# NuMED
# Summary of Safety and Clinical Performance
# SSCP – Stent Placement

*This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device.*

*The SSCP is not intended to replace the Instructions for Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.*

*The following information is intended for users/healthcare professionals.*

| **1. Device identification and general information** | |
|---|---|
| Device trade name(s) | NuMED Stent Placement Family<br>BIB® (Balloon in Balloon) Stent Placement Catheter |
| Model Number | NuMED Stent Placement Family – Model 1500<br>BIB – Model 420.1 |
| Manufacturer's name and address | NuMED, Inc.<br>2880 Main Street<br>Hopkinton, NY 12965<br>USA |
| Manufacturer's single registration number (SRN) | US-MF-000010948 |
| Basic UDI-DI | 08877141500SV |
| Medical device nomenclature description / text | EMDN – C010402020102 – Cardiocirculatory System Devices,<br>Stent Positioning Vascular Balloon Dilatation Catheters |
| Class of device | III |
| Year when first certificate (CE) was issued | 2003 |
| Authorised Representative (AR) | G. van Wageningen B.V.<br>Hallenweg 40, 5683 CT Best,<br>The Netherlands |
| AR SRN | NL-AR-000010437 |
| Notified Body | SGS Belgium NV |
| Notified Body ID number | 1639 |

| **2. Intended use of the device** | |
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| Indications for use | Indicated for stent placement in vessels over 8mm in diameter. |
| Contraindications and/or limitations | There are no contraindications to the use of the BIB Stent Placement Catheters, except for vessels smaller than 8mm in diameter. |

| **3. Device description** | |
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| Description of the device | The BIB Stent Placement Catheter is triaxial in construction with two lumens being used to inflate the balloon while one lumen is being used for tracking over a guidewire. The inner balloon is 1/2 of the outer balloon diameter and 1 cm shorter. The purpose of the double balloon catheter is to apply an incremental inflation for the purpose of dilating a stent. The inner balloon provides initial |

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| | expansion of the stent and also acts as a tool to hold the stent on the catheter prior to the outer balloon being inflated. The outer balloon is then inflated, providing the remainder of the expansion. There are radiopaque platinum marker bands under the balloon shoulders, to aid during placement.<br><br>The balloons are designed to inflate to the diameter and length listed on the label at a specific pressure. Thus, it is recommended that the device be used in conjunction with a mechanism to monitor pressure, an inflation device with pressure gauge. This device is also designed to be used with an appropriately sized introducer and guidewire, and stent.<br><br>Both the inner and outer balloon size is ± 10 % at the Rated Burst Pressure (RBP) and the RBP is not to be exceeded.<br><br>The catheters are supplied sterile, by ethylene oxide gas, and are intended for single use only. The catheters are invasive and intended for transient use (continuous use of <60 minutes) on patients. |
| Reference to previous generation(s) or variants | The BIB also comes in variants with a stent pre-mounted on it: Mounted CP Stent, Covered Mounted CP Stent, G-Armor Mounted Stent, and G-Armor Covered Mounted Stent. There is also a variant in which the Covered CP Stent is mounted on the BIB catheter inside a retractable introducer sheath as an all-in-one device. This variant is known as the NuDEL device. These other variants are covered by NuMED's CoA Stent, RVOT/CoA Stent, and Delivery System SSCPs. |
| Accessories which are intended to be used in combination with the device | There are no accessories that are intended to be used with this device. |
| Description of any other devices and products which are intended to be used in combination with the device | This device is designed to be used with a stent, guidewire, introducer, and an inflation device with pressure gauge. |

| **4. Risks and Warning** | |
|---|---|
| Residual risks and undesirable effects | Side-effects reported in the literature are stent flaring and stent migration.<br><br>All risks identified in the clinical literature as well as the risks detected from the Post Market Surveillance or from clinical data generated and held by the Sponsor, have been considered by the risk management process.<br><br>All significant risks were considered, mitigated as far as possible (AFAP), and are acceptable in regard to the clinical benefit of the device.<br><br>Identified clinical residual risks/undesirable side-effects for the Stent Placement Catheters are:<br><br>**POTENTIAL COMPLICATIONS/ADVERSE EFFECTS**<br>NOTE: Circumferential tear of the delivery balloon catheter prior to complete expansion of the stent may cause the balloon to become tethered to the stent, requiring surgical removal. In case of rupture of an adequately sized balloon after stent expansion, it can be withdrawn and a new balloon catheter exchanged over a guidewire to complete expansion of the stent.<br><br>Cardiac catheterization carries certain risks. Potential complications & adverse effects associated with device use and indication include:<br><br>• Stent misplacement<br>• Stent migration<br>• Minor hematoma<br>• Intraluminal thrombosis<br>• Pseudoaneurysm |

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| | • AV fistula formation<br>• Bleeding requiring transfusion<br>• Sepsis/infection<br>• Distal thromboemboli<br>• Death<br>• Vessel rupture<br>• Cerebrovascular incident<br>• Hematoma requiring repair |
| Warning and Precautions | The following Warnings and Precautions have been identified and are called out in the Instruction for Use:<br><br>**WARNINGS**<br>• Do not exceed the RBP. An inflation device with pressure gauge is recommended to monitor pressure. Pressure in excess of the RBP can cause balloon rupture and potential inability to withdraw the catheter through the introducer sheath.<br>• Confirm that the distal end of the introducing sheath is at least 2.5cm back from the most proximal image markers before inflating the outer balloon. Failure to do so may stretch the outer tubing and severely hinder balloon deflation.<br>• Use two appropriate size inflation devices with pressure gauges for inflation.<br>• Do not advance the guidewire, balloon dilatation catheter, or any other component if resistance is met, without first determining the cause and taking remedial action.<br>• When the stent is crimped onto a balloon delivery catheter, the maximum balloon inflation pressure must not exceed the recommended inflation pressure specified in the manufacturer's instructions.<br>• This catheter is not recommended for pressure measurement or fluid injection.<br>• Do not remove the guidewire from the catheter at any time during the procedure except when the procedure has been completed.<br>• This device is intended for single use only. Do not resterilize and/or reuse it, as this can potentially result in compromised device performance and increased risk of cross-contamination.<br><br>**PRECAUTIONS**<br>• The BIB Stent Placement balloon catheter was tested with the NuMED Cheatham Platinum (CP) Stent (bare & covered).<br>• Dilatation procedures should be conducted under fluoroscopic guidance with appropriate x-ray equipment.<br>• Stents are delicate devices. Care should be exercised while handling to help prevent the possibility of breakage.<br>• Careful attention must be paid to the maintenance of tight catheter connections by aspiration before proceeding to avoid air introduction into the system.<br>• The inflation diameter of the balloon used during stent delivery should approximate the diameter of the obstructive vessel and the intended implant site.<br>• Under no circumstances should any portion of the catheter system be advanced against resistance. The cause of the resistance should be identified with fluoroscopy and action taken to remedy the problem.<br>• If resistance is felt upon removal, then the balloon, guidewire and the sheath should be removed together as a unit, particularly if balloon rupture or leakage is known or suspected. This may be accomplished by firmly grasping the balloon catheter and sheath as a unit and withdrawing both together, using a gentle twisting motion combined with traction.<br>• Before removing the catheter from the sheath, it is very important that the balloon is completely deflated.<br>• Proper functioning of the catheter depends on its integrity. Care should be used when handling the catheter. Damage may result from kinking, stretching, or forceful wiping of the catheter. |

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| Other relevant aspects of safety, including a summary of any field safety corrective actions (FSCA including FSN) if applicable | There have not been any Field Safety Corrective Actions or Field Safety Notices for the BIB Stent Placement Catheter. |

## 5. Summary of clinical evaluation and post-market clinical follow-up (PMCF)

**Summary of clinical data related to equivalent device:**

An equivalent device was not used for the clinical evaluation.

**Summary of clinical data from conducted investigations of the device:**

The COAST, COAST II and PARCS studies were specifically initiated to investigate clinical efficacy and safety of the CP Stent, with the BIB Stent Placement Catheter. The results of these studies demonstrate that a double balloon significantly reduces known risks associated with single balloon stent placement procedures. Devices used in the studies were provided both in unmounted and mounted configurations.

### 1. Study Name: COAST

**Purpose:** to provide information that will support labeling of both the CP bare metal and covered stents to treat native and recurrent CoA in selected children, adolescents and adult.

**Clinical Study Methodology:** Single arm interventional study (open label)
***Reference to the clinical study plan (and amendment) n°:*** NCT00552812

**Investigation site:** 19 pediatric cardiology centers in United States

**Ethics Committee Approval:** Institutional Review Board approvals from all participating institutions

**Regulatory Authority Approvals:** Investigational Device Exemption from US FDA (August 3, 2007)

**Patient Population:** Patients with native or recurrent CoA. A total of 105 patients underwent attempted implantation, median age 16 years (range from 8 to 52 years) and with 69.5% male.

**Clinical Study Results:** Results held on file by Sponsor

| Purpose | Criteria | Results |
|---|---|---|
| Performance | Blood pressure gradient and coarctation minimum diameter: cardiac catheterization before and after CP Stent placement | Average systolic blood pressure difference (mmHg) changed from 29±14 mmHg at baseline to -3±15 mmHg at 24 months follow-up. The Coarctation minimum diameter reported at 7.9 ± 2.7mm at baseline to 14±3 mm after implantation. |
| Safety | Adverse events | No serious adverse events reported, 7% of the patients experienced somewhat serious events.<br>Aortic aneurysms (n=6): 5 were successfully treated with covered stent placement, and 1 resolved without intervention.<br>Stent fractures were seen in 2 patients after one year, 11 patients at two years and 12 additional fractures above 2 years. |

***Reference to the Clinical Study Report n°:*** NCT00552812
**Device Used:** Bare CP Stent and BIB catheter; covered stents were available in case of aortic wall injury.

