# NuMED
# Summary of Safety and Clinical Performance
# SSCP – Stents - CoA

*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 CoA Stent Family<br>CP Stent<br>Mounted CP Stent<br>G-Armor Stent<br>G-Armor Mounted Stent |
| Model Number | NuMED CoA Stent Family – Model 1600<br>CP Stent – Model 425<br>Mounted CP Stent – Model 426<br>G-Armor Stent – Model 431<br>G-Armor Mounted Stent – Model 433 |
| 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 | 08877141600T2 |
| Medical device nomenclature description / text | EMDN – P070402010102 - METALLIC NON-STAINLESS STEEL CORONARY STENTS |
| Class of device | III |
| Year when first certificate (CE) was issued | 2004 |
| 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** | |
|---|---|
| Indications for use | Coarctation of the Aorta (CoA)<br>Indicated for implantation in the native and/or recurrent coarctation of the aorta on patients with the following clinical conditions: |

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| | • Stenosis of the aorta resulting in significant anatomic narrowing as determined by angiography or non-invasive imaging, i.e. echocardiography, magnetic resonance imaging (MRI), CT scan;<br>• Stenosis of the aorta resulting in hemodynamic alterations, resulting in systolic pressure gradient, systemic hypertension or altered left ventricular function;<br>• Stenosis of the aorta where balloon angioplasty is ineffective or contraindicated;<br>• Stenosis diameter <20% of adjacent vessel diameter. Stenosis that would present increased risk of vascular damage or disruption; or aneurysm associated with coarctation of the aorta. |
| Contraindications and/or limitations | Contraindications include:<br>• Patients too small to allow safe delivery of the stent without compromise to the systemic artery used for delivery;<br>• Unfavorable aortic anatomy that does not dilate with high pressure balloon angioplasty;<br>• Occlusion or obstruction of systemic artery precluding delivery of the stent;<br>• Clinical or biological signs of infection;<br>• Active endocarditis;<br>• Known allergy to aspirin, other antiplatelet agents, or heparin;<br>• Pregnancy. |

| **3. Device description** | |
|---|---|
| Description of the device | The Stents are balloon expandable and intended for permanent implant. The Stents are composed of heat treated 90% platinum/10% iridium wire that is arranged in laser welded rows with a "zig" pattern. The number of zigs in a row can be varied and will impact the strength of the stent as well as the eventual expanded diameter and percent stent shortening, while the number of rows will determine the unexpanded length of the stent.<br><br>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 ½ 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 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. 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.<br><br>The devices are supplied sterile, by ethylene oxide gas, and are intended for single use only. The stents are invasive and intended for permanent implant by an adequately trained/experienced healthcare professional. |
| Reference to previous generation(s) or variants | N/A |
| Accessories which are intended to be used in combination with the device | All Stents are designed to be used with the hemostasis valve tools that are provided with the stents. |
| Description of any other devices and products which are intended to be used in combination with the device | All Stents are designed to be used with a balloon catheter, introducer, and guidewire. |

| **4. Risks and Warning** | |
|---|---|
| Residual risks and undesirable effects | The clinical investigations performed on the CP Stent family of devices reported the following side effects:<br>COAST: aortic aneurysm, stent fracture<br>COAST II: iliac artery dissection<br><br>The literature reported the following side effects: Acute wall rupture / dissection, aortic aneurysm / |

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|---|---|
| | pseudoaneurysm, balloon rupture, death, stroke, stent embolization, groin hematoma, late lumen loss, left hemothorax, stent displacement, stent fracture, stent malposition, transitory arrhythmia, and cardiogenic / septic shock.<br><br>Known and foreseeable clinical risks have been considered in accordance with risk management (RM) procedure AP-346 and through the RM files and mitigated as far as possible (AFAP).<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>- Femoral artery injury, thrombosis or psuedoaneurysm<br>- Stent Migration<br>- Aortic Rupture/Tear<br>- Thrombosis/Thromboembolism<br>- Endocarditis<br>- Stent Stenosis<br>- Stent Malposition<br>- AV fistula formation<br>- Bleeding<br>- Stent Fracture<br>- Hematoma<br>- Death<br>- Cell necrosis at the site of implant<br>- Aortic Aneurysm / Pseudoaneurysm<br>- Sepsis/infection<br>- Transitory arrhythmia<br>- Cerebrovascular Incident |
| Warning and Precautions | The following Warnings and Precautions have been identified and are called out in the Instruction for Use:<br><br>**WARNINGS**<br>• Radiofrequency heating during MRI scans on overlapped, 10 zig Stents has not been evaluated.<br>• As with any type of implant, infection secondary to contamination of the stent may lead to aortitis, or abscess. The platinum/iridium stent may migrate from the site of implant. Over-stretching of the artery may result in rupture or aneurysm formation.<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>• The inflated diameter of the stent should at least equal the diameter of the intended implant site.<br>• Excessive force while crimping may weaken welds of the stent.<br>• Crimping the 8 zig stent on a balloon catheter smaller than 12mm, and the 10 zig on a balloon catheter smaller than 26mm, may cause damage to the stent.<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>• Use of an inflation device with pressure gauge is highly recommended during this procedure.<br>• The stent is rigid and may make negotiation through vessels difficult.<br>• Dilatation procedures should be conducted under fluoroscopic guidance with appropriate x-ray equipment.<br>• Guidewires are delicate instruments. 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 and by aspiration before proceeding to avoid air introduction into the system.<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. |
| Other relevant aspects of safety, including a summary of any field safety corrective actions (FSCA including FSN) if applicable | Since commercialization, there has been one recall on the Bare CP Stent in 2003 (#Z-0983-03, completed in 2004) concerning the lack of PMA or 510(k) for the Bare CP Stent. The recall was conducted in the U.S. only.<br><br>There have not been any Field Safety Corrective Actions or Field Safety Notices on any other version of the Stents. |

**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:**

**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). The COAST is a prospective, multicenter, single-arm clinical study involving 19 pediatric cardiology centers in the United States. The study includes patients with native or recurrent CoA treated by physicians at the participating institutions. A total of 105 patients underwent attempted implantation, with 104 successes.

***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.<br>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:** To evaluate 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. Patients were enrolled if they had a history of CoA with pre-existing aortic wall injury (Treatment group) or with increased risk of aortic wall injury (Prevention group). Pre/post-implant hemodynamics and angiography were reported. A core laboratory performed standardized review of all angiograms. One month follow-up was reported.

***Reference to the clinical study plan (and amendment) n°:*** NCT01278303

**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 |

| | | |
|---|---|---|
| | | 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). |

***Reference to the Clinical Study Report n°:*** NCT01278303
**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.

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

| First Author (Year) | Appraisal/Results |
|---|---|
| 1. Baykan et al. (2018) | **Safety & Performance** |

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Control study. Study group was composed of 20 CoA patients who were treated with CP Stent between the dates October 2008 and February 2015, and control group was composed of 20 healthy children with age and sex matched. | To address the presence of hypertension and risk for cardiovascular diseases in patients with CoA who were treated with endovascular stent placement. | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stents (Bare and Covered) |
| Application | - CoA |
| Patient | - Patients who had undergone stent placement for CoA compared with control group (healthy children with a matched).<br>- Sampling: n=20 CoA and n=20 healthy children<br>- Mean age:<br>  - CoA group: 14.2 (SD: 3.9) years<br>  - Control group: 13.7 (SD: 2.7) years<br>- Sex:<br>  - CoA group: 16M; 4F<br>  - Control group: 15M; 5F |
| Report | - High quality |
| | Suitability Grade |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Ambulatory blood pressure | **Yes 1** | No 2 |
| Follow-up | - 6 months and 6 years | **Yes 1** | No 2 |
| Statistical analysis | - Student t-test was used if the two independent group comparisons were normal and the Mann-Whitney U test was used if the normal distribution was not present. Pearson chi-square analysis was performed to determine whether there was a difference in categorical variables between the case and control groups. | **Yes 1** | No 2 |
| Clinical significance | - It was shown that hypertension incidence as demonstrated by ambulatory blood pressure monitorization and risk for cardiovascular diseases as indicated by carotid intima media thickness and pulse wave velocity were higher than those in healthy population even after CoA is corrected.<br>- CoA should be carefully monitored for hypertension, even if it has been completely corrected by any method. This study suggests that CoA is a part of generalized vasculopathy rather than being a localized narrowing. | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | 4 | |

