thrombosis.³⁵⁾ The SVG can also be a cause of acute myocardial infarction in the late postoperative period, likely due to embolism from wall thrombus detachment or thrombosis at the site of intimal thickening.³³⁾ Due to the poor or absent growth potential of SVGs, they can cause traction on the recipient coronary artery, distorting the anastomosis, and resulting in poor run-off to the distal artery.^{33),34)}

Representative graft-coronary angiograms in the late postoperative period (>20 years) are shown in Fig. 12.

With enlarged ITA grafts in association with a patent or non-patent SVG, 5 grown-up patients who developed total occlusion of both the left and right coronary ostia are living at present without symptoms. Two ITA grafts implanted during childhood can maintain the entire blood supply to the heart in adulthood. As demonstrated in Figs. 9 and 10, there was a significant difference ($P < 0.001$) between the 25-year patency rate of the ITA graft (87%) and the SVG (44%).²⁷⁾ Furthermore, as shown in Fig. 11, when used in children <10 years of age, the patency for ITA grafts was 86%, which was essentially the same ($P = 0.163$) as that in patients >10 years old, compared with a patency of 25% for SVGs ($P < 0.004$).^{27),33)} According to the results of the 30-year postoperative follow-up, it was concluded that the pedicled ITA should be the conduit of choice for PCABS, based on persistent graft patency, growth potential, and potential metabolic advantages for many decades.^{42),43)} Overall, the use of SVGs should be avoided in growing children.



Kitamura S, et al. *Circulation* 1988;78:129-39

Fig. 4. Chronological longitudinal growth of the ITA graft with the somatic growth of a child from 1 month to 7 years after PCABS. Growth potential was apparent without any degenerative changes in the graft wall. This figure was reproduced with modifications based on the original literature.³⁰⁾

The negative aspects of the ITA graft

Flow competition causing a string phenomenon of the ITA graft is now well documented and occurs because of insufficient blood flow through the graft when the recipient coronary artery blood flow is unrestricted.⁴¹⁾ This phenomenon has also been observed in adult coronary artery bypass grafting (CABG) for atherosclerotic disease and is the major non-technical cause of ITA graft failure (thrombosis).⁴⁵⁾ However, recanalization of ITA grafts that have been judged as occluded or nonfunctioning after the ITA string phenomenon has been noted to occur with a relatively high incidence of 20–25% in PCABS^{27),41)} compared with that in adult CABG. This phenomenon is endothelium-dependent, and when flow competition between the graft and the recipient coronary artery disappears due to the progression of coronary artery obstructive lesions, the ITA regains its flow and function as a graft, unless the lumen is completely thrombosed⁴³⁾ (Fig. 13).

Measurements of the fractional flow reserve (FFR) with a pressure guidewire may help avoid the ITA string phenomenon due to flow competition. Ogawa *et al.*⁴⁶⁾ reported that an abnormal preoperative FFR normalized after a successful CABG in patients with KD. Botman *et al.*⁴⁷⁾ studied the value of FFR (>0.75 or ≤ 0.75) for ITA graft obstruction in adult CABG and reported that 8.9% of bypass grafts in functionally significant lesions (≤ 0.75) and 21.4% of bypass grafts in functionally nonsignificant lesions (>0.75) were occluded. There was no difference in symptoms, such as angina pectoris, between the groups. The usefulness of FFR in preventing the graft string phenomenon in pediatric coronary artery disease with multiple aneurysms needs further prospective evaluation, and it would be worthwhile to conduct a multicenter trial. Anastomotic stenosis due to technical reasons can be easily managed by simple balloon dilatation, with essentially no recurrence of stenosis.^{38),39)} Stenting is absolutely unnecessary in this setting and should be avoided in children.

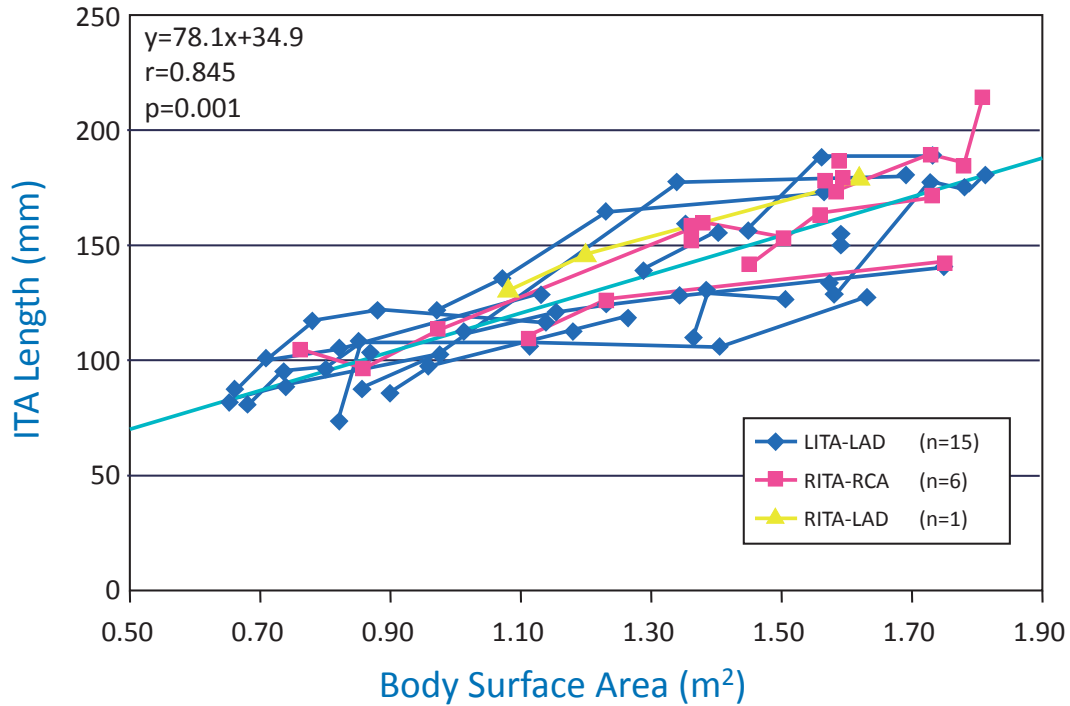


Fig. 5. The relationship between the growth in length of ITA grafts and body surface area (somatic growth). A significant correlation ($r = 0.845$, $p = 0.001$) was present, which clearly showed the growth potential of the living ITA graft. LITA: left ITA, RITA: right ITA, LAD: left anterior descending artery, RCA: right coronary artery. This figure was reproduced with modifications based on the original literature.³¹⁾