**Conclusion:** The CP stent is safe and associated with persistent relief of aortic obstruction. Stent fracture and progression of fracture occur but have not resulted in clinically important sequelae. Reintervention is common and related to early and late aortic wall injury and need for re-expansion of small-diameter stents.

### 2. Study Name: COAST II

**Purpose:** safety and short-term efficacy of the CP Stent in treating or preventing aortic wall injury in patients with aortic coarctation

**Clinical Study Methodology:** Single arm interventional study

**Investigation site:** 19 pediatric cardiac centers in United States

**Ethics Committee Approval:** Johns Hopkins Institutional Review Board and Institutional review boards of all participating centers.

**Regulatory Authority Approvals:** Investigational Device Exemption from US FDA

**Patient Population:** Patients with aortic coarctation at risk of aortic wall injury or with existing aortic wall injury. A total of 158 patients (83 treatment cohort and 75 prevention cohort, median age 19 years (range from 5 to 70 years) and with 103 males and 55 females.

**Clinical Study Results:** Results held on file by Sponsor

| Purpose | Criteria | Results |
|---|---|---|
| Short term efficacy | Blood pressure gradient (at 1 month) | All: from 24 ± 26 mmHg to -1 ± 15 mmHg<br>Treatment group: from 14 ± 24 to -2 ± 14<br>Prevention group: from 35 ± 23 to 1 ± 15 |
| Safety | Adverse events | 17 adverse events; 2 serious (dissection of the iliac artery) and 15 somewhat serious.<br>No deaths.<br>Device related AEs included local stent migration (n=1) and stent malposition (n=1). |

**Device Used:** Covered CP Stent by NuMED, pre-mounted on BIB stent delivery catheter.

**Conclusion:** The CP Stent can effectively treat and potentially prevent aortic wall injury associated with aortic coarctation. Access site arterial injury is the most common important complication. Longer-term follow up is necessary to define mid- and late-term outcomes.

**3. Study Name: PARCS**

**Purpose:** Evaluation of the Covered CP Stent for repair of tears that occur in the pulmonary artery during dilation (enlargement) of a conduit (passageway) connecting the right ventricle of the heart to the pulmonary arteries.

**Clinical Study Methodology:** Single arm prospective study
***Reference to the clinical study plan (and amendment) n°:*** NCT01824160

**Patient Population:** Participants receiving a Covered CP stent for repair of pulmonary artery injury. In the pivotal trial, fifty patients met the inclusion criteria, mean age 17 years (range from 6 to 44 years) and 56% of male patients. In the continued access, seventy patients with mean age of 16 years (range from 7 to 49 years) and 57% of male patients.

**Clinical Study Results:** Results held on file by Sponsor

| Purpose | Criteria | Results |
|---|---|---|
| Pivotal (n=50): Severity of illness | Median improvement by at least 1 level from baseline to post-procedure | Median improvement of 1 level in Severity of Illness Score |
| Pivotal (n=50): Procedure success | ≥ 75% patients, based on both device success and lesion success | Procedure success achieved in 68% of patients |
| Pivotal (n=50): Successful implantation of the Melody TPV | Coverage of conduit disruption defined as either no residual disruption or contained disruption, followed by successful implantation of Melody valve in ≥ 80% patients | Successful implantation achieved in 83% of patients |
| Pivotal (n=50): Adverse events attributed to covered CP Stent within 30 days | ≥ 80% patients free of adverse events attributed to the covered CP Stent within 30 days | At least 80% were free of an adverse event attributed to the covered CP Stent. There was 1 report of stent malposition where the stent became dislodged and migrated into the pulmonary arteries |
| All patients (n=120): Performance | Covered CP Stent Implant success | CCPS implants successfully treated 95% of conduit injuries with either no or minimal residual conduit wall injury. |

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| | | Melody TPVR was successfully performed in 94% of the enrolled cohort, and TPV function was not adversely affected by placement within the CCPS substrate, with 6-month follow-up data comparing favorably with other previously published cohorts. |
| All patients (n=120): Safety | Stent-related AEs | AEs that specifically related to the CCPS and its implantation were uncommon. One serious (stent malposition) and one somewhat serious (stent embolization) AE occurred (both in the same patient who is described above). A device usage issue was identified whereby the expanded poly tetrafluoroethylene covering separated from the stent during attempts to load the CCPS device into the delivery sheath. This was identified before deployment; the stent was removed and replaced with a new CCPS without consequence to the patient. |

***Reference to the Clinical Study Report n°:*** NCT01824160

**Device Used:** Covered CP Stent pre-mounted on BIB

**Conclusion:** The study results demonstrate the safety and efficacy of use of the covered CP Stent when used for pre-stenting in the RVOT prior to Melody TPV implantation.

**Summary of clinical data from other sources:**

| First Author (Year) | Appraisal/Results |
|---|---|
| 1. Delaney et al. (2018) | **Safety & Performance**<br>This publication presents the results from the PARCS trial – Covered CP Stent for Treatment of Right Ventricular Conduit Injury During Melody Transcatheter Pulmonary Valve Replacement (NCT01824160). Please refer information presented in **Table G-1** for safety and performance of the subject devices, Study no. 3. The state of the art information is presented below.<br><br>**State of the Art**<br>**Appraisal** |

| Medical condition | | Alternatives | | Risk/benefit | | Side-effects | | Equivalence | | Surrogate endpoints | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Yes 1** | No 2 | **Yes 1** | No 2 | **Yes 1** | No 2 | **Yes 1** | No 2 | Yes 1 | **No 2** | Yes 1 | **No 2** |

**Overall SOA Appraisal and Disposition**

| SOA Grade (Range 6-12) | 8 | Disposition (select) | **Accepted, < 12**<br>Excluded, 12 |
|---|---|---|---|

| Contribution | |
|---|---|
| S&P | x |
| SOA | x |

**Relevant SOA Results**

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|---|---|
| SOA data | - Current knowledge:<br>o Important conduit injury can occur during ultrahigh pressure angioplasty. Ultra-high pressure angioplasty is often required to dilate conduits effectively for TPVR. Conduit injury, once identified, could preclude further dilation of the conduit out of concern for extension of the area of injury.<br>- Stenting of the conduit before valve implantation improves the durability of the implanted valve.<br>- Covered stents have been used in the vascular space to isolate areas of injury.<br>- RVOT reconstruction:<br>o RVOT reconstruction with a valved conduit or bioprosthetic pulmonary valve placement is necessary during surgical repair of a substantial subset of patients with congenital heart disease.<br>o All valved RVOT substrates, regardless of type, have been associated with functional deterioration, with between 50% and 80% requiring replacement by 10 years.<br>o RVOT dysfunction may be associated with substantial patient morbidity and even mortality.<br>o Transcatheter RVOT conduit rehabilitation using high-pressure angioplasty with or without stent placement has been utilized to delay or defer the need for surgical pulmonary valve replacement. An injury within the wall of the conduit is likely to occur with any successful conduit dilation, although |

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| | minor injuries may not be clinically relevant or recognized with angiography.<br>o Successful RVOT conduit angioplasty often requires the use of ultrahigh pressure noncompliant balloons to effectively relieve the stenosis but with a higher rate of recognized conduit injury (≤33%). The vast majority of these injuries was not associated with hemodynamic compromise.<br>- Melody transcatheter pulmonary valve:<br>o Introduction of the Melody transcatheter pulmonary valve (TPV; Medtronic) led to more frequent percutaneous conduit rehabilitation because cardiologists could effectively treat both stenosis and insufficiency, without the need for open-heart surgery.<br>o Melody TPV implants, without stent reinforcement of the conduit before valve implant, have been associated with a high rate of progressive valve deformity and stent fracture leading to valvular dysfunction.<br>o Conduit wall injury is a known complication of isolated or serial balloon angioplasty of the RVOT conduit. Although bare metal stents may provide some reinforcement of a damaged conduit wall, they are not likely to allow for safe, continued dilation of an injured RVOT conduit that has not been fully prepared (e.g., left with hemodynamically important residual stenosis) for TPVR, and they are not anticipated to be effective in treating catastrophic conduit injuries.<br>o Covered CP Stent (NuMED) is a balloon-expandable, large-diameter, covered stent whose construction and applications for vascular wall injury, tears, or leak have been reported previously. Experience with the Covered CP Stent outside of the United States is extensive and has included its routine use in the pre-stenting process for valve implantation. The European experience has suggested that this practice may reduce the clinical impact of conduit injury.<br>o Some US centers did have access to the Covered CP Stent as participants in the COAST (Coarctation of the Aorta Stent Trial) and could apply for emergency use if an unexpected RVOT wall injury occurred. Non-COAST centers could apply for a single-patient compassionate use exemption if they felt a patient was at high risk for conduit injury. |
| Comments | - High-pressure balloon and stent angioplasty are frequently necessary to prepare the dysfunctional RVOT conduit before transcatheter pulmonary valve replacement (TPVR). Conduit injury can result, which may be catastrophic to the patient or prevent successful TPVR. Severe conduit injury was found to be rare but unpredictable. The covered stent was effective in either treating or mitigating this problem. The vast majority of patients, even with identified conduit injury, was able to complete the valve replacement procedure. The covered stent did not interfere with Melody valve function at short-term, 6-month follow-up. |