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

**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**

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|---|---|
| Safety data | - Hypertensive:<br>  - Daytime: 5% were hypertensive and 20% were pre-hypertensive in the study group compared to 0% in the control group.<br>  - Night: 15% were hypertensive and 15% were pre-hypertensive in the study group compared to 0% in the control group. |
| Performance data | - Mean arterial pressure:<br>  - At 24 hours: 88.5 (81-96) mmHg in study group and 83 (80-86) mm Hg in control group<br>  - Daytime: 91 (84-99) mmHg in study group and 84 (81-88) mmHg in control group<br>  - Night: 78 (76-87) mmHg in study group and 78 (75-81)mmHg in control group |
| Benefits/claims data | - N/A |
| Strengths | - N/A |
| Weaknesses/ Potential bias | - Patients were treated only with “NuMED brand Bare and Covered Stent” types. In the future the authors can do more extensive studies with more cases and different types of stents. |

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| | - Same methodology (blood pressure monitoring with Holter device) in pre-operative period could not be used because at that time they did not have a blood pressure Holter device. |

**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 |
|---|---|
| Device | - NuMED CP Stent (Bare and Covered)<br>- BIB |
| Application | - Severe native CoA |
| 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 |
| Report | - High quality. |
| | Suitability Grade |

2. 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. |

3. Vanagt et al. (2014)

**Safety & Performance**

**Appraisal**

| Level of | Study Method/Design | Question Applied | Oxford LOE 2011 |
|---|---|---|---|

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

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stent (Covered)<br>- BIB |
| Application | - CoA and RVOT pre-stenting for percutaneous revalvulation |
| Patient | - Patients with CoA and RVOT pre-stenting for percutaneous revalvulation. For the RVOT gr (Covered) was chosen for delivery balloon protection after rupture of the pre-dilation ba patients (19%) and 30 (81%) because tear, rupture, or fracture of the conduit was expected, c 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 |
| Report | - High quality. |
| | Suitability Grade |

| Data Contribution | Relevant Data |
|---|---|
| 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 |
| Follow-up | - Not specified. |
| Statistical analysis | - Two-sided p<0.05 was considered significant. |
| Clinical significance | - CP Stents (Covered) can safely be applied in CHD patients. The covering allows adequ existing or expected tears, thereby increasing the safety margin with more complete dilation. |
| | Data Contribution Grad |

**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) |
|---|---|---|

**Relevant S&P Results**

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|---|---|
| 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 rh ventricle), and transient atrioventricular block with nodal escape rhythm (n = 1, while wir<br>  - During follow-up: no stent fractures, nor stent recompression occurred, and none of the pa 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-u |
| 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.<br>- Graft diameter (RVOT Group)<br>  - Increased from graft stenosis diameter of 13 (5-22) mm to 22 (16-26) mm at pre-revalvul |
| 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 soldering. The strut thickness is slightly larger than most other stents, but makes the stent edges<br>- CP Stent (Covered) was hand-crimped on a balloon-in-balloon (BIB, Numed). Hand-inflation c ml syringe on the inner balloon and 20 ml syringe on the outer balloon, automatically limiting i |
| Weaknesses/ Potential bias | - In this retrospective study, there are no control groups with bare stents, the lack of which is inh these procedures would have been impossible, or significantly less safe, if bare stents were used |

4. Alcibar et al. (2013)

**Safety & Performance Appraisal**

| Level of Evidence | Study Method/Design | Question Applied |
|---|---|---|

| | | |
|---|---|---|
| | Retrospective and observational study. | To investigate reduction in aortic wall rupture and dissection, as well as aneurysms by implanting covered stents. |

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

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stent (Covered)<br>- BIB |
| Application | - CoA and re-coarctation |
| Patient | - Patients treated for CoA and re-coarctation (2 adolescents and 15 adults treated between Nover 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 |
| Report | - High quality. |
| | Suitability Grade |

| 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**

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|---|---|
| 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. |

5. Chang et al. (2012)

**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 |

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

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stent (Covered and Bare)<br>- BIB |

| | | |
|---|---|---|
| Application | - Native CoA | |
| 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 | |
| Report | - High quality. | |
| | | Suitability Grade (Range 4-12) |

| 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. |

6. Erdem et al. (2011)

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

**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 |
|---|---|
| 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) |
| Application | - Patients with native or recurrent CoA |
| Patient | - Patients with native CoA (Group 1); recurrent CoA and/or aneurysm developed after either sur balloon angioplasty (Group 2)<br>- Sampling: n=45 (47 CP Stents, Covered or Bare)<br>- Median age: 11 (range: 5-33) years |

| | | |
|---|---|---|
| | - Sex: 34M; 11F | |
| Report | - High quality. | |
| | | Suitability Grade (Range 4-12) |

| 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 |

**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. |

7. Butera et al. (2011)

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Prospective single arm | To evaluate the management of aneurysms associated | 1 | 2 | **3** | 4 | 5 |

| Contribution | | | interventional study. | with CoA by covered stent deployment. | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| S&P | x | | | | | | | | |
| SOA | | | | | | | | | |

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stent (Covered)<br>- BIB or Crystal balloon (not subject device) |
| Application | - Patients with native CoA associated with aortic wall aneurysm |
| 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 angiop with previous bare stent implantation)<br>- Median age: 13 (range: 6-66) years<br>- Sex: Not reported |
| Report | - High quality. |
| | Suitability Grade |

| 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. |

8. Tanous et al. (2010)

**Safety & Performance**

**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 |

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

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stent (Covered) hand-crimped on Z-Med II (NuMED) or pre-mounted on BIB |
| Application | - Native CoA (n=14) and previous treatment (n=8) |
| 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 |

| | | |
|---|---|---|
| Report | - High quality. | |
| | | Suitability Grade (Range 4-12) |

| 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. |

9. Moltzer et al. (2010)

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

**Safety & Performance**
**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 |
|---|---|
| Device | - CP Stent (Bare and Covered)<br>- BIB |
| Application | - Native CoA and re-coarctation |
| 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 |
| Report | - High quality. |
| | Suitability Grade |

| 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 1** | No 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. |

10. Kische et al. (2010)

**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 |
|---|---|
| Device | - BIB |
| Application | - CoA |
| Patient | - Patients with CoA.<br>- Sampling: Not reported.<br>- Mean age: adult CoA patients, specific age not reported.<br>- Sex: Not reported. |
| Report | - High quality. |
| | Suitability Grade |

| 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 | |

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

**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/ | - No conflict of interest reported. |

| | |
|---|---|
| Potential bias | |

**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 |
|---|---|
| Device | - CP Stent (Bare & Covered), crimped on BIB<br>- Palmaz stent, crimped on BIB and simple balloons |
| Application | - Patients with CHD (including CoA/re-coarctation, RVOT) |
| Patient | - Patients with CHD (including CoA/re-coarctation, RVOT and other CHD conditions, such as t 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 |
| Report | - High quality. |
| | Suitability Grade |

11. Agnolett i 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.<br>  - 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. |

| | |
|---|---|
| | - 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 | | | | |
|---|---|---|---|---|---|---|---|
| | Prospective interventional single arm study to evaluate placement of CP Stent (Covered) with smallest possible balloon sizes, then dilation with larger diameter balloons until pressure gradient was <20 mmHg and the stent was opposed to the aortic wall. | To report on the early results of treatment of native CoA by implantation and serial dilations of covered stents. | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stents (Covered) |
| Application | - Native CoA |
| Patient | - Patients with native CoA<br>- Sampling: n=22<br>- Mean age: 15.5 (7.8 – 38.6) years<br>- Sex: 14 M; 8 F |
| Report | - High quality. |
| | Suitability Grade |

12. Bruckheimer et al. (2009)

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

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Increase of coarctation diameter<br>- Reduction of peak pressure gradient<br>- Adverse effects | **Yes 1** | No 2 |
| Follow-up | - Median 18.5 (1.6-31.4) months | **Yes 1** | No 2 |
| Statistical analysis | - P-values reported. | **Yes 1** | No 2 |
| Clinical significance | - Serial dilation of CP Stents (Covered) is feasible, safe and an effective percutaneous method for the treatment of native 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 (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 small tear at the distal stent edge<br>- One femoral pseudoaneurysm which spontaneously resolved |
| Performance data | - Increase of coarctation diameter:<br>  - From 3.6 ± 1.9 mm pre-intervention to 12.6 ±1.9 mm post-intervention, P=0.001<br>- Reduction of peak pressure gradient:<br>  - From 29.4 ± 8.5 to 6.7 ± 5.7 mmHg, P=0.001 |
| Benefits/claims data | - Increase of coarctation diameter<br>- Reduction of peak pressure gradient |
| Strengths | - N/A |
| Weaknesses/ Potential bias | - No conflict of interest reported. |

13. Peters et al. (2009)

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

**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** |

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stent and BIB |
| Application | - Stenting in CoA |
| Patient | - Patients with CoA<br>- Sampling: Not reported.<br>- Mean age: Not reported.<br>- Sex: Not reported. |
| Report | - High quality. |
| | Suitability Grade |

| 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 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. |