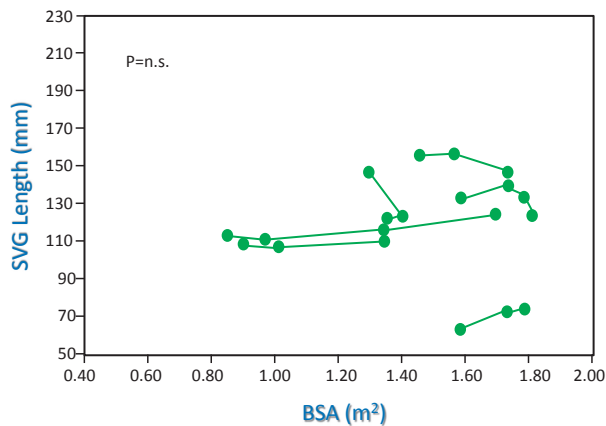


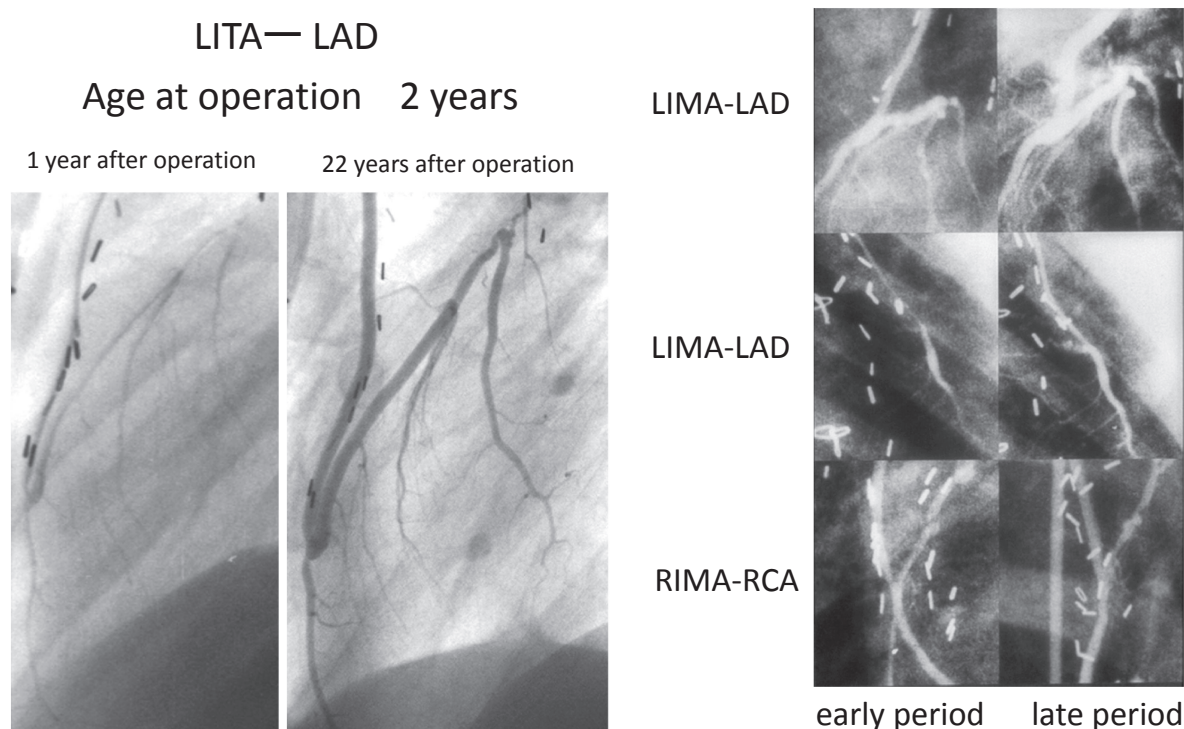
Fig. 6. The relationship between the length of SVGs and body surface area (somatic growth). No significant correlation was observed ($p = \text{n.s.}$), which showed poor or no growth potential of the SVG. This figure was reproduced with modifications based on the original literature.³¹⁾

Survival of children with KD treated by PCABS

PCABS using ITA grafts is a safe procedure for children with severe coronary involvement due to KD. The surgical mortality in over 100 such children has been 0%, and the late mortality in the subsequent

25 years has been 5% (95% CI: 2–12)²⁷⁾ (Fig. 14). Successful surgery often improves cardiac function and coronary blood flow, particularly during exercise, which is quite beneficial for growing children who require progressively increasing exercise capacity.⁴⁸⁾ Approximately one-third of the surgical subjects had a previous myocardial infarction.²⁷⁾ Although a strict comparison is impossible, the 30-year survival of children with KD with previous myocardial infarction was limited and as low as 49% (95% CI: 27–71),⁴⁹⁾ compared with a 95% (95% CI: 88–98) 25- to 30-year survival with PCABS with ITA grafts.²⁷⁾

Late death after PCABS in patients with KD was frequently sudden, mostly occurring in children with both reduced left ventricular function and a history of ventricular tachyarrhythmias.^{27),49),50)} Therefore, early management strategies, such as early reintervention for graft failure, electrophysiologic studies, early ablation therapy, and implantable cardioverter-defibrillator insertion for ventricular tachyarrhythmias, may be critical. The multicenter cooperative study that we conducted^{36),37)} demonstrated that the presence of ITA grafts in the heart was significantly beneficial for the long-term survival of children with KD, as shown in Fig. 15. Cardiac



Kitamura S. et al. J Thorac Cardiovasc Surg 1990;99:708-15

Fig. 7. Circumferential growth potential of the ITA graft. Angiograms taken at two different time points clearly demonstrated that the graft diameter also increased including the anastomotic point. This figure was reproduced with modifications based on the original literature.¹³⁾

transplantation has been performed for KD with severely reduced left ventricular function together with multiple giant coronary aneurysms. Approximately 15 cases have been reported in the literature worldwide,^{51)–54)} and in Japan, at least 3 patients with KD have received a heart transplant.