2. Morgan et al. (2017)

| Contribution | |
|---|---|
| S&P | x |
| SOA | x |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Retrospective data collected of the first NuDEL delivery systems used in patients from three centers (UK and Ireland). | To evaluate the first-in-man use of a new system (NuDEL) for implantation of CP Stent (Covered) in patients with complex structural and CHD. | 1 | 2 | 3 | **4** | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - NuDEL Delivery System | **D1** | D2 | D3 |
| Application | - CoA and RVOT | **A1** | A2 | A3 |
| Patient | - Patients with COA and RVOT<br>- Sampling: n=12 (13 CP Stents, Covered, delivered via 12 NuDELs); with 6 CoA, 5 RVOT, and 1 with severe stenosis of a Mustard systemic venous baffle. Note: "P2" due to one with severe stenosis of a Mustard systemic venous baffle.<br>- Age: 10-43 years<br>- Sex: Not reported | P1 | **P2** | P3 |
| Report | - High quality with minor deficiency as device performance is based on descriptive information. | R1 | **R2** | R3 |
| | Suitability Grade (Range 4-12) | 6 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Procedure complications.<br>- Ease of use. | **Yes 1** | No 2 |
| Follow-up | - Not reported. | Yes 1 | **No 2** |
| Statistical analysis | - Not reported. | Yes 1 | **No 2** |
| Clinical significance | - NuDEL system is a safe and effective means of covered stent deployment in challenging anatomy. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | **6** | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (4) + Suitability (6) + Data Contribution (6) = 16 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21** |
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| | | | Excluded, 22-25 |

**Relevant S&P Results**

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| Safety data | - No procedural complications and no reports of equipment failure or dysfunction. |
| Performance data | - The system required minimal preparation – flushing only; therefore, despite a lack of familiarity, it was ready for deployment in each case in under two minutes after removing the packaging.<br>- Key positive feedback and observations were that the assembly tracked well through the access site and through tortuous and narrowed anatomy in either the outflow tract or the descending aorta.<br>- Stent was easy to uncover, and the markers on the system provided added re-assurance to this process. |
| Benefits/claims data | - Most difficult part of the catherization procedure is getting the stent into the required anatomical position before deploying it. To this end, the NuDEL system has been developed.<br>- NuDEL reported to require minimal preparation and tracked well through the access site and tortuous and narrowed anatomy. |
| Strengths | - Our initial series suggests that the NuDEL system provides a safe, efficient method of deploying a covered stent in patients with complex outflow tract stenosis and those with CoA. Using this system avoids some of the pitfalls associated with stent mounting and management of the stent–balloon–delivery system complex.<br>- Stent was easy to uncover and markers on the system provided added re-assurance of the process. |
| Weaknesses/ Potential bias | - Conflict of interest: None<br>- Financial support: Research received no specific grant from any funding agency or from commercial or not-for-profit sectors |

**State of the Art**
**Appraisal**

| Medical condition | | Alternatives | | Risk/benefit | | Side-effects | | Equivalence | | Surrogate endpoints | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Yes 1** | No 2 | Yes 1 | **No 2** | **Yes 1** | No 2 | Yes 1 | **No 2** | Yes 1 | **No 2** | Yes 1 | **No 2** |

**Overall SOA Appraisal and Disposition**

| | | | |
|---|---|---|---|
| SOA Grade (Range 6-12) | 10 | Disposition (select) | **Accepted, < 12**<br>Excluded, 12 |

**Relevant SOA Results**

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| SOA data | - Conduit rupture is an anxiety-provoking potential complication; the availability of a "ready-to-go" covered stent system may provide an attractive emergency backup. This may be of benefit to operators who perform a low volume of large-caliber stent procedures and are not conversant with the techniques involved, even in the elective setting.<br>- The range of stents available for these therapies has developed well over the last 10–15 years, allowing authors to make semi-quantitative decisions about stent choice for each individual case.<br>- Safety and accuracy of deployment are at least partially dependent on the precise mounting of the stent on its delivery balloon and passing it into and along the delivery sheath to its required position. The most difficult part of the catherization procedure is getting the stent into the required anatomical position before deploying it. A lot of time is taken in getting these essential steps right, and there is potential for safety, efficiency, and efficacy problems at every step. Slipping of the stents off balloons leading to migration of the stent before or during deployment and damage to the balloon or stent during mounting are some of the problems encountered, which may require re-crossing of the target areas, lead to vascular risk of removing and re-inserting a long, large-caliber sheath, and at worst can have major safety consequences. |
| Comments | - Stent implantation in the RVOT and for the treatment of CoA has become standard practice for congenital interventional cardiologists. |

3. Bishnoi et al. (2015)

| Contribution | |
|---|---|
| S&P | x |
| SOA | x |

**Safety & Performance**
**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Retrospective review of incidence and potential predictors of conduit disruption. | To assesses the frequency of RVOT conduit disruption during transcatheter pulmonary valve replacement (TPVR) and the effectiveness and safety of NuMED CP Stents (Covered) for its prevention or treatment. | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - Covered CP Stents (12 to 22mm), pre-mounted on BIB i.e., CP Stents (Covered Mounted) | **D1** | D2 | D3 |
| Application | - NuMED CP Stents (Covered) for prevention or treatment of RVOT conduit disruption during TPVR | **A1** | A2 | A3 |
| Patient | - Population: Patients undergoing TPVR requiring treatment of RVOT conduit disruption (patients with pre-existing tears, patients developed tears after performing conduit dilation, and patients developed tears after transcatheter pulmonary valve implantation, or prophylactically placed in patients of perceived high risk related to degree of calcification and/or | **P1** | P2 | P3 |

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|---|---|---|---|---|
| | severity of homograft stenosis).<br>- Sampling: 50 patients receiving 69 Covered CP Stents during TPVR/PPVI procedures (comparative cohort: 251 implants US Melody transcatheter pulmonary valve IDE Trial, planned for bare metal stenting of supported conduit)<br>Note: overall incidence of conduit disruption requiring intervention was 6% in the study.<br>- Mean Age: 21.4 (SD 3.7) years (5.5 to 56 years)<br>- Sex: not reported | | | |
| Report | - High quality | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | **4** | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Peak-to-peak RVOT gradient<br>- Mean Doppler RVOT Gradient at 6 months<br>- Valve competence with no or trivial pulmonary regurgitation<br>- Safety | **Yes 1** | No 2 |
| Follow-up | - 6 months | Yes 1 | **No 2** |
| Statistical analysis | - Not provided | Yes 1 | **No 2** |
| Clinical significance | - CP Stent (Covered, Mounted) implantation can successfully treat RVOT conduit disruption without negative impact on the transcatheter pulmonary valve function | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 6 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (3) + Suitability (4) + Data Contribution (6) = 13 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21**<br>Excluded, 22-25 |
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**Relevant S&P Results**

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| Safety data | - Stent fracture: 1/50 patients with 2 CP Stents (Covered) developed multiple stent fracture 3 years following implantation. Patient was successfully treated with implantation of a stainless steel stent to support remaining portions of the CP Stent (Covered).<br>- No Covered CP Stent-related acute complications were reported. |
| Performance data | - Peak-to-peak RVOT gradient: Decreased from 45.5 ± 17.5 mm Hg to 10.6 ± 6.3 mm Hg<br>- Mean Doppler RVOT Gradient at 6 months: 12.86 ± 5.0 mmHg compared to 20.0 ± 8.6 mmHg from the Melody TPV IDE trial.<br>- Valve competence with no or trivial pulmonary regurgitation: At follow-up 94% in study group and 93% in comparator group.<br>- Conduit tears: prevented or repaired in 49/50 patients. |
| Benefits/claims data | - N/A |
| Strengths | - CCPS implantation can successfully treat RVOT conduit disruption without negative impact on the TPV function.<br>- This retrospective analysis suggests high RVOT conduit systolic pressure gradient is a risk factor for conduit tears during PPVI. |
| Weaknesses/ Potential bias | - Retrospective analysis of prospectively collected data for other purposes and thus, suffers the biases of such investigations.<br>- Sample size is small and in most cases the follow-up period is short. Long term results are unknown.<br>- Conflict of interest reported:<br>  - Bishnoi RN: none<br>  - Jones T: research grant and consultant for Medtronic; research grant support from NuMED.<br>  - Kreutzer J: research grant support from Medtronic and St. Jude Medical; consultant for Medtronic, Inc.<br>  - Ringel RE: research grant support from Medtronic, Inc. and NuMED. |

**State of the Art**
**Appraisal**

| Medical condition | | Alternatives | | Risk/benefit | | Side-effects | | Equivalence | | Surrogate endpoints | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Yes 1** | No 2 | **Yes 1** | No 2 | **Yes 1** | No 2 | Yes 1 | **No 2** | Yes 1 | **No 2** | Yes 1 | **No 2** |

**Overall SOA Appraisal and Disposition**

| SOA Grade (Range 6-12) | 9 | Disposition (select) | **Accepted, < 12**<br>Excluded, 12 |
|---|---|---|---|

**Relevant SOA Results**

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|---|---|
| SOA data | - Surgical management of patients with CHD such as tetralogy of Fallot, pulmonary atresia, transposition of the great arteries, truncus arteriosus, and those undergoing Ross procedure for treatment of aortic valve disease, often includes implantation of a bioprosthetic valve or RVOT conduit.<br>- The lifespan of bioprosthetic valves or RVOT conduits is limited by progressive obstruction and/or regurgitation due to variety of factors including mechanical fatigue, immunologic reaction to the surgical implant, extrinsic conduit compression and somatic outgrowth on growing children.<br>- Endovascular treatment using balloon dilatation and bare stent implantation has been shown to extend conduit lifespan and reduce a patient's need for repeated open heart surgeries.<br>- While resolving the problem of conduit obstruction, bare stent placement leads to creation or exacerbation of pulmonary regurgitation. |
| Comments | - No further comment |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Prospective randomized controlled trial. | To evaluate outcomes of treatment with Covered versus Bare NuMED CP Stents. | 1 | **2** | 3 | 4 | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - NuMED CP Stent (Bare and Covered)<br>- BIB | **D1** | D2 | D3 |
| Application | - Severe native CoA | **A1** | A2 | A3 |
| Patient | - Patients with severe native CoA<br>- Sampling: n=120 (60 CP Stents versus 60 CP Stents, Covered)<br>- Mean age: 23.6±10.99 (range 12 to 58) years<br>- Sex: 79 M; 41 F | **P1** | P2 | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 4 | | |