14. Tzifa et al. (2006)

**Safety & Performance**

**Appraisal**

| Level of | Study Method/Design | Question Applied | Oxford LOE 2011 |
|---|---|---|---|

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

| Evidence | Single arm interventional study. | To evaluate the use of Covered CP Stents in treatment of CoA. | 1 | 2 | 3 | **4** | 5 |
|---|---|---|---|---|---|---|---|

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stent (Covered)<br>- BIB |
| Application | - CoA |
| 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 |
| Report | - High quality. |
| | Suitability Grade |

| 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. |

15. Cheatham et al. (2001a)

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

**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 | 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 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | balloon). | | | | | | |

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stent and BIB. Note: D1 for subject device (CP Stent and BIB).<br>- Palmaz stent and single balloon. |
| Application | - CoA and re-coarctation |
| 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 |
| Report | - High quality. |
| | Suitability Grade |

| 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. |

| | |
|---|---|
| | - 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 |

16. Cheatham et al. (2001b)

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

**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 |

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stent<br>- BIB |
| Application | - CoA and other conditions. |
| 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 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 |
| Report | - High quality. |
| | Suitability Grade |

| 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. |

| | |
|---|---|
| 17. Meadows et al. (2015)<br><br>Contribution<br>S&P x<br>SOA | **Safety & Performance**<br>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. |

18. Taggart et al. (2016)

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

**Safety & Performance**
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.

19. Sasikumar et al. (2020)

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

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

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Retrospective study. | To study the early and late outcomes after stenting of native and recurrent CoA with uncovered and covered stents. | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data |
|---|---|
| Device | - CP Stent (Bare and Covered) – "D1" for subject devices<br>- Other devices, including Advanta V12 stent (covered), Andra XL and XXL stents, Palmaz XL |
| Application | - CoA (native and recurrent) |
| Patient | - Patients with CoA (native and recurrent)<br>- Sampling: n=45 (20 covered stents, 25 non-covered stents)<br>  - Covered stents used were covered 7 CP Stent; 13 Advanta V12 Stent<br>  - Non-covered stents used were 17 CP Stent, 6 Andra XL and XXL stents, and 2 Palmaz X<br>- Mean age: 28±17.5 (range 8 to 65) years. Age per device group was not reported.<br>- Sex: 32 M, 13 F. Sex per device group was not reported. |
| Report | - High quality with deficiencies |
| | Suitability Grade |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Safety | **Yes 1** | No 2 |
| Follow-up | - Covered stent group: 57 months<br>- Non-covered stent group: 35 months | **Yes 1** | No 2 |
| Statistical analysis | - Statistical analysis was done by the Statistical Package for Social Sciences (version 21.0). Quantitative data were presented as mean ± SD or as median and range and qualitative data were presented as frequency (percentages). The categorical parameters were compared by chi-square test, and the continuous variables were compared by Student t test for independent continuous data and Manne Whitney U test for nonparametric data. | **Yes 1** | No 2 |
| Clinical significance | - Not reported specifically for subject devices. | 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 | **Outcomes** | **Covered (n=18)** |
| | Late lumen loss (no or mild) | 2 (Advanta 1, CP 1) |
| | Late lumen loss (moderate) | 12 (Advanta 7, CP 4, Andra 1) |
| | Late lumen loss (severe) | 4 (Advanta 3, CP 1) |
| | Fracture | 1 Advanta |
| Performance data | - Not reported specially for subject devices. | |
| Benefits/claims data | - Not reported | |
| Strengths | - Not reported. | |
| Weaknesses/ Potential bias | - Not reported. | |

**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) | 8 | Disposition (select) |
|---|---|---|

**Relevant SOA Results**

| | |
|---|---|
| SOA data | - Patients in the covered stent group were older and had greater basal pressure gradient. More residual gradient >10 mm Hg after the procedure.<br>- No mortality or aortic wall injury in either group.<br>- Mean number of anti-hypertensive was 1.38 ± 0.74 in the covered goup and 1+0.7 in the uncov<br>- Greater incidence of severe late lumen loss (>30% lumen loss) in the covered stent group on f phenomenon was brand specific (Advanta V12 stent). Single strut fracture which was not c noted in one Advanta V12 stent. The stents have an open cell stent geometry with consequent l<br>- A previous study on Advanta stent implantation in 25 patients did not show any complicat median period of follow-up in that study was only 4.9 months and longer follow-up is neede formation.<br>- Another study described 2 patients with Advanta stent implantation who developed in-foldi follow-up and both the cases were managed by re-stenting. The authors had a similar proxi Advanta stent implantation, which was managed by balloon angioplasty. Though the residual g the balloon angioplasty, the gradient increased to 25mmHg on follow-up and he underwent result. |
| Comments | - Uncovered stents can be safely implanted with minimal risk of aortic wall injury in patients w stent implantation is associated with higher incidence of planned and unplanned re-intervention |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Single center retrospective study. | The aim of this study was to compare surgical and stenting effectiveness in terms of re-coarctation rate at trans-thoracic echocardiography and incidence of late arterial hypertension at 24-hour ambulatory blood pressure monitoring in the long-term follow-up of a large cohort of pediatric and adult patients. | 1 | 2 | **3** | 4 | 5 |

20. Yammine et al. (2021)

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

| Suitability | Relevant Data |
|---|---|
| Device | - All patients treated with aortic stenting performed the same percutaneous procedure with implantation of ballo expandable Cheatham-Platinum (CP) Stent (NuMED, Inc., Hopkinton, NY, USA) at the site of CoA. This corr CoA-PS group.<br>- Surgical group (CoA-S): patch aortoplasty, subclavian flap repair or end-to-end anastomosis<br>- Hybrid group (CoA-H): with multiple aortic procedures with or without balloon angioplasty |
| Application | - CoA (native and recurrent) |
| Patient | - Patients with CoA (native and recurrent)<br>- Population of 212 patients divided into 3 groups depending on CoA treatment type:<br>-Surgical group (CoA-S): included 139 patients (66%) who underwent one-time surgical aortic repair via patch subclavian flap repair or end-to-end anastomosis.<br>-Percutaneous stenting group (CoA-PS): included 18 patients (8%) with CoA repair by means of one-time endo aortic stent positioning (NuMED CP Stent).<br>-Hybrid group (CoA-H): included 55 patients (26%) who underwent multiple aortic procedures (with or without angioplasty) because of reCoA recurrence.<br>- 4 patients (7%) had multiple surgical procedures<br>- 5 patients (9%) had multiple percutaneous procedures<br>- 46 patients (84%) had surgical and percutaneous procedures<br>- Male: 152 (72%)<br>- Median follow-up: 17 years (IQ range 11-24) (previous aortic repair with first stent positioning in 2002)<br>- Mean age at data collection: 19 ± 8.7 years (OQ range 12-26) with 47% patients in the pediatric age (<18 years |
| Report | - High quality report |
| Suitability Grade (Range 4-12) | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Primary end-point was to identify which aortic repair technique (CoA-S versus CoA-PS versus CoA-H) was predictive of re-coarctation during a long-term follow-up. | **Yes 1** | No 2 |

| | | | | |
|---|---|---|---|---|
| | | Secondary end-point was to evaluate the incidence of late arterial hypertension at ABPM after different types of aortic repair.<br>- Re-coarctation rate at trans-thoracic echocardiography and incidence of late arterial hypertension at 24-hour ambulatory blood pressure monitoring. | | |
| Follow-up | - | Long-term: 17 years (IQ range 11-24) | **Yes 1** | No 2 |
| Statistical analysis | - | All continuous variables were assessed for normality with the Shapiro-Wilk test and by examination of their histogram. Variables with normal distribution were expressed as means and standard deviations and tested for differences using ANOVA with post-hoc Bonferroni correction and Student-T test, as appropriate. Non-parametric variables were expressed as median and interquartile range and differences tested using Kruskall-Wallis test and Mann-Whitney test, as appropriate. Categorical variables were expressed as percentages and analyzed by chi-squared test. Survival curves were estimated using the Kaplan-Meier product-limit estimator and compared using the log-rank test. Cox proportional hazard analysis was used to calculate the adjusted hazard ratios for each clinical variable. The final multivariable Cox regression model was selected via a stepwise approach based on minimization of Akaike Information Criterion. Only p values lower than 0.05 were considered statistically significant. All tests were 2-tailed and analyses were performed using computer software packages (SPSS-22.0, IBM, NY, USA). | **Yes 1** | No 2 |
| Clinical significance | - | The magnitude of the treatment effect observed was clinically significant. | **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