Event incidence after PCABS for KD

Cardiac events after PCABS were precipitated by: 1) ITA graft stenosis at the anastomosis; 2) graft obstruction of any cause, including the string phenomenon of ITA grafts; 3) fibroproliferative intimal thickening and atherosclerosis of the SVG; 4) late thrombosis of the remaining coronary aneurysms; and 5) post-inflammatory progression of coronary artery fibro-obstructive disease.²⁷⁾ The incidence of these coronary events increased as the postoperative period lengthened, and the total cardiac event-free rates at 5, 10, 20, and 25 postoperative years were 87%, 81%, 70%, and 62% (95% CI: 48–74),²⁷⁾ respectively (Fig. 14). Tsuda *et al.*⁵⁰⁾ reported that the 30-year overall cardiac event-free rate in patients with giant aneurysms (≥ 8 mm in diameter) was only

36% (95% CI: 28–45, $n = 245$), whereas it was 62% (95% CI: 48–74, $n = 114$) with PCABS.²⁷⁾ Although the cardiac event-free rates reported in 2 different series^{27),50)} were not comparable, children who had suffered multiple giant aneurysms prior to PCABS were found to have fewer cardiac events during the subsequent 25–30 years after PCABS with at least 1 ITA graft.

Although cardiac events at 25 years were not uncommon, events resulting in death were rare in surgical patients when early and adequate interventions were carried out, either by reoperation or percutaneous coronary intervention.^{27),32),33)} Furthermore, because most of the patients had reached adulthood by the time the second intervention was required, reoperation utilizing either the radial artery, the gastroepiploic artery, or both, and percutaneous coronary intervention using coronary stents could be applied more safely and effectively than in children.^{55)–58)}

Analysis of long-term follow-up data emphasized the need for prolonged and close postoperative medical supervision of patients with KD with

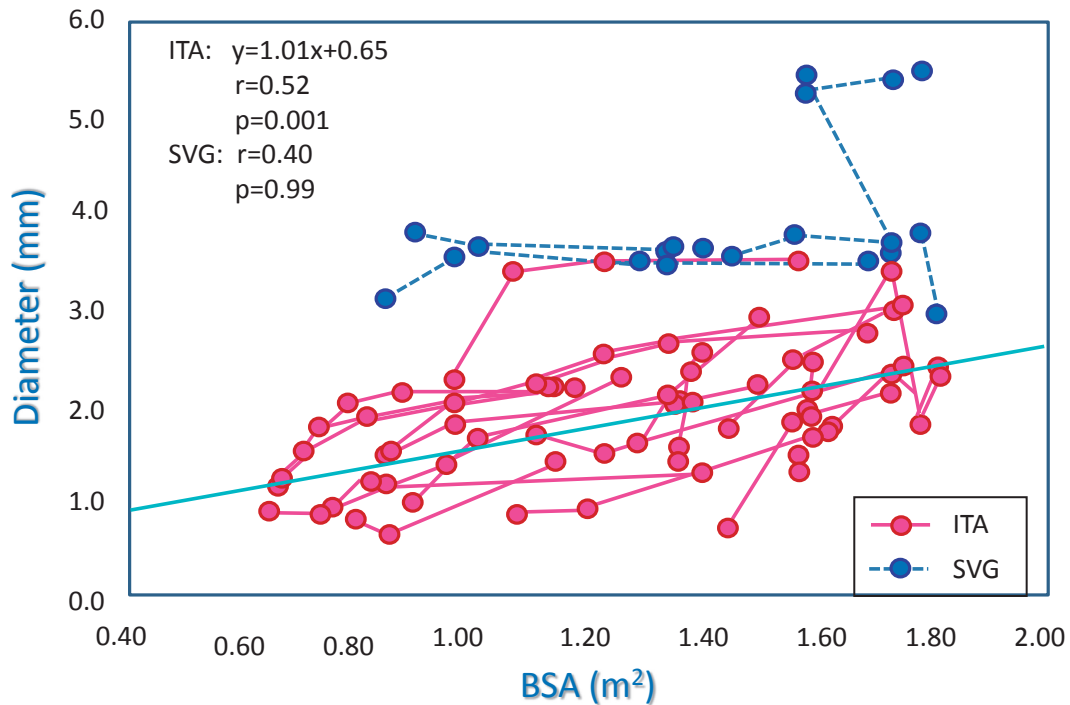


Fig. 8. The relationship between the minimal diameter of the vein graft and body surface area (somatic growth). For the ITA, a significant correlation was present ($r = 0.52$, $p = 0.001$); however, a correlation was not found for SVGs ($r = 0.40$, $p = 0.99$). This figure was reproduced with modifications based on the original literature.³¹⁾