4. Sohrabi et al. (2014)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Procedural success<br>- Reduction in systolic blood pressure gradient<br>- Reduction in mean diameter of coarctation segment<br>- Adverse effects | **Yes 1** | No 2 |
| Follow-up | - 31.1 ± 19.2 months | **Yes 1** | No 2 |
| Statistical analysis | - A p-value <0.05 was considered significant. | **Yes 1** | No 2 |
| Clinical significance | - Implanting CP Stent (Bare) and CP Stent (Covered) have very high success rates with remarkable hemodynamic effects in severe native CoA patients, with no significant complication during the procedure and hospitalization.<br>- Patients undergoing CP Stent (Covered) implantation experienced a non-significantly lower re-coarctation rate and a higher occurrence of pseudoaneurysm formation with respect to CP Stent (Bare) stenting during follow-up.<br>- In both groups, blood pressure was significantly reduced after intervention.<br>- These findings indicate that CoA stenting is a safe procedure. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 4 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (2) + Suitability (4) + Data Contribution (4) = 10 | Disposition and Weighting (select) | **Accepted and Pivotal 9-12**<br>Accepted but not Pivotal, 13-21<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - Pseudoaneurysms: 0 (CP Stent, Bare) versus 2 (CP Stent, Covered)<br>- Mortality: 1 (CP Stent, Bare) versus 0 (CP Stent, Covered) |
| Performance data | - Successful placement: successful in all patients<br>- Mean systolic blood pressure gradient reduction: from 54.61 (CP Stent, Bare) and 54.42 (CP Stent, Covered) to 3.47 and 3.36 mmHg respectively; no significant difference between the two types of stent, P<0.001<br>- Mean diameter of coarctation segment reduction: From 3.34 (CP Stent, Bare) and 3.30 (CP Stent, Covered) to 16.07 and 15.82 mm respectively; no significant difference between the two types of stent, P<0.001<br>- Recurring coarctation: 4 (CP Stent, Bare) versus 0 (CP Stent, Covered), non-significant |
| Benefits/claims data | - Reduction in mean systolic blood pressure gradient<br>- Reduction in diameter of coarctation segment |
| Strengths | - The CP Stent was hand-crimped down onto a balloon-in-balloon catheter (NuMED), which allows a |

| | | |
|---|---|---|
| | | precise and safe stent delivery |
| Weaknesses/ Potential bias | - | Although the first randomized clinical trial in this respect, study was limited in some aspects. First, during follow-up, patients did not undergo 24-hour ambulatory blood pressure monitoring, which could have diagnosed the normotensive state more accurately. Second, evaluation of the blood pressure response during exercise testing could have been more valuable in defining the procedure outcome. |

5. Vanagt et al. (2014)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Single-center retrospective study (CHD database of all CP Stent, Covered, during 2003-2012) | To evaluate possibilities and safety of CP Stent (Covered) in CHD. | 1 | 2 | 3 | **4** | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent (Covered)<br>- BIB | **D1** | D2 | D3 |
| Application | - CoA and RVOT pre-stenting for percutaneous revalvulation | **A1** | A2 | A3 |
| Patient | - Patients with CoA and RVOT pre-stenting for percutaneous revalvulation. For the RVOT group, CP Stent (Covered) was chosen for delivery balloon protection after rupture of the pre-dilation balloon in 7/37 patients (19%) and 30 (81%) because tear, rupture, or fracture of the conduit was expected, or further stent expansion following somatic growth was anticipated.<br>- Sampling: n= 51 (CoA group), n=37 (RVOT group)<br>- Mean age:<br>  - CoA group: 19 (range from 8 to 69) years<br>  - RVOT group: 16 (range from 6 to 43) years<br>- Sex:<br>  - CoA group: 38M; 13F<br>  - RVOT group: 26M; 11F | **P1** | P2 | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 4 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Increase in diameter at coarctation (CoA group)<br>- Decrease in peak to peak gradient (CoA group)<br>- Number of procedures for pre-stenting and pulmonary valve delivery (RVOT Group)<br>- increase in graft diameter (RVOT Group)<br>- Adverse effects | **Yes 1** | No 2 |
| Follow-up | - Not specified. | Yes 1 | **No 2** |
| Statistical analysis | - Two-sided p<0.05 was considered significant. | **Yes 1** | No 2 |
| Clinical significance | - CP Stents (Covered) can safely be applied in CHD patients. The covering allows adequate sealing of existing or expected tears, thereby increasing the safety margin with more complete dilation. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 5 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (4) + Suitability (4) + Data Contribution (5) = 13 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21**<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - CoA Group:<br>  - No acute bleeding, aneurysm formation or life-threatening complications.<br>  - Mild procedure related-complications included groin hematoma (n = 3), transient nodal rhythm (n = 1, no wire present in left ventricle), and transient atrioventricular block with nodal escape rhythm (n = 1, while wire was present in left ventricle).<br>  - During follow-up: no stent fractures, nor stent recompression occurred, and none of the patients had limb ischemia or signs of vessel occlusion at the puncture site.<br>- RVOT group:<br>  - No procedure-related complications and no extravasation.<br>  - No embolization nor fracture of CP Stent (Covered) found on annual chest X-ray follow-up. |
| Performance data | - Diameter at coarctation (CoA group):<br>  - Increased from 6 (0-15) to 14 (7-20) mm, P<0.001.<br>- Peak to peak gradient (CoA group):<br>  - Reduced from 23 (0-86) to 2 (0-25) mm Hg, P<0.001.<br>- Number of procedures for pre-stenting and pulmonary valve delivery (RVOT Group):<br>  - 22/37 single procedure and 15/37 in a second procedure. |

| | |
|---|---|
| | - Graft diameter (RVOT Group)<br>  - Increased from graft stenosis diameter of 13 (5-22) mm to 22 (16-26) mm at pre-revalvulation, P<0.001. |
| Benefits/claims data | - Increase in luminal diameter in CoA patients. |
| Strengths | - CP Stent (Covered) frame is made from 90% platinum and 10% iridium 0.013″ wire, welded in a zig pattern with additional gold soldering. The strut thickness is slightly larger than most other stents, but makes the stent edges relatively atraumatic.<br>- CP Stent (Covered) was hand-crimped on a balloon-in-balloon (BIB, Numed). Hand-inflation of the balloon was performed with a 10 ml syringe on the inner balloon and 20 ml syringe on the outer balloon, automatically limiting inflation pressures to 4–6 atmospheres. |
| Weaknesses/ Potential bias | - In this retrospective study, there are no control groups with bare stents, the lack of which is inherently related to the fact that some of these procedures would have been impossible, or significantly less safe, if bare stents were used. |

6. Alcibar et al. (2013)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Retrospective and observational study. | To investigate reduction in aortic wall rupture and dissection, as well as aneurysms by implanting covered stents. | 1 | 2 | 3 | **4** | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent (Covered)<br>- BIB | **D1** | D2 | D3 |
| Application | - CoA and re-coarctation | **A1** | A2 | A3 |
| Patient | - Patients treated for CoA and re-coarctation (2 adolescents and 15 adults treated between November 2005 and January 2012).<br>- Sampling: n=17 (11 native CoA and 6 re-coarctation)<br>- Mean age: 35 (range 14-65) years<br>- Sex: 4 M; 13 F | **P1** | P2 | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 4 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Reduction in blood pressure<br>- Reduction in lumen diameter<br>- Reduction of hypertensive medications at follow-up<br>- Adverse effects | **Yes 1** | No 2 |
| Follow-up | - 2.5 years | **Yes 1** | No 2 |
| Statistical analysis | - Significance was considered as P<0.05. | **Yes 1** | No 2 |
| Clinical significance | - CP Stents (Covered) are effective in treating CoA and re-coarctation in adolescents and adults, are the treatment of choice in patients with complex anatomy, and must be available in the operating room as a rescue device when implanting a conventional stent. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 4 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (4) + Suitability (4) + Data Contribution (4) = 12 | Disposition and Weighting (select) | **Accepted and Pivotal 9-12**<br>Accepted but not Pivotal, 13-21<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - One death: patient died two days post-op due to massive hematemesis as a result of the combination of an extreme increase in blood pressure and an existing aneurysm.<br>- No local complications occurred, except one hematoma that resolved spontaneously.<br>- No patient had any complication at the iliac-femoral level that required stenting. |
| Performance data | - Blood pressure gradient: Reduced from 40 to 2 mmHg (P<0.001)<br>- Lumen diameter: Increased from 4 to 15 mm (P<0.001)<br>- At follow-up (2.5 years):<br>  - All good initial outcome persisted without any signs of re-obstruction.<br>  - 13/17 patients underwent imaging study; no aneurysms, dissections, and/or obstructive processes were observed.<br>  - Medication for hypertension was reduced in 5 patients and in 2 patients could not be discontinued. |
| Benefits/claims data | - Increased in luminal diameter<br>- Decreased in antihypertensive medication use |
| Strengths | - Having observed the case of aortic rupture, and with the aim of reducing these complications in patients |

| | |
|---|---|
| | who have had CoA and re-coarctation since their youth, the authors decided to electively implant a NuMED (Hopkinton, New York, United States) ePTFE CP Stent (Covered). This stent is mounted on a balloon catheter and protects the vascular wall when expanded. |
| Weaknesses/ Potential bias | - Retrospective and observational study with no control group of patients receiving conventional stents. Although all patients underwent clinical follow-up, this did not include an imaging study in all cases, and so authors cannot determine with certainty the incidence of potential aneurysms. |