- Not reported

Performance data

24-Hour Ambulatory Blood Pressure Monitoring (ABPM):

| | CoA-S group (n = 139) | CoA-PS group (n = 18) | CoA-H group (n = 55) | p S *vs.* PS | p PS *vs.* H | p S *vs.* H |
|---|---|---|---|---|---|---|
| Mean 24hSBP, mmHg (mean ± SD) | 116 ± 10 | 121 ± 8 | 118 ± 10 | ns[b] | ns[b] | ns[b] |
| 24h Pulse Pressure, mmHg (mean ± SD) | 52 ± 11 | 58 ± 8 | 57 ± 11 | 0.085 | ns | 0.020 |
| Day-time SBP, mmHg (mean ± SD) | 120 ± 10 | 125 ± 8 | 121 ± 10 | ns[b] | ns[b] | ns[b] |
| Number of mean daytime SBP values > 95$^{th}$ centile, n (%) | 9 (6) | 4 (22) | 3 (5) | **0.045**[a] | ns[a] | ns[a] |
| Night-time SBP, mmHg (mean ± SD) | 106 ± 10 | 112 ± 11 | 107 ± 10 | 0.075[b] | ns[b] | ns[b] |
| Nocturnal dipping, mmHg (mean ± SD) | 11 ± 5 | 10 ± 7 | 11 ± 4 | ns[b] | ns[b] | ns[b] |

Note: PP: Pulse Pressure. SBP: Systolic Blood Pressure. [a]Chi square, [b]ANOVA with Bonferroni correction.

It was observed 9% of the whole population with elevated 24-hour SBP values, 7.5% with elevated daily SBP values and 9% with elevated nocturnal SBP values. CoA-PS patients had a higher proportion of mean day-time SBP values exceeding the normal value compared to CoA-S patients (22% vs. 6%, respectively; p = 0.045). Also, mean 24-hour PP values were significantly different in all study groups, as shown in the figure as above. No significant difference in nocturnal dipping was recorded.

Trans-Thoracic Echocardiography (TTE)

- Echocardiography showed that the number of patients with significant aortic gradient was higher in CoA-PS (50%) and CoA-H (73%) groups compared to CoA-S (33%) group (p < 0.0001) and median 95% CI gradient was significantly different in all study groups. Moreover, a correlation between aortic gradient and mean 24-hour PP values was found (rho: 0.399, p < 0.0001). Besides, TTE evaluation of left ventricular mass did not show significant differences among the 3 study groups. However, CoA-PS patients demonstrated a tendency to have higher relative wall thickness values compared to CoA-S patients (median 0.35 mm [IQ range 0.29–0.38] vs. 0.30 mm [IQ range 0.27– 0.34], p = 0.065), which is consistent with a concentric left ventricular adaptation to pressure overload.

Freedom from re-coarctation rate: Kaplan-Meier Survival Estimates

- At Kaplan Meier survival analysis, CoA-PS group significantly showed a higher re-coartaction rate (log rank p < 0.0001) compared to CoA-S and CoA-H groups. Finally, at multivariate regression Cox analysis adjusted for gender, age at first CoA repair, body mass index (BMI) > 90th centile and hypertension

| | |
|---|---|
| | (HTN) therapy, stenting treatment was the best independent predictor of echocardiographic evidence of re-coarctation during a long term follow up (H.R. 14.653, 95% CI 6.432–33.377; p ≤ 0.001). |
| Benefits/claims data | - Not reported |
| Strengths | - Long term follow up<br>- Comparative study |
| Weaknesses/ Potential bias | - The main limitation of the study is the heterogeneity of groups, mostly regarding age at first repair, which is higher in patients with aortic stenting. This is not perfectible because percutaneous treatment needs by definition higher age and weight of patients, compared to surgery. Thus, age-matched groups are not feasible. As much as possible, this discrepancy was reduced by applying multivariate Cox regression analysis, and primary end-point proved to be irrespective of age at repair. |

**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) | 7 | Disposition (select) |
|---|---|---|

**Relevant SOA Results**

| | |
|---|---|
| SOA data | CoA:<br>- CoA is the sixth most common cardiovascular malformation, accounting for 5-8% of all congenital heart di infancy and early childhood.<br>- Since the first surgery performed in 1944 by Crawford, surgical repair has been the standard of care for isola evolution of approaches following the excision of the aortic coarcted segment, including subclavian flap re common used technique, the end-to-end anastomosis. Despite excellent surgical results, patients still experience morbidity related to restenosis, aneurysm formation and most of all chronic arterial hypertension, left ventri increased cardiovascular disease. As an alternative to surgery, percutaneous CoA treatment came to light in the in the early 1990s with CoA stenting, aiming at reducing surgical-related morbidity and acute complications. Sin and stent technology have improved the success rate, the safety and thus the popularity of endovascular CoA tr intervention and even for re-stenosis in both pediatric and adults ages. However, long-term complications occu re-coarctation (reCoA) is seen in 4–14% of patients, more frequently after stent placement or balloon angioplast patients with aortic stenting, irrespective of the absence of residual obstruction. In recent decades, aortic stentin surgery for both native aortic coarctation and re-stenosis in children and adults. However, comparative investigated. Despite the large number of studies comparing outcomes of balloon angioplasty versus surgery fo about which technique could be best for the treatment of native CoA and mostly of reCoA.<br>- Surgical repair has been for many years the treatment of choice in neonates, infants and young children. Ho potentially leading to early or mid-term complications and also long-term complications may occur despite suc is known to persist after intervention in 1/3 of patients irrespective of the absence of re-coarctation. Hence, a (balloon angioplasty and/or percutaneous stenting) has recently emerged as a promising technique both for secondary restenosis. However, some concerns must be pointed out regarding percutaneous stenting in the pedia age/weight limitations, major complications (mostly aneurysm formation, aortic dissection and stent migration growing aorta during childhood. |
| Comments | - Although being yet far from the solution of the problem (i.e., which technique is best for isolated CoA rep probably be still the best option for native CoA in the pediatric age. On the other hand, looking at recoarctation tailored to each patient. Children and adolescents before puberty may experience the cons of stent positionin dilation procedures with multiple radiation exposures, stent's failure to adapt to a growing aorta, hypertensive b patients after pubertal development may be akin to adults and stenting procedure may be the best choice for reC |

**Safety & Performance**

**Appraisal**

21. Stassen et al. (2021)

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Single center retrospective study. | The aim of this study was to investigate the impact and safety of covered stent placement for treatment of (re)CoA during a longer follow-up period. | 1 | 2 | **3** | 4 | 5 |

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

| Suitability | Relevant Data |
|---|---|
| Device | - Only 8-zig covered Cheatham Platinum (CCP) stents (NuMED Inc. Hopkinton, NY, USA) wer the study; 8z22 (1.1%), 8z28 (18.0%), 8z34 (25.8%), 8z39 (25.8%), 8z45 (28.1%) and 8z55 (1 |
| Application | - CoA (recurrent) |
| Patient | - Patients with CoA who were treated with 102 covered stents from 2003 to 2017<br>- All patients with a covered stent implantation for a native CoA or reCoA after surgical or trans repair were included. |

| | | |
|---|---|---|
| | - 89 patients with 102 covered stents in 93 procedures<br>- Mean age 23.9±15.8 years (5.1-71.6)<br>- 35 patients <16 years and 54 patients ≥16 years<br>- 60 (67.4%) male and 29 (32.6%) female | |
| Report | - High quality report | |
| Suitability Grade (Range 4-12) | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Short-term pre/post-implant hemodynamics and angiographic data were reported. Changes in blood pressure, the use of antihypertensive drugs and complications were recorded during follow-up. | **Yes 1** | No 2 |
| Follow-up | - Mean follow-up time was 6.6±3.7 years (min max range 0.2-15.7 years). | **Yes 1** | No 2 |
| Statistical analysis | - Continuous variables are presented as mean plus minus standard deviation (range minimum–maximum). In case of an asymmetric distribution of data, results are reported as median (interquartile range (IQR)). Proportions are noted as number and percentage. Comparison of individual parameters before and after stenting was performed using the two-tailed paired t test. Categorical data were compared with a McNemar. A p value of less than 0.05 was considered statistically significant. Statistical analysis was done using the SPSS software version 26 package (SPSS Inc., Chicago, IL USA). | **Yes 1** | No 2 |
| Clinical significance | - The magnitude of the treatment effect observed was clinically significant. | **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 | - Long-term adverse events were found in 4.5% of patients (covered stent fracture (n=3), aneurysm formation (n=2)). |
| Performance data | - The procedural success rate was 100%.<br>- The mean invasive ascending-to-descending aorta systolic gradient under general anaesthesia decreased from 25 ± 16mmHg to 4 ± 7mmHg (p<0.001). After a mean follow-up time of 6.6 ± 3.7 years, there was a persistent improvement of the mean systolic blood pressure gradient between right arm and leg (~7 ± 18 vs 38 ± 24mmHg; p<0.001). A larger proportion of patients required antihypertensive medication (33.7% vs 50.0%, p=0.017) and needed ≥ two drugs (20.2% vs 27.4%, p=0.066) to control blood pressure. |
| Benefits/ claims data | - Covered stent implantation for CoA is highly successful, safe and results in a persistent hemodynamic improvement in the immediate and long-term outcome. Lifelong follow-up with additional antihypertensive drug treatment is mandatory to maintain favourable hemodynamic results after stenting. |
| Strengths | - Patients were followed for a mean period of 6.6±3.7 years (maximum follow-up time 15.7 years). To authors knowledge, this is the largest study with the longest follow-up of the use of covered stents in (re)CoA. |
| Weaknesses/ Potential bias | - Retrospective design<br>- Single centre design<br>- Incomplete follow-up achieved: 14 of the 89 patients had no follow-up data. Among the 75 remaining patients, 47 had 5 years follow-up (so with imaging). |