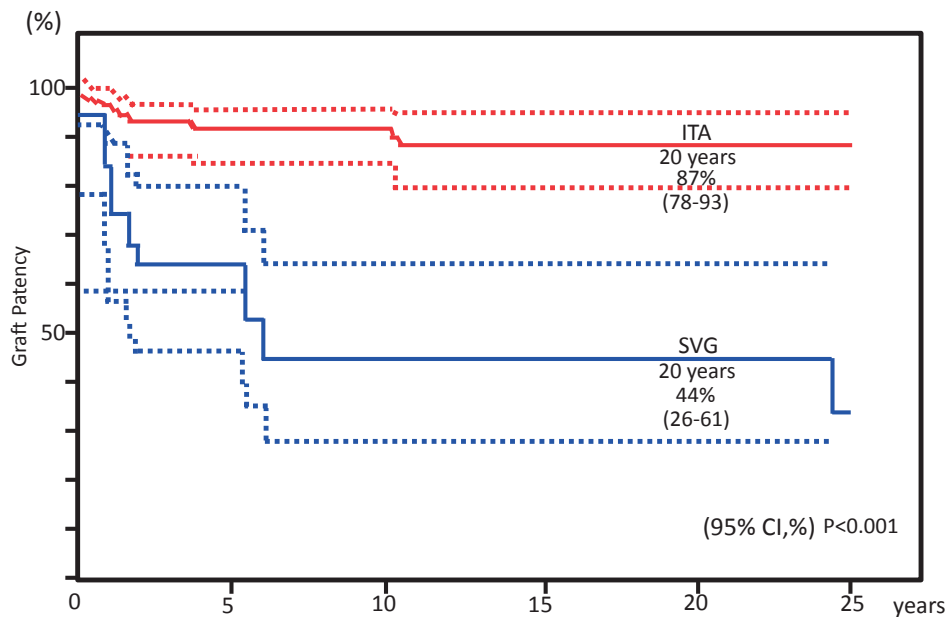


Fig. 9. Long-term graft patency up to 25 years after PCABS. A very significant difference ($P < 0.001$) in patency was observed between ITA grafts (87%, 95% CI 78–93%) and SVGs (44%, 95% CI 26–61%). However, a few SVGs maintained patency, particularly for the LAD, but degeneration of SVGs became obvious over 20 years after PCABS. This figure was reproduced with modifications based on the original literature.^{27),33)}

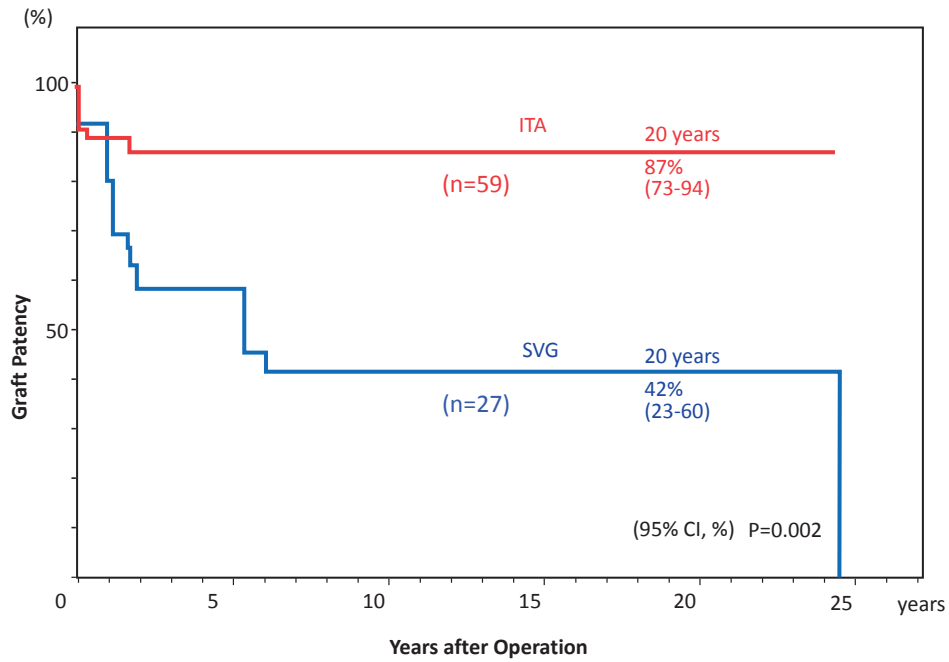


Fig. 10. Long-term patency was compared between ITA grafts and SVGs for non-LAD arteries (RCA and LCX), because the LAD was exclusively revascularized with the ITA. Again, the ITA showed far better long-term patency than SVGs ($p = 0.002$) for the non-LAD coronary arteries. This figure was reproduced with modifications based on the original literature.^{27),33)}

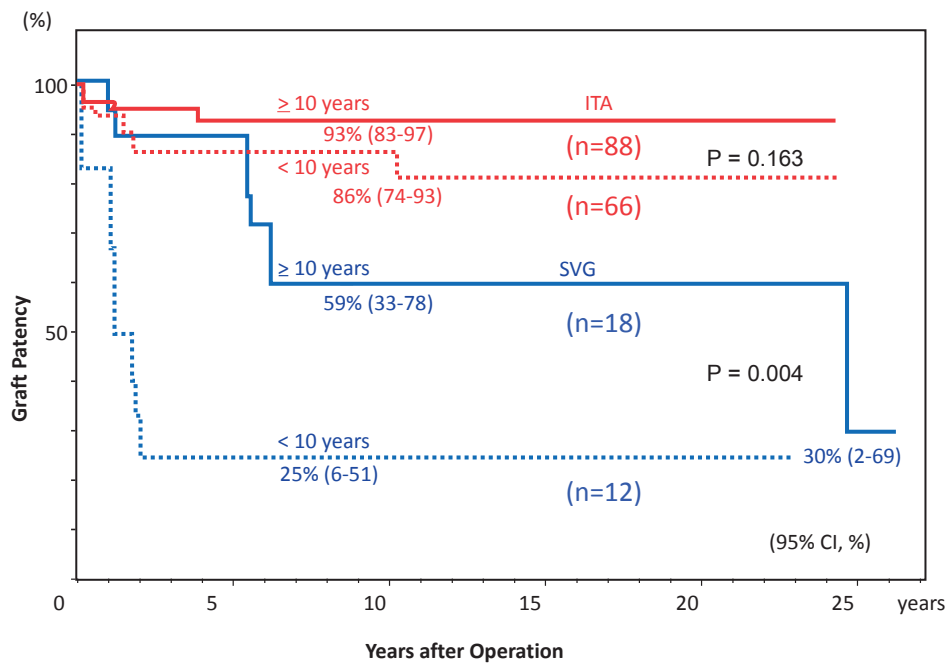


Fig. 11. Long-term graft patency of ITA grafts and SVGs according to the age of patients at operation of older and younger than 10 years. For ITA grafts, there was no significant difference ($p = 0.163$) in graft patency between children older and younger than 10 years. However, for SVGs, children younger than 10 years showed a significantly lower patency than those older than 10 years (59% vs. 25%, $p = 0.004$). SVGs were proven to be inappropriate for PCABS, particularly for small children. This figure was reproduced with modifications based on the original literature.^{27),33)}