7. Chang et al. (2012)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

**Safety & Performance**
**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Single arm interventional study. | To evaluate the use of CP Stent (Covered) as the primary modality in the treatment for native CoA. | 1 | 2 | 3 | **4** | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent (Covered and Bare)<br>- BIB | **D1** | D2 | D3 |
| Application | - Native CoA | **A1** | A2 | A3 |
| Patient | - Patients with native CoA without previous treatment<br>- Sampling: n=25<br>- Mean age: 22.5 (range 14-46) years<br>- Sex: 16 M; 9 F | **P1** | P2 | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 4 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Decrease in systolic gradient<br>- Increase in stenotic segment diameter | **Yes 1** | No 2 |
| Follow-up | - 32 (7-72) months | **Yes 1** | No 2 |
| Statistical analysis | - P<0.05 was set as statistically significant. | **Yes 1** | No 2 |
| Clinical significance | - Implantation of CP Stent (Covered) as the primary modality is safe and effective in the treatment for native CoA in adolescents and adults.<br>- Treatment modality of native CoA in adolescents and adults acquired excellent results, such as significant reduction in peak systolic gradient across CoA, successful relief of anatomic stenosis, and reduction of systemic hypertension.<br>- Above all, no adverse events were encountered during the procedure or during the follow-up period of up to 72 months. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 4 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (4) + Suitability (4) + Data Contribution (4) = 12 | Disposition and Weighting (select) | **Accepted and Pivotal 9-12**<br>Accepted but not Pivotal, 13-21<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - No acute complications were observed.<br>- During a follow-up period of up to 72 months (median, 32 months and quartile range, 51 months), no adverse effects (e.g., dissection, aneurysm formation, stent migration, stent fracture) were encountered.<br>- In the patient with the implantation of three CP stents, the aneurysm formation related to the bare CP stent was not encountered, the left subclavian artery crossed by the bare CP stent presented patent without thrombosis, and the left arm ischemia was not detected. |
| Performance data | - Peak systolic gradient across the lesion:<br>  - Decreased from median 67.5 mmHg to median 2 mmHg (P<0.0001)<br>- Stenotic segment diameter<br>  - Increased from median 5.0mm to median 17.9mm (P<0.0001)<br>- At follow-up (up to 72 months):<br>  - Most patients (21/25) were normotensive; except from 4/25 patients still required antihypertensive medication during follow-up |
| Benefits/claims data | - Reduced in peak systolic gradient.<br>- Reduced in luminal diameter.<br>- BIB offered precise and safe control over the stent implantation without any stent migration |
| Strengths | - Use of covered CP stents as the primary treatment modality may reduce the risk of significant complications related to stent implantation. |
| Weaknesses/ Potential bias | - Conflict of interest: not reported. |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Single arm interventional study. | To present author's institutional experience of endovascular CP Stent implantation in children and adults with native and recurrent CoA. | 1 | 2 | 3 | **4** | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent (16 Covered or 31 Bare) – n=47<br>- BIB (n=29) or single balloon catheter (n=18), Z-med (not subject device) | D1 | **D2** | D3 |
| Application | - Patients with native or recurrent CoA | **A1** | A2 | A3 |
| Patient | - Patients with native CoA (Group 1); recurrent CoA and/or aneurysm developed after either surgery or balloon angioplasty (Group 2)<br>- Sampling: n=45 (47 CP Stents, Covered or Bare)<br>- Median age: 11 (range: 5-33) years<br>- Sex: 34M; 11F | **P1** | P2 | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 5 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Decrease in invasive and echocardiographic gradients<br>- Increase in lesion diameter<br>- Adverse effects | **Yes 1** | No 2 |
| Follow-up | - 12.1±7.1 months; median 11 month (range 2-29) | **Yes 1** | No 2 |
| Statistical analysis | - A p value <0.05 was considered statistically significant. | **Yes 1** | No 2 |
| Clinical significance | - Early and short- term follow-up results indicate that stent implantation is safe and very effective in reducing coarctation gradient and increasing lesion diameter both in native and recurrent CoA.<br>- Some serious complications do occur and hypertension remains in some patients.<br>- Aortic disruption and stent displacement are potentially catastrophic complications of stenting but implanting a second covered stent can seal the ruptured wall and parking in a safe area or replacement of displaced stent carried by half-inflated balloon could solve the problem. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 4 | |

8. Erdem et al. (2011)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (4) + Suitability (5) + Data Contribution (4) = 13 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21**<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - No procedure related death.<br>- Two immediate complications relating to stenting:<br>  - One an acute wall rupture, successfully managed immediately in the same session with implantation of a second covered stent<br>  - One stent was displaced before it was completely opened. It was carried with support of partially inflated balloon and long sheath, and repositioned into the correct place.<br>- No femoral arterial complications<br>- No difficulty in catheter manipulation.<br>- None of the patients required intensive care following the procedure, and all were discharged home the following day except the patient with aortic rupture and after stenting with covered stent this patient was followed two days in intensive care unit. |
| Performance data | - Considering all cases, a statistically significant decrease in both the invasive and echocardiographic gradients (p<0.001 for both)<br>- Statistically significant increase in lesion diameter (p<0.001) were detected.<br>- Before the procedure, the invasive gradient was significantly higher and the lesion diameter was significantly lower in Group I than in Group II (p=0.002 and p=0.005, respectively).<br>- Percentage of decrease in gradient and increase in diameter was statistically higher in group 1 than in group 2 (p=0.04 and p=0.04).<br>- When the stent was in good position, the balloon was inflated to fix the stent in the coarctation site. |
| Benefits/claims data | - Increase in luminal/lesion diameter. |
| Strengths | - CP stent is the one of the most commonly used stent in pediatric cardiology<br>- This stent has excellent radial strength even at larger diameters and also has brilliant visibility on fluoroscopy. |

| | | |
|---|---|---|
| | Weaknesses/ Potential bias | - Some limitations have to be noted about this study:<br>  - Firstly, there is a need a greater number of patients have undergone stent implantation and their long-term results.<br>  - Secondly, population included both children and adult.<br>  - Thirdly, this was a single-center report and patients were not compared with surgery or balloon angioplasty alone.<br>  - Fourthly, 24-hour ambulatory blood pressure monitoring before stenting was not performed in any patients.<br>  - Finally, radiologic imaging for aneurysm was done in limited number of patients after procedure.<br>- Conflict of interest: None declared. |

9. Butera et al. (2011)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Prospective single arm interventional study. | To evaluate the management of aneurysms associated with CoA by covered stent deployment. | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent (Covered)<br>- BIB or Crystal balloon (not subject device) | D1 | **D2** | D3 |
| Application | - Patients with native CoA associated with aortic wall aneurysm | **A1** | A2 | A3 |
| Patient | - Patients with CoA associated with aortic wall aneurysm<br>- Sampling: n=11 (3 native CoA, 3 with previous surgical repair, 3 with previous balloon angioplasty, and 2 with previous bare stent implantation)<br>- Median age: 13 (range: 6-66) years<br>- Sex: Not reported | P1 | **P2** | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 6 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Systolic pressure gradient reduction<br>- Increase in aortic diameter<br>- Adverse effects | **Yes 1** | No 2 |
| Follow-up | - Median follow-up 50 (16-61) months | **Yes 1** | No 2 |
| Statistical analysis | - P-value less than 0.05 was considered to be statistically significant | **Yes 1** | No 2 |
| Clinical significance | - CP Stent (Covered) are a safe and effective treatment with low risk of complication for the treatment of CoA associated with aortic wall aneurysm.<br>- CP Stents (Covered, e-PTFE) may be considered the treatment of choice for native CoA associated with aortic wall aneurysm. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 4 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (3) + Suitability (6) + Data Contribution (4) = 13 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21**<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - No early complications observed. |
| Performance data | - Successful device deployment: Achieved in all patients.<br>- Successful relief of stenoses and complete sealing of all aneurysms.<br>- Systolic pressure gradient reduction: From median 30 (25-50) to 5 (0-20) mmHg, P<0.01<br>- Increase of aortic diameter: From median 6 (0.5 – 11) to 12 (10-22) mm, P<0.001<br>- Re-dilatation required at follow-up: four patients developed systemic hypertension (one intrastent restenosis secondary to significant endothelial growth, three showed restenosis secondary to somatic growth). Re-dilatation with a larger balloon was performed without complication in all cases. |
| Benefits/claims data | - Increase in luminal diameter<br>- Reduce systolic pressure gradient<br>- Reduce/prevent aortic wall injury (patients associated with aortic wall aneurysm) |
| Strengths | - Covered CP stents are manufactured with an alloy of 90% platinum and 10% iridium. Theoretically, this combination is more malleable and with good radial strength, which is enhanced by being designed in a ‘‘zig’’ pattern. The CP stent has rounded edges, decreasing the risk of balloon rupture or injury to the vessel wall and, in addition, the platinum component makes it more radio-opaque. Furthermore, the e-PTFE protects the stenotic and diseased segment. |
| Weaknesses/ Potential bias | - No conflict of interest reported. |

10. Tanous et

**Safety & Performance**

al. (2010)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Single arm interventional study. | To determine the safety and efficacy of the CP Stent (Covered) in adults with CoA. | 1 | 2 | 3 | **4** | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent (Covered) hand-crimped on Z-Med II (NuMED) or pre-mounted on BIB | D1 | **D2** | D3 |
| Application | - Native CoA (n=14) and previous treatment (n=8) | **A1** | A2 | A3 |
| Patient | - Patients with native CoA and CoA with previous treatment<br>- Sampling: 14 native CoA; 8 CoA (with previous treatment)<br>- Mean age: 39±14 (range 19 to 67) years<br>- Sex: 11 M; 11 F | **P1** | P2 | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 5 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Reduction in peak systolic gradient across coarctation site<br>- Adverse effects | **Yes 1** | No 2 |
| Follow-up | - 12 (9-15) months | **Yes 1** | No 2 |
| Statistical analysis | - A P-value <0.05 was considered significant. | **Yes 1** | No 2 |
| Clinical significance | - Covered stents are safe, durable, and efficacious in the management of CoA. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 4 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (4) + Suitability (5) + Data Contribution (4) = 13 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21**<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - One pseudoaneurysm. Patient was treated successfully.<br>Note: this problem may have been caused because the stent was hand crimped. When pre-mounted stents were used the problem did not reoccur. |
| Performance data | - Reduction in peak systolic gradient across coarctation site: From average 29 ± 17 to 3 ± 5 mmHg immediately post intervention and 6 ± 9 mmHg at follow up, P<0.001 |
| Benefits/claims data | - Reduction in peak systolic gradient |
| Strengths | - N/A |
| Weaknesses/ Potential bias | - This review is limited by the small sample size and lack of a randomized comparison group.<br>- This study was not intended to demonstrate the efficacy of percutaneous therapy, or the superiority of covered stents, but rather to document a single-center experience as an alternative and safe treatment option in a broad spectrum of patients with aortic coarctation. |