**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) | 7 | Disposition (select) |
|---|---|---|

**Relevant SOA Results**

| | |
|---|---|
| SOA data | CoA:<br>- CoA is a congenital cardio-vascular malformation, characterised by a restriction of the lumen of the thoracic aorta. It occurs in approximately 4 of 10,000 live births and comprises 5% to 8% of CHD.<br>- Mostly, CoA is detected in childhood and repaired surgically or by endovascular therapy. Occasionally it is diagnosed in adolescence or adulthood by investigations done for systemic hypertension.<br>- The natural history of CoA carries a poor prognosis due to complications such as left ventricular failure, |

| | |
|---|---|
| | intracranial haemorrhage, aortic rupture or dissection, premature coronary artery disease and sudden death.<br>- Smaller and younger infants are typically treated surgically but remain at risk for recurrent obstruction with up to 10% requiring further intervention during adulthood.<br>- In older children and adults, the preferred treatment method depends on the individual anatomy and nature of the lesion, but endovascular therapy with either balloon angioplasty or stent implantation is commonly preferred over surgery. Although balloon angioplasty results in excellent acute hemodynamics, it is associated with a high rate of aortic wall injury and recurrent obstruction. Because of these concerns, stent implantation is usually favoured to avoid overdilation or the elastic recoil of the aorta. Bare stent implantation has become a worthy alternative to surgery and balloon angioplasty and seems to lead to better results and fewer complications. However, although interventions with bare stent implantation seem efficient and generally safe, major complications such as local aneurysm formation, aortic rupture, dissection and even death may occur. To prevent these aortic wall injuries (AWI) during the stent procedure, covered stents are increasingly used and their safety and efficacy for immediate and intermediate follow-up have been demonstrated. However, long-term results remain limited.<br>Covered stents:<br>- Covered stents are increasingly used in severe and complex coarctations of the aorta, mainly to avoid the risk of aortic wall injuries such as local aneurysm formation, dissection and aortic rupture. Nevertheless, the aorta can still rupture with a covered stent, but no unlimited bleeding will occur, unless there was insufficient sealing, the covering was torn or in case of vessel tear with retrograde bleeding from collaterals. |
| Comments | - Not reported |

**Safety & Performance**

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Included in this report are the 5-year follow-up data from patients in these 2 trials and those treated through their Continued Access protocols. Data was prospectively collected during the 2 multi-center studies. | To report the late-term follow-up data and to compare this to earlier follow-up data. For the purpose of this study, follow-up was defined as:<br>- Immediate (1 month),<br>- Early (12 months),<br>- Late (48 or 60 months).<br>To identify possible predictors of late-term outcome post-stent implantation. | 1 | 2 | **3** | 4 | 5 |

22. Holzer et al. (2021)

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

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | - CP Stent (Bare and Covered)<br>- 52% received covered stents and 48% received bare stents.<br>- The minimum stent diameter was 14.4mm (interquartile range (IQR), 12.6-16.0mm) with a minimum stent diameter to the aorta at diaphram ratio of 0.87 (IQR, 0.77-1.0). | **D1** | D2 | D3 |
| Application | - CoA (native or recurrent)<br>- Native coarctation was present in 49%, postsurgical in 24% and postcatheterization in 27%.<br>- The minimum coarctation diameter was 8.0mm (IQR, 5.4-10.5mm), and median aortic diameter at the diaphragm was 16.0mm (IQR, 14.0-19.0mm). | **A1** | A2 | A3 |
| Patient | - All patients enrolled in the COAST or COAST II trials and their Continued Access extensions were included. Patients without late follow-up data were excluded from analysis, except for analyzing the estimated cumulative incidence of stent fractures, aortic wall injury, and reinterventions.<br>- Cohort of 248 patients<br>- COAST: 105 patients enrolled in COAST with 16 Continued Access patients (n=121)<br>- COAST II: 82 participants from COAST II with an additional 45 Continued access patients (n=127).<br>- From the 180 patient cohort, the median age at implant was 17 years (IQR, 13-28 years), the median weight (66.3kg, IQR, 53.8-78.1kg). | **P1** | P2 | P3 |
| Report | - High quality report | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | 4 | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | - Parameters used to assess aortic stent outcomes:<br>- Hemodynamic<br>- Systemic systolic hypertension<br>- Use of antihypertensive medication<br>- Upper limb to lower limb blood pressure difference of ≥20mm Hg | **Yes 1** | No 2 |

| | | | |
|---|---|---|---|
| | - Reinterventions<br>- Stent fractures<br>- Aortic wall injury<br>- Predictor variables used to assess late-term results:<br>- Demographics<br>- Type of coarctation<br>- Preimplantation clinical data<br>- Baseline characterization data<br>- Type of stent<br>- Poststent catherization data<br>- Postcatheterization data | | |
| Follow-up | - Follow-up data was collected at 1, 6, 12, 24, 36, 48 and 60 months and included MRI at 12 and 24 months, and fluoroscopy at 12, 24, 48 and 60 months.<br>- 96% of patients returned for 1-month follow-up, 86% for 12-month follow-up, and 63% for 60-month.<br>- A total of 180 patients (73%) had either 48- or 60-month follow-up data.<br>- Out of the 180 patients with late follow-up, 177 (98%) had also immediate and 180 (100%) early follow-up data available for analysis.<br>- Aortic imaging (either MRI, computed tomography, or angiography) was available for 180/180 (100%) at immediate follow-up, 177/180 (98%) at intermediate follow-up, and 41:180 (23%) at late follow-up. Fluoroscopy was available for 180/180 (100%) at immediate follow-up, 178/180 (99%) at intermediate follow-up, and 136/180 (76%) at late follow-up. | **Yes 1** | No 2 |
| Statistical analysis | - Categorical variables are summarized as frequencies and percentages, and continuous variables as either means and SDs or medians with interquartile range (IQR) as noted. For the entire cohort, the cumulative incidence of stents fractures, aortic wall injury, and reinterventions at immediate, early and late follow-up was estimated using the Kaplan-Meier method. Patients who did not have an outcome event were censored at time. Changes in hemodynamic measures over time were evaluated using tests of trend. For patients with late follow-up, associations between patient and procedure characteristics and 4 binary outcome variables – suboptimal hemodynamic outcome, stent fractur, catheter reintervention, and aortic wall injury – were assessed using Fisher exact test. Characteristics significant at the 0.20 level were considered for inclusion in multivariable logistic regression models. Forward selection was used, and P <0.05 was required for retention in the final model. To assess generalizability, characteristics of patients with and without late follow-up were compared using Fisher exact and Wilcoxon rank sum tests; no significant differences were found. All analytics were performed using SAS software version 9.4. | **Yes 1** | No 2 |
| Clinical significance | - Coarctation stenting is effective at maintaining obstruction relief up to 60 months postimplant with reduction in the number of patients requiring antihypertensive medication. However, an increase in-stent fractures and reinterventions were observed between medium and long-term follow-up. Covered stents appear to confer some protection from the development of stent fractures but do not provide complete protection from late aneurysm formation. | **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 | Aortic Wall Injury:<br>- 13 patients were identified as having aneurysms or pseudo-aneurysms (COAST: 6/121 [5%], COAST II: 7/127 [5.5%].<br>- No dissections were found.<br>- The cumulative incidence was 1.2% by early and 6.3% by late follow-up.<br>- In 3 patients, the aneurysm was proximal to the implanted stent, in one patient the location was not specified, and in the reminder, the aneurysm was within the borders of the implanted stent.<br>- In 4 of 13 patients, aneurysms were identified on MRI or computed tomography before reintervention, while in 9 patients the aneurysms were diagnosed by angiography during catheterization performed for other reasons such as elective stent re-expansion.<br>- 17 patients had covered stents implanted to treat the aneurysm; 2 did not.<br>- By univariate analysis, coarctation minimum diameter <6mmm was the only factor significantly associated with aortic wall injury (12% versus 2%, P=0.007). |