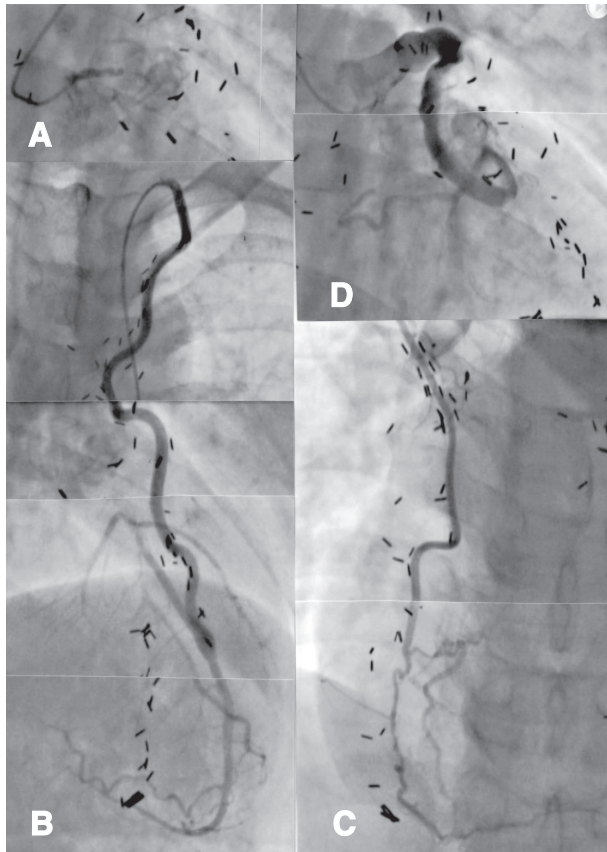


Fig. 12. Post-PCABS (24 years) angiographic evaluation of the coronary artery and grafts. **A:** The left and right coronary arteries were totally obstructed at their origins. **B:** The left ITA-LAD graft was perfect, with an increased diameter and smooth wall configuration. **C:** The right ITA-RCA graft was also patent, with very good wall configuration. **D:** The SVG-LCX was patent but showed very poor perfusion state with graft degeneration (wall irregularity), wall thrombosis, and poor distal perfusion, resulting in small posterolateral myocardial infarction at 24 years after PCABS. This figure was reproduced with modifications based on the original literature.³³⁾ Degeneration is unavoidable in SVGs implanted in childhood. *PCABS, pediatric coronary artery bypass surgery; ITA, internal thoracic artery; LAD, left anterior descending artery; RCA, right coronary artery; SVG, saphenous vein graft; LCX, left circumflex artery.

functioning but degenerated SVGs, as well as those with persistently patent coronary aneurysms.^{27),50)} Conversely, when the graft was functioning well, 84% of children could enjoy athletic programs at school, and 16% of them participated in sport clubs^{27),33)} despite the fact that they had been strictly excluded from school athletic programs prior to surgery because of fear of sudden collapse or death in the playground due to repeat coronary events. Upon reaching adulthood after PCABS, many

patients have successfully engaged in jobs and several female patients have had successful pregnancies and deliveries. Long-term, careful observation showed that PCABS with unilateral or bilateral ITA grafts could offer effective and long-lasting treatment and improve quality of life for children compromised by coronary lesions.

Treatment for coronary aneurysms with no stenotic lesions

There are no indications for PCABS in the absence of stenosis or obstruction. The string phenomenon will occur when the ITA is anastomosed to such arteries. In this setting, the main purpose of treatment is to prevent acute thrombotic obstruction within coronary aneurysms. Several interventions have been attempted for this purpose in addition to anticoagulation therapy, which is mostly based on the combined use of warfarin and aspirin.

1. Ligation of the outlet of coronary aneurysms and placement of distal coronary bypass grafts. Atherosclerotic coronary aneurysms carry a risk of rupture, and either resection of the aneurysm or ligation of the inlet and/or outlet segments must be performed.^{59),60)} In contrast, aneurysm rupture has hardly occurred in KD except in the acute inflammatory phase; consequently, very few ligations of the coronary artery distal to aneurysms combined with a distal bypass graft have been performed⁶¹⁾ in light of the risk of myocardial damage if the graft function is not perfect. In 1 patient who underwent ligation of the outlet of a right coronary aneurysm combined with placement of a distal ITA bypass graft, the aneurysm rapidly thrombosed, with a persistent right bundle branch block and increased efflux of cardiac enzymes.³³⁾ Particularly when a single ITA is used for bypass, the initial blood flow may not be sufficient for the recipient coronary area because of the small caliber of the ITA in children. Small side-branches arising from the aneurysm may also simultaneously thrombose. In my series, I have not ligated a coronary artery, because coronary aneurysms caused by KD do not rupture in the post-inflammatory phase and the ITA string phenomenon is clinically benign, causing no discernible harm except for the mortification of the surgeon. In contrast, coronary ligation can lead to certain acute cardiac events that may worsen the late prognosis.³³⁾ The optimal surgical strategy for this situation may involve the use of unilateral or bilateral ITAs, depending on the comparative sizes of the coronary artery and the ITA, or use of the bigger SVG despite the high likelihood of late SVG failure.

