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Stenting of the Arterial Duct in Newborns with Duct-dependent Pulmonary Circulation

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ABSTRACT

OBJECTIVE. To evaluate the feasibility and the results of stenting of the arterial duct in newborns with duct-dependent pulmonary circulation using low-profile and high-flexibility pre-mounted coronary stents.

DESIGN. Prospective interventional and clinical follow-up study.

SETTING. Tertiary referral centre.

PATIENT POPULATION. Between April 2003 and December 2006, 26 neonates [age 15.2(19.9) days, weight 3.3(0.8) kgs] underwent attempts at stenting of the arterial duct.

MAIN OUTCOME MEASURES. Procedural success and complication rates. Early and mid-term follow-up results.

RESULTS. The procedure was successfully completed in 24/26 (92.3%) of cases. Minor complications occurred in 2/26 (7.7%) of cases. No mortality occurred. After stenting, the ductal diameter increased from 1.2(1.0) to 3.1(0.4) mm ($p<0.0001$) and the percutaneous O_2 saturation increased from 70(14) to 86(10)% ($p<0.00001$), respectively. Over a mid-term follow-up, 2/24 patients (8.3%) needed a systemic-to-pulmonary artery shunt because of inadequate ductal flow and 4/24 patients (16.7%) underwent stent re-dilatation after 6.0(4.4) months, but prior to corrective surgery. Cardiac catheterization prior to corrective surgery in 9 patients showed an increase of the Nakata index from 112(49) to 226(108) mm/mm2 ($p<0.001$), without any left-to-right unbalance of the pulmonary artery size. In the subset of 11 patients who improved without needing an additional source of pulmonary blood supply, the stented arterial duct closed uneventfully in 45.5% of cases after 4.0(2.2) months.

CONCLUSIONS. Stenting of the arterial duct is a feasible, safe and effective palliation in newborns with duct-dependent pulmonary circulation, supporting the spontaneous improvement process or promoting significant and balanced pulmonary artery growth for subsequent corrective surgery.

INTRODUCTION

Despite current trends toward early primary repair, surgical systemic-to-pulmonary artery shunt is still an invaluable palliative option in some high-risk patients with cyanotic congenital heart defects. However, shunt-related complications such as pleural effusion, chylothorax, phrenic and vagal nerve palsy, distortion and differential growth of the pulmonary arteries are well-known and potentially increase morbidity and mortality of the subsequent corrective surgery. [1][2][3][4] Since the early 1990s, stenting of the arterial duct has been proposed as an alternative to achieving stable ductal patency, [5][6] allowing the stent to conform to the size and angulations of the pulmonary arteries, thereby avoiding any unbalance of lung perfusion and distortion of the pulmonary arteries. After the initial discouraging experience, technical advances in the design of the stents and delivery systems allowed us to evaluate its role as a reliable alternative to surgery for palliation of duct-dependent cardiac defects.

The aims of our study are to evaluate the feasibility and report the results of primary stenting of arterial duct in newborns with duct-dependent pulmonary circulation using low-profile, high-flexibility pre-mounted coronary stents in a single tertiary referral centre.

METHODS

Patient population. Between April 2003 and December 2006, 26 neonates with congenital heart defects producing duct-dependent pulmonary circulation underwent stent implantation of the arterial duct on an intention-to-treat basis. Their clinical data are summarized in the **Tab.1**. Twenty-three patients were neonates and 3 were small, low-weight infants previously submitted to non-cardiac surgical interventions. Parental informed consent to the procedure and agreement on the management plan with the cardiac surgeon were always obtained. In the same observation period, 61 patients [age 48(60) days, range 6-270; weight 3.9(1.5) kg, range 2.2-8.4] underwent primary systemic-to-pulmonary artery shunt. At the beginning of our experience, arterial duct stenting was performed only in newborns at high surgical risk. However, due to the excellent results and low procedural risks, this approach was then progressively extended to patients with an anticipated need for a short-term support to the pulmonary circulation and finally to newborns at low risk for surgical palliation (see below).

Inclusion criteria. The criteria for inclusion into the study included (a) a high-risk profile for conventional surgery in 11 patients, (b) an anticipated need for short-term support to the pulmonary circulation in 12 patients and (c) an elective alternative to systemic-to-pulmonary artery shunt in low-risk neonates in whom early surgical repair had been planned in 3 patients.
a) The defects were considered to be high-risk if the patient was of low-weight and/or in a critical clinical condition in 6 patients or if there was an unusual anatomic arrangement of the pulmonary arteries in 5 patients.
b) A short-term support to pulmonary circulation was anticipated in those patients with pulmonary atresia and intact ventricular septum after a successful radio-frequency pulmonary valve perforation or in critically cyanosed neonates due to Ebstein's anomaly and functional pulmonary atresia. In all neonates with pulmonary atresia and intact ventricular septum, elective stenting of the arterial duct was performed approximately 2 weeks after catheter valvotomy because of failure to wean from prostaglandin infusion. In neonates with Ebstein's anomaly, stenting of the arterial duct was performed in critically cyanotic, mechanically-ventilated neonates who were unresponsive to pulmonary vasodilator therapy with prostaglandin infusion, inhaled nitric oxide and high-frequency ventilation.
c) late in the series, stenting of the arterial duct was suggested as alternative to systemic-to-pulmonary artery shunt in 3 cases of complex congenital disease with uni-ventricular physiology as a bridge toward an early cavo-pulmonary anastomosis. In these patients, a small arterial duct

was present beyond the neonatal period but was inadequate to warrant the systemic oxygen saturation.