| | | |
|---|---|---|
| | | - There was a borderline relationship between minimum stent to aortic diameter at the diaphragm <0.7 and aortic wall injury (19% versus 5%, M=0.059).<br>- Aneurysms did not just occur in patients with bare metal stents, but equally in patients who had covered stents implanted. As such, the notion that covered stent implantation confers long-term protection from the development of aneurysm, may not be the case. Data are in contrast with Butera et al.[1] who did show a significant difference in the incidence of aneurysm formation when comparing patients bare versus covered stents, albeit in a much smaller cohort. Also, the median follow-up in that study was significantly longer for those with bare stents compared with covered stents (85 versus 35 months). This is important as the current study demonstrates that the majority of aneurysms were not identified until late follow-up.<br>- Most aneurysms developed within the borders of the stent, including covered stents. One possible explanation is that pressure within the aorta distributes flow between the stent and the aortic wall, eventually leading to aneurysm formation. Another possibility is that the expanded polytetrafluoroethylene became damaged during initial implantation.<br>- Current study did not investigate the benefit of a covered stent to reduce the risk of acute aortic wall injury during stent implantation because cases have not been randomly assigned and high-risk patients were excluded for bare stent implantation and received covered stents.<br>Other Adverse Events:<br>- Over the follow-up period, 2 patients had additional adverse events that were captured in the data set. One patient had a self-resolving neurological adverse event (possible transient ischemic attack) 2 weeks after the procedure without any clear relationship to the procedure itself. Another patient developed cardiogenic/sceptic chock 7 months after the procedure. No other serious adverse events were documented in any patients. |
| | Performance data | Hemodynamic Outcome:<br>- The number of patients with suboptimal hemodynamic outcome was 59% at immediate and early follow-up and decreased to 44% at late follow-up (P=0.001; median age, 21.7 years).<br>- When comparing immediate, to early and late follow-up, there was no significant difference in SBP. Hypertension remained fairly constant at about 20% of patients.<br>- Systolic arm-leg blood pressure gradients did not change significantly between immediate, early and late follow-up (median of -1 to -2mm Hg) with 91% to 95% <20mm Hg, 85% to 89% <15mm Hg, and 77% to 80% <10mm Hg.<br>- There was a significant decrease in use of hypertension medication, from 53% at immediate, to 42% at early, and 29% at late follow-up (P<0.001).<br>- By univariate analysis, none of the predictor variables had a significant association with suboptimal hemodynamic outcome at late follow-up.<br>- No association was found between the ratio of minimum stent diameter to aortic diameter at the diaphragm <0.7, and residual arm-leg SBP gradients >10, 15, or 20mm Hg at late follow-up.<br>Stent Fractures:<br>- There were 50 patients with stent fractures.<br>- The cumulative incidence was 0% by immediate, 2.9% by early, and 24.4% by late follow-up.<br>- There were no stent segment embolization and no complete circumferential or longitudinal stent fractures.<br>- The CP stent fractured in multiple locations leading to loss of stent integrity in only 3 patients.<br>- No patient with stent fracture had a reintervention at immediate or early follow-up, but 12 had reinterventions at late follow-up (estimated incidence 6.0%.<br>- By multivariate analysis, independent predictors of stent fracture by late follow-up were age: < 18 years (odds ratio [OR], 3.33 [95%CI, 1.38-8.03], P=0.008), male sex (OR, 3.11 [95% CI, 1.15-8.47], P=0.026), minimum stent diameter at implantation ≥12 mm (OR, 5.13 [95% CI, 1.38-19.1], P=0.015), and use of a bare metal stent (OR, 3.14 [95%, 1.37-7.20], P=0.007).<br>Reinterventions:<br>- 45 patients required catheter-based reinterventions (n=21 balloon angioplasty, n=24 stent implantation).<br>- The cumulative incidence was 1.6% by immediate, 5.1% by early, and 21.3% by late follow-up.<br>- Where data was available, reasons for intervention included staged re-expansion (n=5), aortic wall injury (n=11), restenosis (n=15).<br>- Stent fractures were noted in 12 patients undergoing reintervention, only one with loss of structural integrity.<br>- By multivariate analysis, independent predictors of reinterventions at late follow-up were: age <18 years (OR, 3.76 [95% CI, 1.10-12.9], P=0.035), coarctation minimum diameter <6mm (OR, 3.47 [95% CO, 1.21-9.98], P=0.021), minimum stent diameter at implantation <12 mm (OR, 4.16 [95% CI, 1.37-12.7], P=0.012); and post-implantation systolic arm-leg BP gradient ≥10 mm Hg (OR, 3.25 [95% CI, |

[1] Butera G, Manica JL, Marini D, Piazza L, Chessa M, Filho RI, Sarmento Leite RE, Carminati M. From bare to covered: 15-year single center experience and follow-up in trans-catheter stent implantation for aortic coarctation. Catheter Cardiovasc Interv. 2014 May 1;83(6):953-63. doi: 10.1002/ccd.25404. Epub 2014 Feb 4. PMID: 24459104.

| | |
|---|---|
| | 1.13-9.35], P=0.029).<br>Native Versus Recurrent Coarctation:<br>- Study did not find significant differences of any outcome variable when comparing native, postsurgical, or postcatheterization coarctation. However, subtle differences in the need for reintervention and presence of aortic wall injuries are noted.<br>- Reintervention incidence was 7% for postsurgical coarctation, 22% and 23% for native and postcatheterization.<br>- Aortic wall injuries were not seen in the postsurgical group compared with 6 to 7% in native and postcatheterization coarctation. |
| Benefits/claims data | - At late follow-up, freedom from surgical intervention was 100%, catheter reintervention 78.7%, stent fracture 75.6%, and freedom from aortic wall injury 93.7%.<br>- 44% of patients had suboptimal long-term hemodynamic outcomes.<br>- It has documented that hemodynamic results are generally maintained over the follow-up period. Stent fractures, catheterization reinterventions, and aortic wall injuries, all increase in frequency between medium and long-term follow-up. Overed stents appear to confer some protection from the development of stent fractures, but they do not provide complete protection from late aneurysm formation. |
| Strengths | - The largest study to date with comprehensive follow-up data up to 60 months post-procedure. |
| Weaknesses/ Potential bias | - Small sample size<br>- Did not have the statistical power to evaluate all parameters contributing to long-term morbidity in these patients, such as aortic wall injury.<br>- Once the COAST studies were closed, it was not permissible to contact centers for additional data regarding stent fractures, indications for reintervention and other clinical data elements.<br>- There were inherent differences between COAST and COAST II enrollment indications and the way some of the data was collected.<br>- While this study defined 48 to 60 months follow-up as long-term, this is still a relatively short time period.<br>- This study only analyzed the outcome of stent implantation for coarctation using CP stents. Ot did not compare the outcome of stent implantation to other treatment modalities, as was done in the Congenital Cardiovascular Interventional Study Consortium Report.[2] |

**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) | 7 | Disposition (select) |
|---|---|---|

**Relevant SOA Results**

| | |
|---|---|
| SOA data | CoA:<br>- CoA is repaired during the neonatal period and infancy by surgery. Beyond infancy, percutaneous treatment using either balloon angioplasty or stent implantation are more frequently employed to treat native or recurrent coarctation.<br>- The Cheatham-Platinum (CP) Stent was developed by NuMED (Hopkinton, NY) specifically designed to treat aortic coarctation. It has rounded edges to reduce the incidence of aortic wall injury and can be expanded to 24mm diameter.<br>- Stent implantation, balloon angioplasty, and surgery are all treatment options for coarctation in patients beyond infancy.<br>- Treated coarctation is associated with long-term morbidity irrespective of treatment strategy.<br>COAST Trials:<br>- The FDA pivotal trials COAST (Coarctation of the Aorta Stent Trial; 2007-2016) and COAST II (Covered Cheatham-Platinum Stents for Prevention or Treatment of the Aorta; 2010-2016) demonstrated safety and efficacy of the bare and Covered CP Stents when used to treat aortic coarctation. Short- and medium-term results have been previously reported (Meadows et al. *(48)* and Taggart et al. *(49)*).<br>- The Covered CP Stent is a CP stent covered by a 0.28'' sleeve of 0.005'' thick expanded polytetrafluoroethylene tubing and was available to centers participating in the COAST trial for compassionate and emergency use for aortic wall injury occurring during aortic interventions. |