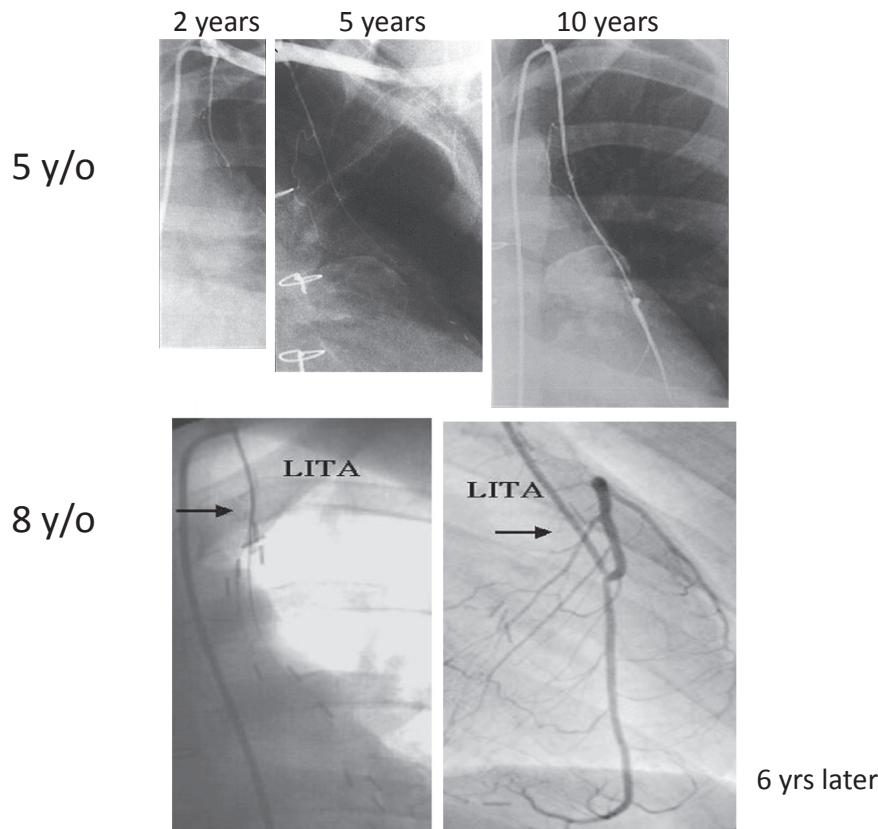


Fig. 13. The ITA graft could be recanalized after a string phenomenon once judged as a nonfunctioning or closed graft, when stenosis of the recipient coronary artery progressed. The incidence of ITA graft recanalization or reopening was higher for children than adults, being approximately 20–25%. This figure was reproduced with modifications based on the original literature.⁴¹⁾

2. Coronary aneurysmorrhaphy or size reduction of coronary aneurysms. This procedure was first reported by Abe and Ochi,⁶²⁾ who excised the uncalcified anterior wall of a long and large right coronary aneurysm and resutured the wall, maintaining the lumen using a probe of adequate size. The luminal dilatation and irregularity was consequently corrected, resulting in less turbulent blood flow within the aneurysm. This procedure may prevent blood clotting inside the aneurysm and may be effective in selected patients. Some patients were successfully weaned from warfarin; others, however, suffered complications from coronary artery thrombosis after the procedure,⁶²⁾ as endothelial function within the aneurysm might have remained impaired. Certainly, a longer follow-up with more patients is needed.

Current status of PCABS for KD

In Japan, more than several hundred patients with KD have undergone a bypass operation, and the

main graft for PCABS has completely shifted from the SVG to the ITA,^{63),64)} based upon the results of our studies. The annual number of new patients with KD in Japan, mostly children, has been increasing progressively over the last 2 decades. In Japan, 20,000 new patients per year have been reported; cardiac or coronary lesions were found in 9.3% of patients in the acute inflammatory phase, and this resolved to 2.8% in the late phase (coronary sequelae) in 2011.⁶⁵⁾ The gender ratio remains the same, with male dominance at a ratio of 1.5–2:1. Recently, in the U.S.A., more than 8,000 new patients with KD have been hospitalized each year.^{66),67)} Reports of PCABS for KD from the U.S.A., Europe, and Asian countries other than Japan have been increasing significantly, and in fact, PCABS with the use of ITAs for children with KD is referred to as the “Kitamura operation”.^{38),68)–70)} Over the last 15 years, consultations have been requested by many pediatric cardiologists and surgeons from all over the world, including the U.S.A., Canada, South America, Germany, Italy,

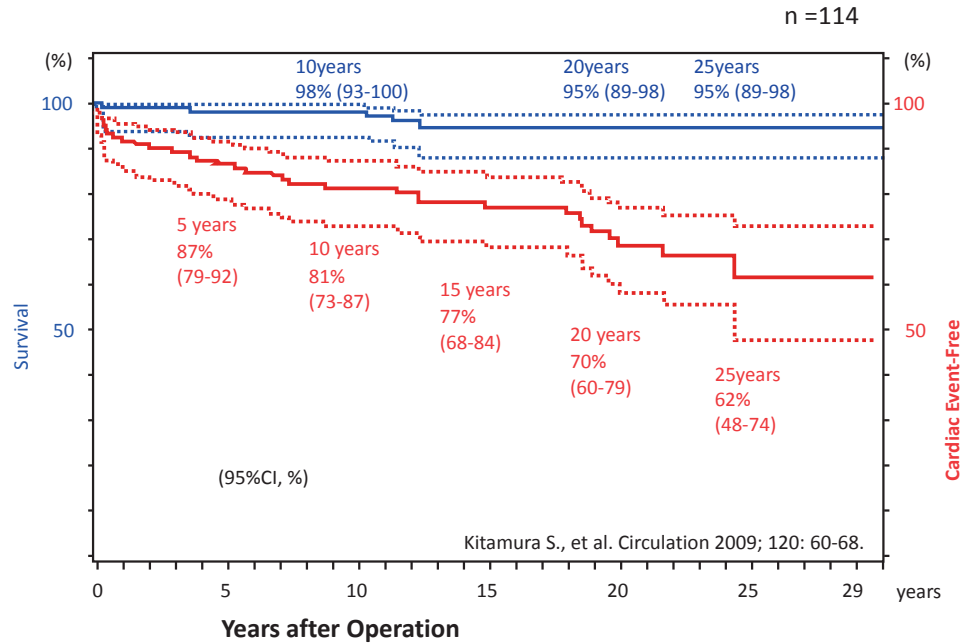


Fig. 14. Long-term survival and cardiac event-free rates after PCABS for children with KD. Although, the cardiac event-free rate slowly but progressively declined over 25 years, early interventions maintained the excellent survival rate, 95% (95% CI 89–98%) at 30 years. Clinical observation is required for a long period after PCABS for KD because of the remaining coronary aneurysms, presence of SVGs and reduced left ventricular function with ventricular tachyarrhythmias. This figure was reproduced with modifications based on the original literature.²⁷⁾