11. Moltzer et al. (2010)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

**<u>Safety & Performance</u>**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Prospective observational study. | To evaluate the intermediate-term outcome of stent implantation for CoA in adults. | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent (Bare and Covered)<br>- BIB | **D1** | D2 | D3 |
| Application | - Native CoA and re-coarctation | **A1** | A2 | A3 |
| Patient | - Patients with native CoA and re-coarctation<br>- Sampling: n=24<br>- Mean age: 36 (18-60) years<br>- Sex: 12 M; 12 F | **P1** | P2 | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 4 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Decrease in systolic gradient<br>- Increase in minimum aortic diameter<br>- Adverse effects | **Yes 1** | No 2 |
| Follow-up | - 24 hours post intervention and 33 (8-77) months | **Yes** | No |

| | | | |
|---|---|---|---|
| | | **1** | 2 |
| Statistical analysis | - All statistical tests were two-sided and a p-value <0.05 was considered statistically significant | **Yes 1** | No 2 |
| Clinical significance | - Stenting in adults results in significant blood pressure gradient decrease and increase in vessel diameter. However, serious complications do occur and hypertension remains in the majority of patients. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 4 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (3) + Suitability (4) + Data Contribution (4) = 11 | Disposition and Weighting (select) | **Accepted and Pivotal 9-12**<br>Accepted but not Pivotal, 13-21<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - One death due to aorta ruptured.<br>- Two groin hematoma post-op. |
| Performance data | - Systolic gradient: Decreased to < 10 mmHg in 21 patients, P<0.001<br>- Minimum aortic diameter: Increased from median 10 (2-17) to 16 (10-28) mm, P<0.001 |
| Benefits/claims data | - Reduced in systolic gradient<br>- Increased in minimum aortic diameter |
| Strengths | - N/A |
| Weaknesses/ Potential bias | - Only a small number of patients have undergone stent implantation since the authors started this procedure in 2003. This was a single-center report and patients were not compared with surgery or balloon angioplasty alone. Finally, 24-hour blood pressure monitoring before stenting was not performed in the majority of the patients. Post-stent 24-hour ambulatory blood pressure monitoring is therefore difficult to translate in terms of blood pressure reduction. |

12. Kische et al. (2010)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

**Safety & Performance Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Technical review. | To report the technique of interventional repair in adult CoA. | 1 | 2 | 3 | 4 | **5** |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - BIB | **D1** | D2 | D3 |
| Application | - CoA | **A1** | A2 | A3 |
| Patient | - Patients with CoA.<br>- Sampling: Not reported.<br>- Mean age: adult CoA patients, specific age not reported.<br>- Sex: Not reported. | P1 | **P2** | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 5 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Stent placement (delivery of large-diameter stents).<br>- Safety. | **Yes 1** | No 2 |
| Follow-up | - Not applicable. | Yes 1 | **No 2** |
| Statistical analysis | - Not applicable. | Yes 1 | **No 2** |
| Clinical significance | - Not applicable. | Yes 1 | **No 2** |
| | Data Contribution Grade (Range 4-8) | 7 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (5) + Suitability (5) + Data Contribution (7) = 17 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21**<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - BIB catheters require a larger arterial sheath for introduction, however, which needs to be upsized by 1F if a hand-crimped balloon is mounted on the balloon. Thus, although BIB catheters prevent stent flare and offer more precise control over stent placement, single-balloon catheters are still sometimes preferable in smaller patients to reduce the risk of femoral artery injury at the access site.<br>- The use of a BIB catheter will generally prevent technical complications such as balloon rupture and stent migration. |
| Performance data | - One of the most important technical refinements for delivery of large-diameter stents has been the NuMED Balloon-in-Balloon (BIB) catheter.<br>- These catheters have an inner balloon and a longer outer balloon that is double the diameter of the inner balloon and are available in outer-balloon sizes of up to 24 mm.<br>- The inner balloon of the BIB catheter is inflated, and an angiogram can be performed through the sheath |

| | |
|---|---|
| | or through an anterograde catheter in the proximal aorta to confirm position of the stent. With the stent in the desired position, the outer balloon is inflated to fix the stent in the lesion. Once the stent is expanded, both the outer and inner balloons are deflated as rapidly as possible. |
| Benefits/claims data | - BIB catheters offer more precise control over stent placement |
| Strengths | - BIB offers the important advantage of opening the stent more uniformly along its length, thereby eliminating the risk of unintended stent protrusion that has been documented by the use of single balloons. |
| Weaknesses/ Potential bias | - No conflict of interest reported. |

**Safety & Performance**
**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Two arms comparative interventional study. | To compare the CP Stent and the Palmaz stent for treatment of native and postoperative lesions of CHD patients. | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent (Bare & Covered), crimped on BIB<br>- Palmaz stent, crimped on BIB and simple balloons | **D1** | D2 | D3 |
| Application | - Patients with CHD (including CoA/re-coarctation, RVOT) | A1 | **A2** | A3 |
| Patient | - Patients with CHD (including CoA/re-coarctation, RVOT and other CHD conditions, such as transposition of the great arteries, ventricular septal defect, single ventricle, etc.)<br>- Sampling: n= 153<br>  - 89 CP Stents (crimped on 77 BIB & 12 other balloons)<br>  - 64 Palmaz Stents (crimped on 23 BIB and 41 simple balloons)<br>- Mean age:<br>  - CP Stents: 15.4 (SD: 9.2) years<br>  - Palmaz Stents: 11.6 (SD: 8.1) years<br>- Sex: Not reported | P1 | **P2** | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 6 | | |

13. Agnoletti et al. (2009)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Blood pressure gradient reduction<br>- Vessel diameter reduction<br>- Adverse effects | **Yes 1** | No 2 |
| Follow-up | - Not reported. | Yes 1 | **No 2** |
| Statistical analysis | - A P-value less than 0.05 was considered statistically significant for stent group comparison. | **Yes 1** | No 2 |
| Clinical significance | - The use of the CP Stents to treat stenotic lesions of CHD is effective and relatively safe. The overall efficacy of CP Stents for the treatment of stenotic lesions is superior to that of the Palmaz stent.<br>- CP Stents' overall safety is higher than that of the Palmaz stent; but Palmaz stents have a lower profile when inserted. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 5 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (3) + Suitability (6) + Data Contribution (5) = 14 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21**<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - Stent-related complications:<br>  - CP Stents (n=89 patients): 4 mild, 1 moderate, 1 severe.<br>  - Palmaz (n=64 patients): 10 mild, 2 moderate, 2 severe.<br>- Stent migration:<br>  - CP Stents: 7.<br>  - Palmaz: 4.<br>- Non stent related complications:<br>  - CP Stents: 1 mild, 2 moderate.<br>  - Palmaz: 1 mild, 2 moderate, 5 severe.<br>- Urgent surgery:<br>  - CP Stents: 2 due to homograft rupture and stent migration.<br>  - Palmaz: 1 for aortic dissection.<br>- Balloon related complications: Balloon burst<br>  - CP Stents: 0. |

| | |
|---|---|
| | - Palmaz: 7 (3 in BIB, 3 with simple balloons, and 1 on pre-mounted stent).<br>- |
| Performance data | - Blood pressure gradient reduction (P<0.004)<br>- CP: from 45.4 ± 25.7 to 8.7 ± 15.7 mmHg.<br>- Palmaz: from 37.7 ± 28.3 to 12.3 ± 15.1 mmHg.<br>- Vessel diameter (P<0.002)<br>- CP: from 7.4 ± 2.6 to 13.3 ± 3.4 mm.<br>- Palmaz: from 5.8 ± 2.7 to 13.3 + 4.5 mm. |
| Benefits/claims data | - Decreased in blood pressure gradient.<br>- Increased in vessel diameter. |
| Strengths | - Efficacy of CP Stents was similar to that of Palmaz stent for stenting of the right ventricular outflow, and higher than that of Palmaz for the stenting of aorta, but the difference was not statistically. |
| Weaknesses/ Potential bias | - Study presented retrospective results obtained in 153 consecutive patients.<br>- CP stents were used for patients weighing more than 15 kg; and thus two populations were different concerning age, weight, indication for stenting; however, none of these differences were related to occurrence of complications.<br>- Subgroup analyses were not performed. |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Technical review. | To discuss the available stents and balloons in stenting in regard to their advantages and disadvantages for common applications in CHD. | 1 | 2 | 3 | 4 | **5** |