[2] Forbes TJ, Kim DW, Du W, Turner DR, Holzer R, Amin Z, Hijazi Z, Ghasemi A, Rome JJ, Nykanen D, Zahn E, Cowley C, Hoyer M, Waight D, Gruenstein D, Javois A, Foerster S, Kreutzer J, Sullivan N, Khan A, Owada C, Hagler D, Lim S, Canter J, Zellers T; CCISC Investigators. Comparison of surgical, stent, and balloon angioplasty treatment of native coarctation of the aorta: an observational study by the CCISC (Congenital Cardiovascular Interventional Study Consortium). J Am Coll Cardiol. 2011 Dec 13;58(25):2664-74. doi: 10.1016/j.jacc.2011.08.053. PMID: 22152954.

| | | |
|---|---|---|
| | | - COAST II included patients who received a Covered CP stent as an emergency or compassionate use during the initial COAST trial (legacy arm) and prospectively enrolled patients between 2010 and 2011.<br>- COAST II included higher-risk groups, such as patients with aortic wall injuries and those with nearly atretic descending aorta of 3mm or less diameter. |
| | Comments | Hemodynamic Outcome:<br>- Study corroborates the results from the largest multi-center study of stenting for coarctation from the Congenital Cardiovascular Interventional Study Consortium, which reported 23% systolic hypertension at 12 to 60 months of follow-up, 9% arm-leg blood pressure gradient ≥20 mm Hg, 23% need for antihypertensive medication and the presence of any of these 3 in 37%.[3]<br>Stent Fractures:<br>- Previous studies of the bare metal CP stent documented stent fractures of 2% at 12 months, and 12% at 24 months (Meadows et al. *(48)*). While the design and metallic composition of the CP stent may contribute, stents fractures are not limited to CP stents.[4] Boe et al.[5] reported a 21% fracture rate for Palmaz Genesis XD stents when used for coarctation therapy in children < 20Kg at a mean follow-up of 75 months.<br>- It is unclear whether somatic growth can add additional force and loading conditions to the implanted stent, or whether participation in contact sports might impact the incidence of stent fractures.<br>- Bare metal stents have a s significantly higher fracture rate than covered CP stent. Possible explanations could be that the struts of a bare stent become more solidly embedded into the aortic wall, and that the expanded polytetrafluoroethylene covering more equally distributes the radial force to multiple struts or that it reduces the transmission of aortic pulsability to the struts.<br>Reinterventions:<br>- Previously reported data documented transcatheter reinterventions of about 5% by 24 months follow-up (Meadows et al. *(48)*).<br>- There is no expert consensus defining when a reintervention should be performed.<br>- Reinterventions in this patient population are not unexpected and do not represent a poor outcome.<br>Aortic Wall Injury:<br>- Aneurysms did not just occur in patients with bare metal stents, but equally in patients who had covered stents implanted. As such, the notion that covered stent implantation confers long-term protection from the development of aneurysm, may not be the case. Data are in contrast with Butera et al.[6] who did show a significant difference in the incidence of aneurysm formation when comparing patients bare versus covered stents, albeit in a much smaller cohort. Also, the median follow-up in that study was significantly longer for those with bare stents compared with covered stents (85 versus 35 months). This is important as the current study demonstrates that the majority of aneurysms were not identified until late follow-up.<br>- Most aneurysms developed within the borders of the stent, including covered stents. One possible explanation is that pressure within the aorta distributes flow between the stent and the aortic wall, eventually leading to aneurysm formation. Another possibility is that the expanded polytetrafluoroethylene became damaged during initial implantation.<br>- Current study did not investigate the benefit of a covered stent to reduce the risk of acute aortic wall injury during stent implantation because cases have not been randomly assigned and high-risk patients were excluded for bare stent implantation and received covered stents. |

[3] Holzer R, Qureshi S, Ghasemi A, Vincent J, Sievert H, Gruenstein D, Weber H, Alday L, Peirone A, Zellers T, Cheatham J, Slack M, Rome J. Stenting of aortic coarctation: acute, intermediate, and long-term results of a prospective multi-institutional registry--Congenital Cardiovascular Interventional Study Consortium (CCISC). Catheter Cardiovasc Interv. 2010 Oct 1;76(4):553-63. doi: 10.1002/ccd.22587. PMID: 20882661.

[4] McElhinney DB, Marshall AC, Schievano S. Fracture of cardiovascular stents in patients with congenital heart disease: theoretical and empirical considerations. Circ Cardiovasc Interv. 2013 Oct 1;6(5):575-85. doi: 10.1161/CIRCINTERVENTIONS.113.000148. PMID: 24129934.

[5] Boe BB, Loccoh E, Stockmaster K, Holzer RJ, Cheatham SL, Cheatham JP, Armstrong A, Berman DP. Median and long-term outcomes of stent implantation for coarctation of the aorta in small patients (<20 kg). [Abstract presented at PICS 2019]. *J Struct Heart Dis. 2018;4:140.*

[6] Butera G, Manica JL, Marini D, Piazza L, Chessa M, Filho RI, Sarmento Leite RE, Carminati M. From bare to covered: 15-year single center experience and follow-up in trans-catheter stent implantation for aortic coarctation. Catheter Cardiovasc Interv. 2014 May 1;83(6):953-63. doi: 10.1002/ccd.25404. Epub 2014 Feb 4. PMID: 24459104.

**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 Stents has been carried out and documented in the clinical evaluation report. Based on the results of that evaluation, 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 Stents, including the IFUs, are 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 Stents 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 Stent Device Family has been on the market since 2004 in the EU and 1999 in other markets. Over time variants of the Stent Device Family have been introduced to these markets. Since then, the devices are likely to have been used in a variety of patients and populations. The Stents have been subjected to several clinical investigations where efficacy and safety has been demonstrated.

A PMCF study was not warranted at this time due to the fact that the long-term safety and clinical performance has been established via device use and ample clinical experience. This experience would likely have identified any rare complications or problems that would become apparent only after widespread device use. Continued PMS activities will provide sufficient data to adequately address clinical risks, and detect emerging risks on the basis of evidence. Additional clinical studies were conducted in the U.S. under the COAST and COAST II clinical trials.

A PMCF study was initiated in 2018 for the additional sizes that were added to the product line, and another one in 2021 for the new G-Armor devices, to determine if there were any new complications which were previously not addressed through actual clinical use, or if any new risks are introduced. The target study size was 59 patients, based on a confidence level of 95%. The study was conducted by issuing a form to the treating physician and collecting data. The results of this study are included in the clinical data that is used for the clinical evaluation.

**6. Possible diagnostic or therapeutic alternatives**

Alternative treatments for CoA include surgery or balloon angioplasty.

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

The COA Stent Device Family is intended for use by 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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# NuMED
# Summary of Safety and Clinical Performance
# SSCP – Stents - CoA

Document Revision: 00
Date issued: 21 June 2022

*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 information presented below is intended for patients or lay person. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.*

*The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an Implant card or the Instructions for Use to provide information on the safe use of the device.*

| **1. Device identification and general information** | |
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| Device trade name(s) | CP Stent<br>Mounted CP Stent<br>G-Armor Stent<br>G-Armor Mounted Stent |
| Manufacturer's name and address | NuMED, Inc.<br>2880 Main Street<br>Hopkinton, NY 12965<br>USA |
| Year when first certificate (CE) was issued | 2004 |
| Basic UDI-DI | 08877141600T2 |
| **2. Intended use of the device** | |
| Intended purpose | The Stents are intended for implantation in the native and/or recurrent coarctation of the aorta.<br>An aortic coarctation is a partial blockage or narrowing in the aorta, the body's main blood vessel distributing blood to all parts of the body. This blockage of the aorta makes the heart work harder to pump blood to your body and can weaken the heart muscle. Furthermore, this blockage can cause severe upper body hypertension (high blood pressure), increasing the risk of stroke. This blockage is present from birth. |
| Indications and intended patient groups | The device is used to treat any patients that have an aortic coarctation as long as none of the below listed contraindications and/or limitations are applicable. |
| Contraindications and/or limitations | The following patients should NOT receive the Stent:<br>• Patients who are too small to allow the stent to pass through their arteries without damaging the artery;<br>• Patients with a stiff aorta that does not get larger with balloon dilation.<br>• Patients with blocked leg arteries making it difficult or unsafe to move the catheter and stent to the narrowed aorta;<br>• Patients with any signs of infection;<br>• Patients with active infection in the heart or blood vessels (endocarditis);<br>• Patients with a known allergy to aspirin, other antiplatelet agents, or heparin;<br>• Pregnancy. |