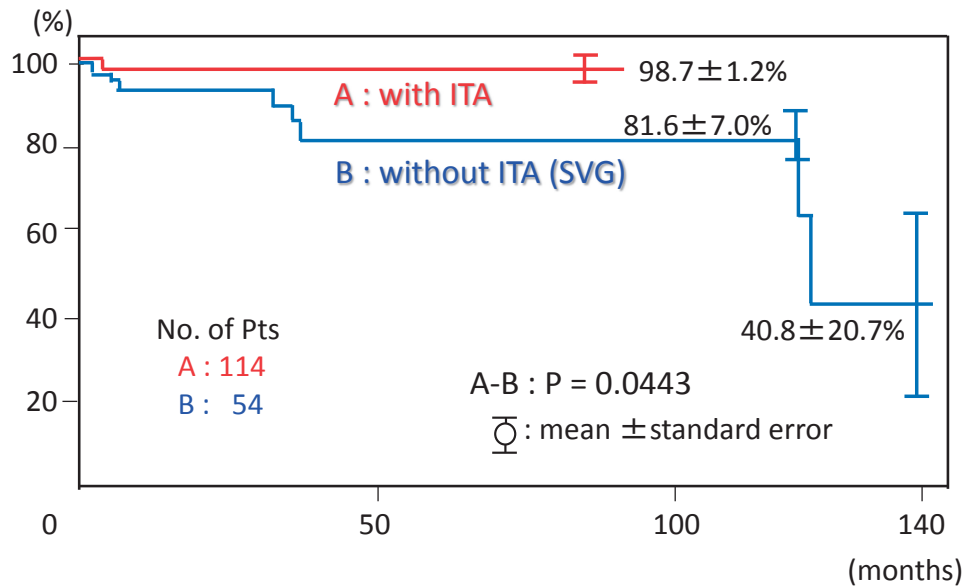


Fig. 15. Survival comparison between children after PCABS with an ITA-LAD graft and those with a SVG-LAD bypass (a multi-center cooperative study of Japan). The presence of the ITA graft to the LAD was important for better survival of KD patients ($p = 0.0445$). Conversely, the absence of an ITA graft was a strong negative factor for postoperative survival ($p = 0.003$). This figure was reproduced with modifications based on the original literature.³⁶⁾

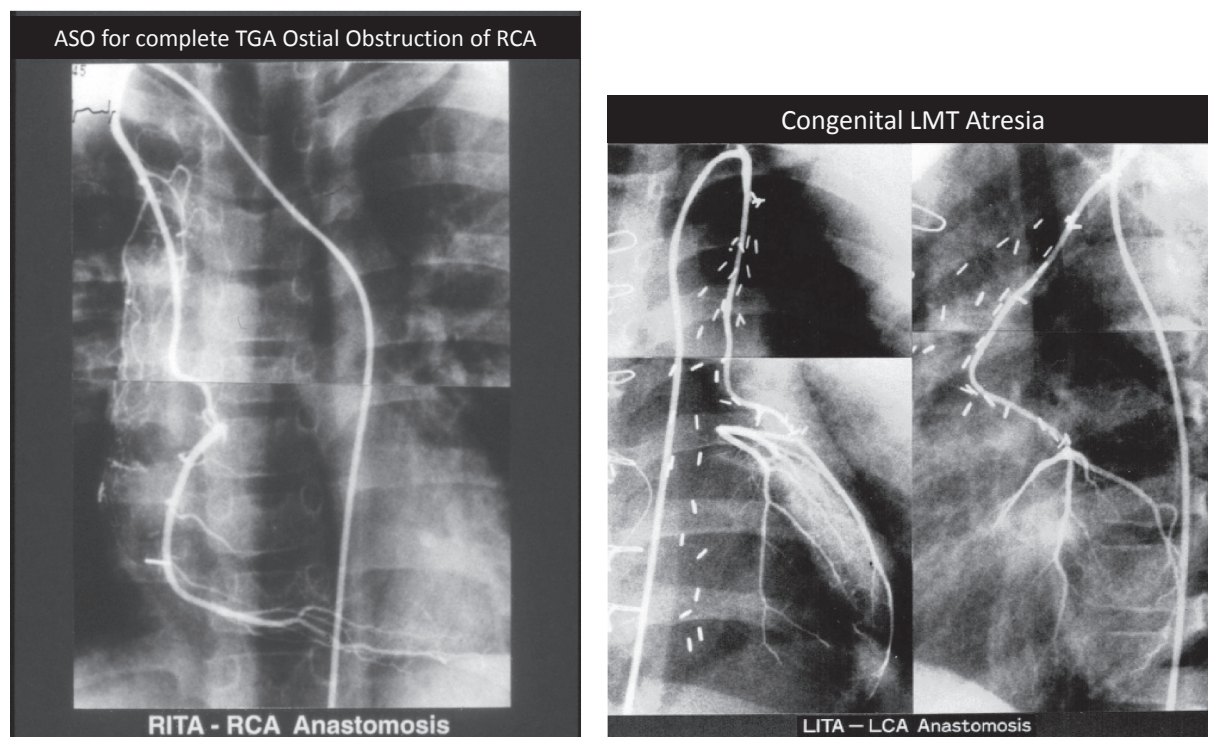


Fig. 16. Post-PCABS angiograms for congenital heart diseases. Left panel: right ITA-RCA bypass for coronary obstruction after the arterial switch operation (ASO) for complete transposition of the great arteries (TGA); right panel: left ITA-LAD bypass for congenital atresia of the left main coronary trunk (LMT). Unlike KD coronary artery disease, the coronary artery itself is quite normal without any distal lesions in congenital heart diseases; therefore, the ITA bypass can function very well, probably with much less late cardiac morbidity than in KD coronary disease. This figure was reproduced with modifications based on the original literature.⁵⁾

France, New Zealand, Australia, Turkey, Malaysia, Indonesia, India, Iran, China, Taiwan, Korea, Philippines, and Singapore, with regard to the surgical indications for their pediatric patients with complications of KD. Severe coronary lesions were often seen and many of them required surgery; however, the exact number of such patients around world remains unknown.