14. Peters et al. (2009)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent and BIB | **D1** | D2 | D3 |
| Application | - Stenting in CoA | **A1** | A2 | A3 |
| Patient | - Patients with CoA<br>- Sampling: Not reported.<br>- Mean age: Not reported.<br>- Sex: Not reported. | P1 | P2 | **P3** |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 6 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Design advantages or disadvantages (technical description)<br>- Safety | **Yes 1** | No 2 |
| Follow-up | - Not applicable. | Yes 1 | **No 2** |
| Statistical analysis | - Not applicable. | Yes 1 | **No 2** |
| Clinical significance | - Large-diameter single-balloon catheters tend to expand first at their ends and thereby evert the stent ends such that they protrude radially from the stent center. Deploying a stent in this orientation can cause injury to the vessel wall and may be a risk factor for development of aneurysm or dissection. One of the most important developments in equipment for the delivery of large-diameter stents has been the Balloon-in-Balloon (BIB; NuMED) catheter, the first balloon specifically designed for stent delivery in the CHD population. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 6 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (5) + Suitability (6) + Data Contribution (6) = 17 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21**<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - BIB:<br>- Stent foreshortening can be much higher if stents are expanded with a single large balloon directly to 15 or 18 mm. The reason for this is that the ends of the stent are compressed toward each other due to the typical "dumb-belling" of the balloon at the end of inflation while the center of the stent is expanding to its full diameter. This results in significant shrinkage of the overall length of the stent. Thus, if final length is critical, the delivery requires sequential balloon dilatation with increasing diameters or, even better, the use of a Balloon-in-Balloon (BIB™ catheter; NuMED).<br>- Balloon rupture with inadequate stent expansion may be prevented by avoiding kinking of the balloon/stent assembly by the use of newer stents with softer ends and by the use of BIB systems. |
| Performance data | - BIB:<br>- These catheters have an inner balloon and a longer outer balloon that is double the diameter of the |

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|---|---|
| | inner balloon. The BIB catheters offer the important advantage of opening the stent more uniformly along its length but require a larger arterial sheath for introduction.<br>- While BIB catheters prevent stent flare and offer more precise control over stent placement, single-balloon catheters are still sometimes preferable in smaller patients to reduce risk of injury to the femoral artery at the access site. |
| Benefits/claims data | - BIB offers more precise control over stent placement |
| Strengths | - CP Stent:<br>- These stents have excellent visibility on fluoroscopy and maintain excellent radial strength even at larger diameters. |
| Weaknesses/ Potential bias | - No conflict of interest reported. |

15. Tzifa et al. (2006)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Single arm interventional study. | To evaluate the use of Covered CP Stents in treatment of CoA. | 1 | 2 | 3 | **4** | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent (Covered)<br>- BIB | **D1** | D2 | D3 |
| Application | - CoA | **A1** | A2 | A3 |
| Patient | - Patients with CoA (fully grown patients)<br>- Sampling: n=30<br>- Mean age: 28±17.5 (range 8 to 65) years<br>- Sex: not reported | **P1** | P2 | P3 |
| Report | - High quality. | R1 | **R2** | R3 |
| | Suitability Grade (Range 4-12) | 5 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Reduction in blood pressure gradient<br>- Reduction in coarctation diameter | **Yes 1** | No 2 |
| Follow-up | - 11 months | **Yes 1** | No 2 |
| Statistical analysis | - Statistical significance was defined as P<0.05. | **Yes 1** | No 2 |
| Clinical significance | - CP Stents (Covered) may be used as the therapy of choice in patients with complications after CoA repairs, whereas they provide a safe alternative to conventional stenting in patients with severe and complex CoA lesions or advanced age. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 4 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (4) + Suitability (5) + Data Contribution (4) = 13 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21**<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - Two stent fractures in the "old" design of the stent, no fractures in the "new" stent design<br>Note: Since May 2002, the CP Stents (Covered) have been produced with reinforced golden soldering joints as the "new" stent design |
| Performance data | - Blood pressure gradient: From 36 + 20 mmHg to 4 + 4 mmHg, P<0.0001<br>- Diameter at coarctation: From 6.4 +3.8 mm to 17.1 + 3.1 mm, P<0.0001 |
| Benefits/claims data | - Reduction in blood pressure gradient<br>- Reduction in coarctation diameter<br>- BIB allows readjustment of position after inflation of the inner balloon. |
| Strengths | - Covered stents were chosen:<br>1) as a rescue treatment in patients with CoA aneurysms or previous stent-related complications; and<br>2) in patients at risk of complications because of complex CoA anatomy or advanced age (defined as >65 years)<br>- Covered CP stents are made of a framework of platinum iridium wire welded in a zig pattern. The addition of a gold soldering to each weld spot fills any voids caused by the welding and transfers the stresses to a larger area of the stent. The gold also serves to encapsulate the welded area, once again adding to the total strength of the weld. The stent is then fitted with a covering of ePTFE to achieve a solid tubular structure that retains fluid. The ePTFE covering is initially approximately 7 mm in diameter and will stretch over the range of diameters of expansion (usually from 12 to 24 mm diameter), and will always be taut over the stent when expanded. When the covering is mounted, it is folded over the crimped stent and expands |

| | |
|---|---|
| | uniformly when the balloon is inflated.<br>- The BIB allows for readjustment of position after inflation of the inner balloon. |
| Weaknesses/ Potential bias | - Not reported. |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Comparative, two single arm interventional study (CP Stent/BIB versus Palmaz stent/single balloon). | To demonstrate effectiveness of CP Stent, in combination with BIB, for treating aortic coarctation in comparison with the Palmaz stent. | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent and BIB. Note: D1 for subject device (CP Stent and BIB).<br>- Palmaz stent and single balloon. | **D1** | D2 | D3 |
| Application | - CoA and re-coarctation | **A1** | A2 | A3 |
| Patient | - Patients with CoA and re-coarctation<br>- Sampling: n=46 (21 Palmaz Stent, 25 CP Stent)<br>- Mean age:<br>  - Palmaz Stent: 12 (range: 4.5 to 16) years old<br>  - CP Stent: 24.1 (range: 10.5 to 60) years old<br>- Sex: M;F<br>  - Palmaz Stent: 15M; 6F<br>  - CP Stent: 15M; 10F | **P1** | P2 | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 4 | | |

16. Cheatham et al. (2001a)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Decrease in peak systolic gradient<br>- Safety | **Yes 1** | No 2 |
| Follow-up | - Limited follow-up because of the relatively short-elapsed time and multiple, out of country institutions involved | Yes 1 | **No 2** |
| Statistical analysis | - Statistically significant achieved when P<0.05. | **Yes 1** | No 2 |
| Clinical significance | - Both the Palmaz and the NuMED CP Stents offer an effective, nonsurgical treatment for both native and recurrent CoA, regardless of site or severity of obstruction.<br>- Native CoA tends to be more severe, with tighter stenosis and higher gradients compared to recurrent coarctation. Aneurysm development may occur in these patients after Palmaz stent implantation. Therefore, graduated serial stent dilation and/or covered stent implantation should be considered in high-risk patients. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 5 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (3) + Suitability (4) + Data Contribution (5) = 12 | Disposition and Weighting (select) | **Accepted and Pivotal 9-12**<br>Accepted but not Pivotal, 13-21<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - Intraoperative complications:<br>  - Two cases of stent embolization in Palmaz Stent group versus one case of left hemothorax in CP Stent (Covered) group<br>- Late complications:<br>  - Aortic aneurysm in Palmaz Stent Group (n=3)<br>  - 9/21 (43%) continued to require antihypertensive medication<br>- Adverse effects:<br>  - Flaring of the Palmaz Stent as a result of the single balloon that first expands at the ends, not from the middle.<br>  - Premature BIB rupture reported using Palmaz stent, believed to be due to inadvertent puncture of outer balloon by the sharp-edged Palmaz stent during hand crimping. |
| Performance data | - Peak systolic gradient<br>  - Palmaz Stent<br>  - Native coarctation: 46.8 to 1.5 mmHg (P<0.05)<br>  - Recurrent coarctation: 35 to 1.2 mmHg (P<0.05)<br>  - CP Stent<br>  - Native coarctation of the aorta: 53 mmHg to 2 mmHg (P<0.001)<br>  - Recurrent coarctation: 41 mmHg to 1.2 mmHg (P<0.001) |

| | |
|---|---|
| Benefits/claims data | - BIB significantly improves stent delivery and final deployment of any stent. The inner balloon is always inflated first, partially expanding the stent without flaring and allows repositioning of the stent before final deployment, when the outer balloon is inflated. |
| Strengths | - The zig design of the NuMED CP Stent improved strength and flexibility while minimizing stent shortening and vessel/balloon trauma.<br>- The tempered platinum/iridium wire and zig design of the NuMED CP Stent improved strength, flexibility, and radiopacity while minimizing stent shortening and vessel/balloon trauma.<br>- The NuMED CP stent offers a wider range of expanded diameters and lengths than the Palmaz stent, which is necessary to ensure an adequate adult vessel diameter in growing children and young adults and reduces the need for multiple stents in long segment obstruction.<br>- The BIB catheter is selected so that the inner balloon is always shorter than the stent while the outer balloon is slightly longer. The BIB delivery catheter significantly improves stent delivery and final deployment of any stent while minimizing stent migration and flaring. This in turn decreases the incidence of ventricular tachycardia in interventional pediatric cardiologists. |
| Weaknesses/ Potential bias | N/A |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Report results collected 45 patients underwent CP stent implantation from August 1998 through August 1999. | To report the CP Stent and BIB development, including results from clinical study conducted from August 1998-August 1999. | 1 | 2 | 3 | **4** | 5 |