| 3. Device description | |
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| Description of the device | The Stents are balloon expandable and intended to permanently stay in your body. The Stents are used for coarctation of the aorta.<br>The Stents are composed of heat-treated metal (90% platinum and 10% iridium) wire that is arranged in laser welded rows with a "zig" pattern. The number of rows determines the unexpanded length of the stent.<br>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 ½ 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 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. 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. |
| Medicinal Substances | The Stents do not contain any medicinal substances. |
| Mode of Action | The Stents are implanted using a thin hollow tube (catheter) with a balloon on the end. Your physician will place the stent on the balloon at the start of your procedure. The catheter with the stent is then placed through the skin, typically into the artery in your upper leg. The balloon and stent are moved to the appropriate position at the narrowed part of your aorta. Once in place, the balloons are inflated to expand the stent. The catheter is then removed from the body and the stent stays in place. |
| Description of Accessories | All Stents are packaged and shipped to the physician with hemostasis valve tools. These tools are hollow tubes that are placed in the valve of the introducer to help the Stent move through that valve without any issues. The valve of the introducer is very tight to prevent blood loss during the procedure, so the tools help the Stent move through the valve without causing damage to the stent or moving the stent on the catheter. |

| 4. Risks and Warning | |
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| *Contact your healthcare professional if you believe that you are experiencing side effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.* | |
| How potential risks have been controlled or managed | The Stent Device Family has been developed in accordance with documented processes to ensure that it is designed, manufactured, packaged, and labelled in accordance with the current state of the art and meets all requirements of the appropriate regulations. Design verification activities were performed and include pre-clinical testing and clinical investigations. A clinical literature review has also been performed on the Stent Device Family. All risks identified during these activities were mitigated as far as possible and are considered acceptable in regards to the clinical benefit of the device. Continued review of all Post Market Surveillance and Post Market Clinical Follow-up Data is performed to identify any additional risks that may be identified after the device was placed on the market. |
| Remaining risks and undesirable effects | Cardiac catheterization and stent insertion carry certain risks. Potential complications & adverse effects associated with device use and indication include:<br>• Femoral Artery Injury, Thrombosis or Psuedoaneurysm – injury or weakening of femoral artery, or development of a blood clot in femoral artery<br>• Stent Migration – movement of the stent away from original implant site<br>• Stent Stenosis – growth of tissue within the stent, leading to return of the blockage<br>• Stent Fracture – break in the frame of the stent<br>• Aortic Aneurysm/Pseudoaneurysm – weakening or injury of the aorta wall |

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| | • Aortic Rupture/Tear – perforation or tearing of the aorta, causing internal bleeding<br>• Stent Malposition – poor position of stent, requiring a 2nd stent<br>• Hematoma - bruising at the site where the device is introduced into the body<br>• Sepsis/infection - infection<br>• Thrombosis/Thromboembolism - formation or presence of a blood clot<br>• AV fistula formation - abnormal passageway between an artery and a vein<br>• Transitory arrhythmia - irregular heartbeat<br>• Endocarditis - infection within the stent<br>• Bleeding - at the site of where the device is introduced into the body<br>• Cell necrosis at the site of implant - death of cells at the implant site<br>• Cerebrovascular Incident - stroke<br>• Death |
| Warning and Precautions | The majority of warnings and precautions listed for the Stents pertain to the placement and use of the device in the cath. lab by the physician.<br><br>MRI Conditional information is applicable to the Stents after they are implanted. This information should be used by any MRI technician that is performing an MRI procedure on any patient with a NuMED Stent implanted. All patients will be provided with an Implant Card after their procedure. This Implant Card will give the location of where to find the most up to date MRI parameters to be used for patients that have a NuMED Stent implanted. |
| Summary of any field safety corrective actions (FSCA including FSN) if applicable | Since commercialization, there has been one recall on the Bare CP Stent in 2003 (#Z-0983-03, completed in 2004) concerning the lack of PMA or 510(k) for the Bare CP Stent. The recall was conducted in the U.S. only.<br><br>There have not been any Field Safety Corrective Actions or Field Safety Notices on any other version of the Stents. |

| **5. Summary of clinical evaluation and post-market clinical follow-up** | |
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| Clinical background of the device | The NuMED Stent Device Family has been sold globally since 1999.<br><br>The following data is based on the NuMED CP Stent®. It was tested and found to be safe and effective to widen the narrow part of the aorta related to coarctation of the aorta. A study was conducted with 105 patients weighing more than 77 lbs at the time of implant. Most patients (98%) were treated with one CP Stent®.<br><br>On average arm systolic blood pressure was 27 mmHg higher than the leg pressure before the procedure. A reduction of a gradient to 15mmHg or less following the procedure suggests that the blockage is reduced effectively. By one month after bare metal stent placement the average leg pressure was 1 mmHg higher than the arm pressure. Two years after implant, 91% of patients had arm blood pressures less than 15 mmHg above their leg blood pressure which suggests that most of the treated aortas did not re-narrow. An overview of complications and additional treatments provided after the stenting procedure is shown below:<br><br>• Serious complications related to the CP Stent® or implant procedure, such as: injury to the aortic wall and leg artery-vein fistula (an abnormal passageway between the artery and vein), were identified in 1 out of 20 (5%) patients within the first month of implant.<br>• No patients needed surgery to repair the aorta, remove the stent or repair the arterial access site.<br>• 1 out of 20 (5%) patients developed small aneurysms (weakened areas of the aorta) in the area of stent placement in the years following stent therapy, making CT or MRI imaging an |

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| | important part of follow up care. However, none of the patients who developed aneurysms demonstrated symptoms or required surgery. All were successfully treated with covered stent placement.<br>• Approximately 3 out of 20 (15%) patients required repeat cardiac catheterization for a second dilation of the stent, mostly to keep up with the size of the patient as he/she grew and for some to repair aortic wall injuries as noted above. |
| The clinical evidence for the CE marking | CE marking is based on data from three clinical studies, a review of published literature, and a review of post market surveillance data. Additional pre-clinical testing was performed as part of the development and design of the device. In vitro (on the bench) testing was performed on the devices as part of the Design History File. Biocompatibility testing was also performed on the materials used to manufacture this device to determine if it met the requirements for an implant in the human body. The device passed all tests. |
| Safety | The clinical data and pre-clinical study data demonstrated that the device performed as intended in the clinical setting; the device does not pose unacceptable safety concerns in the clinical setting; and any risks associated with clinical use of the device are acceptable when weighed against the benefits to the patient. |

**6. Possible diagnostic or therapeutic alternatives**

*When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.*

**Coarctation of the Aorta**

Your cardiologist believes that relief of the blockage is important for your health and safety. There are three ways to relieve the blockage: by surgery, by stent implantation without surgery, or by balloon angioplasty.

**Surgical Therapy**

Surgical treatment of the blockage is usually performed through an incision on the side of the chest, approaching the aorta by spreading the ribs. The narrowed portion of the aorta is removed and then the aorta is sewn back together. For more complicated coarctation, surgery might be performed from the front of the chest, opening the breast bone and using heart lung bypass. For some patients a benefit of a surgical approach is that the repair can be performed without the use of man-made materials. However, for other (especially adult) patients a man-made tube graft or patch may be needed. Please consult with your surgeon regarding his or her approach. For younger patients, surgery results in a lower need for a second procedure to keep up with growth when compared to balloon or stent therapy.

Risks of surgery include: pain from the surgical incision, prolonged fluid drainage from the chest after surgery, chest or wound infection, longer recovery time compared to stent therapy, prolonged postoperative rib discomfort and increased risk of very high blood pressure occurring after immediately after surgery, requiring intravenous therapy in an ICU, compared to stent repair. There is a low risk, probably less than 5%, of developing an aneurysm (weakened areas of the aorta) in the area of surgery in the years following stent therapy, making CT or MRI imaging an important part of follow up care.

**Stent Therapy (without surgery)**

A stent is an expandable metal tube that is implanted into your aorta to keep it open. Surgery is not required for this procedure. The stent is implanted using a thin hollow tube (catheter) with a balloon on the end. The catheter with stent is inserted through the artery in the upper leg. The balloon and stent are then moved to the appropriate position to the narrowed part of your aorta. Once in place, the balloons are inflated to expand the stent against the aortic wall. The catheter is then removed from the body and the stent remains in place.

**Balloon Angioplasty**

A specially designed catheter with a tiny balloon is carefully guided through the artery to the blockage, then inflated to widen the opening and increase blood flow to the heart.

| 7. Suggested profile and training for users |
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| The Stent Device Family is intended for use by cardiology and surgical professionals undertaking stent implantation. |