Expanding indications for PCABS for congenital heart diseases and their surgical complications

PCABS utilizing the ITA is certainly applicable for coronary artery problems other than KD, such as coronary obstruction after arterial switch operations for complete transposition of the great arteries, congenital agenesis of the left coronary trunk, anomalous origin of the left coronary artery from the pulmonary artery, iatrogenic injury of the coronary artery during cardiac operations, and other congenital coronary anomalies.^{3)-5),71)-76)} Coronary ostial transfer problems after an arterial switch operation for complete transposition of the great

arteries or the Taussig-Bing anomaly are the main cause of early operative death which occurs in 7–8% of neonate and infant cases. Moreover, the incidence of late coronary stenosis or occlusion was not infrequent (11.3%).⁷⁷⁾ In this situation, emergency or elective PCABS utilizing the unilateral or bilateral ITAs has become the most important salvage procedure. We also utilized this operative procedure for congenital coronary malformations, which we reported in 1992.⁵⁾ Figure 16 shows postoperative angiograms of children who underwent PCABS for congenital heart diseases. In this situation, PCABS utilizing the ITA is a suitable choice of treatment because, in contrast to the coronary sequelae secondary to KD with many distal coronary lesions, the coronary artery itself is quite normal in congenital diseases. An ITA bypass can function very well in this scenario, probably with significantly less late cardiac morbidity.

In 1996, Mavroudis *et al.*^{71),72)} reported on the expansion of the indications for PCABS to congenital coronary anomalies in infants and children, with

good results. In 2010, Viola *et al.*⁷³⁾ reported on their experience with PCABS utilizing ITA grafts as applied to a variety of pediatric coronary lesions, with no operative deaths. At present, there is essentially no age limitation for this surgery, and PCABS with ITA grafts is now successfully carried out in infants and even neonates,^{71)–76)} with the concomitant revival of the use of a surgical microscope.^{28),29)}

PCABS as a new arena in cardiac surgery and future perspectives

The development of PCABS utilizing pedicled ITAs for KD coronary lesions and congenital heart diseases has contributed to the standardization of surgical coronary revascularization procedures in children. The procedure using unilateral or bilateral ITAs has now been accepted worldwide as the ideal choice of treatment for neonates, infants, and children with coronary artery obstructive lesions, either due to KD or congenital coronary disorders, thus creating a new surgical arena for children. Vida *et al.*²⁸⁾ commented in their recent publication that PCABS with the use of ITA grafts should represent a fundamental part of the training of contemporary congenital heart surgeons. This surgery carries a very low surgical mortality and confers long-term benefits for growing children. PCABS has been included in many English and Spanish language textbooks that have been published around the world,^{78)–85)} and has created a new subspecialty in modern cardiac surgery. We first used a surgical microscope for PCABS utilizing ITA grafts on a small child in 1994,^{9),10),39)} and very recently, the use of a surgical microscope for PCABS has been revived in Europe²⁸⁾ and North America.²⁹⁾ The operation utilizing the pedicled ITA can now be successfully applied regardless of age, and has conferred significant benefits to children affected by coronary problems worldwide. The use of vein grafts should be avoided in small children, and we believe that the ITA graft should continue to function for the entire lifetime of the patient, adapting to the changing body from childhood to the geriatric age.

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Profile

Soichiro Kitamura was born in Kure-city, Hiroshima in 1941, and graduated from the Osaka University School of Medicine in 1965. After completing his internship at Osaka University Hospital, he entered the First Department of Surgery, where he underwent initial training in general surgery for 2 years before majoring in cardiovascular surgery.

From 1969 to 1972, he trained in cardiovascular surgery at the University of Southern California and its affiliated St. Vincent's Hospital in Los Angeles, California, U.S.A. After returning to Japan, he received the title of Doctor of Medical Science in 1976 for his research on the analysis of left ventricular function before and after left ventricular reconstructive surgery for left ventricular noncontractile areas following myocardial infarction. In 1981, he was appointed as Professor of Surgery at the Department of Surgery III, Nara Medical University, where he established a new Department of Thoracic and Cardiovascular Surgery. At this university hospital, he further promoted investigations on pediatric coronary artery revascularization surgery using unilateral or bilateral internal thoracic arteries.

In 1997, when new legislation regarding organ transplantation from brain-dead donors was set forth in Japan, he was assigned to be the Deputy Director of the National Cardiovascular Center (presently National Cerebral and Cardiovascular Center) for the purpose of establishing a cardiac transplantation program at the center. His team, together with that of Osaka University Hospital, successfully conducted initial heart transplant projects, and in 1999, heart transplantation in Japan began smoothly, though in very limited numbers. He also established the first cryopreserved tissue bank in Japan for homograft utilization in the treatment of complicated cardiovascular diseases, such as destructive infective endocarditis and complex congenital heart diseases. This surgical option is now considered as a standard surgical therapy and was included in the social insurance system of Japan in 2016.

He was then assigned as the Director of the Center Hospital in 2000, and was soon promoted to the President of the National Cardiovascular Center in 2001. Since then until his retirement, he served as a chair or member of many committees established by the Ministry of Health, Labor and Welfare of Japan. In addition, he served as the president or congress president of many cardiology and cardiovascular surgical societies or associations, such as the 48th Japanese College of Cardiology (2000), the 54th Japanese Association for Thoracic Surgery (2001), the 39th Japanese Transplantation Society (2002), the Japanese Society for Cardiovascular Surgery (2003–2005), and the 14th Asian Society for Cardiovascular Surgery (2006). For his accomplishments, he has received many honors, such as the Japan Medical Association Award (1991), Richard D. Rowe Memorial Lecture Award (American Heart Association) (1999), Shiju-houshou (medal with purple ribbon for academic excellence) (2003), the Takeda Science Award (2006), and the Japan Academy Award (2017).

In 2008, he retired from the center and received the title of President Emeritus from the Ministry of Health, Labor and Welfare of Japan. From 2009 to 2016, he served as the president of the Sakai City Hospital Organization and Sakai City General Hospital, Sakai, Osaka. In 2014, he was honored with Zuihou-Juhkou-Shou (the Order of the Sacred Treasure), and at present, he is the President of the Cardiovascular Research Foundation, which funds research on cerebral and cardiovascular diseases.