17. Cheatham et al. (2001b)

| Contribution | |
|---|---|
| S&P | x |
| SOA | |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent<br>- BIB | **D1** | D2 | D3 |
| Application | - CoA and other conditions. | A1 | **A2** | A3 |
| Patient | - Patients with CoA and other conditions:<br>  - CoA (n=25; 17 native CoA and 8 Re-coarctation),<br>  - Right pulmonary artery (RPA) stenosis (n=5),<br>  - Isolated left pulmonary artery (LPA) stenosis (n=2),<br>  - Bilateral branch stenosis (n=6),<br>  - Recurrent right ventricle to pulmonary artery (RV-PA) homograft stenosis (n=4),<br>  - Blalock-Taussig shunt stenosis (n=1),<br>  - Multiple sites of left-to-right shunt inside a lateral tunnel Fontan repair (n=1),<br>  - Obstructed superior vena cava (SVC) baffle limb after Mustard repair for transposition of the great arteries (n=1)<br>- Sampling: n=45 patients (CP Stent, n=57)<br>- Mean age: 19 (range 1.8-60) years<br>- Sex: 25 M; 20 F | P1 | **P2** | P3 |
| Report | - High quality. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 6 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Peak systolic gradient reduction<br>- Procedural complications | **Yes 1** | No 2 |
| Follow-up | - Minimal follow-up due to short study period and large number of institutions involved | Yes 1 | **No 2** |
| Statistical analysis | - P-values reported. | **Yes 1** | No 2 |
| Clinical significance | - NuMED CP stent (placed by BIB stent placement catheter) offers an effective, non-surgical treatment for a wide variety of vascular obstructions associated with congenital heart disease.<br>- The NuMED BIB catheter is an innovative concept that has significantly improved operator control during intravascular stent delivery. It minimizes stent flaring, migration, and shortening, while effectively eliminating catheter movement during deployment. It also allows the partially expanded stent to be repositioned before final expansion, which is a significant benefit to the interventionalist to maintain control and precisely position the stent. We currently use the BIB catheter for all stents. Although more data and longer follow-up are required, the NuMED CP stent and BIB delivery catheter offer great promise in the future treatment of children and adults with congenital heart disease. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 5 | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (4) + Suitability (6) + Data Contribution (5) = 15 | Disposition and Weighting (select) | Accepted and Pivotal 9-12<br>**Accepted but not Pivotal, 13-21**<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| | |
|---|---|
| Safety data | - Two procedural complications, both considered avoidable and there were no further sequelae<br>  - One with severe native CoA requiring a covered stent, there was transient left hemothorax.<br>  - One traumatic stent fracture during attempted entry of the long, covered CP stent in the Fontan patient using a modified 'front-load' technique. The stent was inadvertently pushed out of the delivery sheath in the groin with the first row of 10 zigs being traumatized and fractured.<br>- Follow-up:<br>  - Stent fatigue fracture and fragment embolization in two patients<br>  - Two patients with severe native CoA and stenoses <2 mm had immediate residual gradients of 20 and 25 mmHg secondary to limited stent expansion to avoid excessive vessel trauma and possible aneurysm formation with planned stent re-dilation later.<br>  - One patient had a 30 mmHg residual aortic gradient 10 months post implant secondary to an intimal flap that was successfully treated with a second CP stent |
| Performance data | - Peak systolic gradient was reduced in 17 patients with native CoA from 56.2 mmHg to 4.6 mmHg, while in the 8 patients with recurrent aortic obstruction, the gradient was reduced from 41.8 mmHg to 0.9 mmHg, both statistically significant at P<0.001 using paired t-tests<br>- Isolated RPA and LPA stenoses were also effectively treated with peak systolic gradient reductions from 54.6 to 5 mmHg and 52.5 to 6.5 mmHg respectively P<0.001<br>- In the six children with combined RPA and LPA stenoses, 'kissing stents' reduced the peak systolic gradients from 43.5 and 45 mmHg to 6.8 and 6.0 mmHg, respectively P<0.01.<br>- The four patients with recurrent RV-PA homograft obstruction also had effective relief of their<br>- gradients from 55 to 14.3 mmHg P<0.01.<br>- After stenting the stenotic right Blalock-Taussig shunt in the young man with complex cyanotic congenital heart disease, O2 saturations increased from 78 to 88%. The implantation of the long covered CP stent was also clinically effective in treating the young man with multiple leaks in the lateral tunnel by improving resting O2 saturations from 80 to 96%.<br>- Finally, the 9 mmHg mean gradient across the obstructed SVC baffle after Mustard's repair was completely eliminated. |
| Benefits/claims data | - The BIB effectively eliminating catheter movement during deployment. It also allows the partially expanded stent to be repositioned before final expansion, which is a significant benefit to the interventionalist to maintain control and precisely position the stent. |
| Strengths | - CP Stent versus Palmaz Stent<br>  - The advantages of the NuMED CP stent compared to the Palmaz stent are as follows: (1) superior radiopacity secondary to the platinum composition; (2) superior 'compression' or radial hoop strength secondary to the tempered wire and zig design; (3) less rigidity because of the malleability of the tempered platinum-iridium wire; (4) less potential trauma to the delivery balloon and target vessel secondary to the rounded edges of the zig pattern; (5) wider range of expanded diameters from 8 to 24 mm (10 zig can be expanded to 30 mm) while maintaining ≤20% stent shortening; (6) superior selection of stent lengths to meet the demands of a wide range of target lesions; and (7) maximal stent shortening of <20% will minimize chances of missing the target site or need of multiple serial stents.<br>- BIB versus single balloon catheter:<br>  - Careful observation of how a single balloon catheter may actually create significant problems during any stent deployment, but is exaggerated in the aorta. Conventionally, the balloon is chosen to be longer than the stent to avoid stent migration during delivery or deployment. Unfortunately, the proximal and distal ends of the balloon catheter expand first and well before the stent. This leads to flaring of the edges of the stent, which in the Palmaz stent's case is dangerous because of the sharp leading and trailing edges approaching the vessel wall and balloon leading to trauma of both. In addition, the partially expanded balloon acts as a floatation catheter, allowing catheter and stent movement prematurely during deployment. Finally, there is no ability to reposition the stent during deployment.<br>  - In November 1997, the NuMED Balloon In Balloon (BIB) catheter was designed with an inner Tyshak balloon and an outer Z-Med balloon. The inner balloon is very low profiled and expands to half the outer balloon diameter, while the length is 1 cm shorter than the outer balloon. The inner balloon is always inflated first using a twisting action of the locked endoflator that expands the stent to 0.5 of the target vessel diameter without flaring of ends of the stent, since the balloon is shorter than the stent. Because the stent is still in contact with the unexpanded outer balloon material, the entire stent-balloon delivery catheter system can be repositioned before final deployment by expanding the outer balloon. |
| Weaknesses/ Potential bias | A Tower, DJ Villnave and R Normile (NuMED) provided technical support for this publication. |

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| 18. Meadows | **Safety & Performance** |

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| et al. (2015)<br><br>Contribution: S&P x; SOA | This publication presents the results from the COAST trial for CP Stent (Bare and Covered) to treat native and recurrent CoA in selected children, adolescents and adult (NCT00552812). Please refer information presented in **Table G-1** for safety and performance of the subject devices, Study no. 1. |
| 19. Taggart et al. (2016)<br><br>Contribution: S&P x; SOA | **Safety & Performance**<br>This publication presents the results from the COAST II trial to evaluate the safety and short-term efficacy of the CP Stent in treating or preventing aortic wall injury in patients with CoA (NCT01278303). Please refer information presented in **Table G-1** for safety and performance of the subject devices, Study no. 2. |

**An overall summary of the clinical performance and safety:**

A comprehensive, systematic, and critical evaluation of the pertinent clinical data and pre-clinical study data in relation to the BIB Stent Placement catheter has been carried out and documented in the clinical evaluation report. Based on the results of the clinical evaluation report, it is considered that:

a) Conformity with relevant general safety and performance requirements set out in MDR Annex I under the normal conditions of the intended use of the device has been confirmed.
b) Undesirable side-effects and acceptability of the benefit-risk ratio have been evaluated and are acceptable according to the current knowledge/the state of the art in the medical fields concerned and according to available medical alternatives.
c) The information materials supplied by NuMED, and the risk reduction measures are adequate taking into account the intended purpose of the device.
d) Usability aspects have been adequately considered and the BIB, including the IFUs, is suitable for the intended users.
e) The claims foreseen in the information materials provided with the CER are adequate taking into account the intended purpose of the device.
f) The information materials supplied and the RM documentation for the device under evaluation are consistent with the clinical data and pre-clinical study data presented in the CER and with the current knowledge/state of the art.

Overall, it is concluded that the risks associated with the use of the BIB Stent Placement catheter are acceptable when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art; that the intended clinical performances are achieved by the device; and that known and foreseeable risks and undesirable side-effects are considered acceptable when weighed against the benefits from performance achieved by the device.

**Ongoing planned post-market clinical follow-up:**

The BIB Stent Placement Catheter has been commercialized since December 2003 in the EU. Since then, the device is likely to have been used in a variety of patients and populations. A PMCF Study is not warranted at this time due to the fact that long-term safety and clinical performance has been established via device use and ample clinical experience. Continued post-market surveillance activities will provide sufficient data to adequately address clinical risks, and detect emerging risks on the basis of evidence.

The addition of the 26mm, 28mm, and 30mm size in 2014 warranted a PMCF Study just for those sizes. The study investigated procedural and device complications and compared that with currently available data from the use of the smaller BIB Stent Placement Catheter sizes. Based on the findings from the PMCF study, NuMED determined the BIB Stent Placement Catheter (larger sizes) to be safe and effective when used for the approved indication. No changes were required to the risk analysis as there were no new risks identified, and no changes were required to the instructions for use based on the results of the PMCF Study.

**6. Possible diagnostic or therapeutic alternatives**

Alternative therapies to balloon dilatation / stenting include balloon angioplasty without a stent and surgical intervention.

**7. Suggested profile and training for users**

The device is intended to be used by trained cardiology and surgical professionals undertaking stent implantation.

**8. Reference to any harmonised standards and CS applied**

There are no Common Specifications for this type of device.

The following harmonised standards are followed for this device:

- EN ISO 11135:2014 – Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices.
- EN ISO 11737-1:2018/A1:2021 – Sterilization of medical devices – Microbiological methods – Part 1: Determination of a population of microorganisms on products
- EN ISO 13485:2016/A11:2021 – Medical devices – Quality management systems – Requirements for regulatory purposes
- EN ISO 15223-1:2021 – Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements.

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**10. Revision History**

| SSCP revision number | Date Issued | Change Description | Revision validated by Notified Body |
|---|---|---|---|
| 00 | 21 June 2022 | Initial implementation | ☐ Yes<br>Validation Language: English<br>☒ No |
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