Interventional procedure. Cardiac catheterization was performed under general anaesthesia in all patients. Prostaglandin infusion was stopped 6 hours before the procedure, in order to achieve a stable constriction of the arterial duct to grip the stent after its deployment. In 2 cases, the arterial duct was completely occluded at the time of the procedure and was re-canalized by local prostaglandin infusion and manipulation of a chronic occlusion guide-wire before the stent implantation. Vascular access to image the arterial duct was obtained from the femoral artery. Based on the origin and shape of the arterial duct, stent implantation was attempted from the same route in 24 patients, the axillary artery in 1 patient and via a right carotid arteriotomy in one low-weight neonate with atypical origin of the arterial duct from the underside of the aortic arch. [7] The morphology of the arterial duct, its size and length were assessed in multiple angiographic projections and the measurements were made using the catheter as reference.

After imaging of the arterial duct, a 0.014" coronary guide-wire (Crosswire NT, Terumo Corporation, Tokyo, Japan; Balance Middleweight, Guidant Corporation, Santa Clara, CA, USA) was passed and anchored in a distal lower lobe pulmonary artery branch. Positioning and deployment of the stent were angiographically-guided by repeat injections through the introducer sheath (transradial 11 cm-long or 23 cm-long 4Fr Avanti+ Introducer, Cordis Europe, Roden, The Netherlands), without the use of guiding-catheter. Open-cell, high-flexibility cobalt-chromium stents (Vision, Guidant Corporation, Santa Clara, CA, USA; Driver, Medtronic Inc., Minneapolis, MN, USA) were used. The length of the stent was chosen to cover the entire length of the arterial duct, while the diameter of the stent was chosen individually, based on the size of the patient and the expected time for which palliation was needed. However, the stent diameter was always about 75% of the proposed surgical shunt size in the belief that it acted more as a central shunt than a Blalock-Taussig shunt. After deployment of the stent, repeat angiography was performed in multiple views to exclude any incomplete covering of the duct, to evaluate any potential stent-related pulmonary artery stenosis and to calculate the diameter ratio of the left pulmonary artery to the right pulmonary artery and the Nakata index.

Antibiotic prophylaxis (cefotaxime 50 mg/kg//day) was given at vessel entry and continued for 48 hours. Heparin (100 units/kg) was given at vessel entry and continued for 24 hours at the dose of 100 UI/kg/day, followed by aspirin treatment at 3-5 mg/kg/day for 6 months. Post-procedure clinical and echocardiographic assessments were scheduled monthly and cardiac catheterization was performed prior to corrective surgery.

Statistical analysis. Results are expressed as mean ± standard deviation. Statistical analysis was performed using the paired and unpaired Student t-test. Significance was defined as a p value <0.05.

RESULTS

Procedural outcome. The stenting procedure was successfully completed in all except 2 patients (92.3%). The two failures were one patient with tetralogy of Fallot and one patient with Ebstein's anomaly, in both of whom the extreme tortuosity of the arterial duct precluded stent implantation (**Fig. 1**). A total of twenty-eight coronary stents were implanted in the remaining 24 patients. The procedural and fluoroscopy times were 133(46) min (range 60-240, median 120) and 24(24) min (range 6-70, median 14), both of these significantly longer in the cases with stenting of a tortuous arterial duct compared with other morphologies [200(69) vs 120(29) min and 56(24) vs 12(7) min, $p <0.0001$ for both comparisons]. The total X-ray dose exposure (fluoroscopic plus

angiographic) was 42(31) Gray/cm2 (range 9-119). There was no mortality. The rate of morbidity was 2/24 patients (8.3%). One patient developed local infection at the puncture site and one patient had transient femoral artery pulse loss.

Stent implantation increased the diameter of the arterial duct from 1.2(1.0)(range 0-3.5) to 3.1(0.4) mm (range 2.2-3.5)($p<0.0001$) and the percutaneous O2 saturation increased from 70(14)(range 20-80) to 86(10)% (range 50-94)($p<0.00001$). After the procedure, 1 patient was given anti-congestive therapy for two weeks, due to a generous ductal flow, whilst the remaining patients showed an adequate and balanced pulmonary blood flow.
The shape of the arterial duct significantly affected the success rate of the stenting procedure, with 60% success rate in those with tortuous arterial ducts (**Fig. 2**) compared with 100% in those with conical or tubular ducts (**Fig. 3**).

Follow-up. After the procedure, no patient needed recovery at the intensive care unit and one low-weight patient needed anti-congestive therapy for a few weeks, due to a generous ductal flow. During a mid-term follow-up of 15(9) months (range 3-27, median 12), 2 patients (8.3%) underwent a surgical systemic-to-pulmonary artery shunt due to sub-acute, late-onset stent thrombosis in 1 patient and inadequate ductal flow in 1 patient after 2 weeks from stent implantation of a very tortuous arterial duct. Four patients (16.7%) underwent successful redilatation of the stent or implantation of a further stent inside the original stent after 6.0(4.4) months (range 2-11). To date, 7 patients have undergone successful corrective surgery after 9.0(5.0) months (range 2-14) and 5 patients are waiting for surgical repair. At surgery, no significant technical problems were encountered in removing the stents as these were easily removed from the pulmonary artery opening using gentle traction. Cardiac catheterization has been performed in 9 patients prior to surgical correction, showing an increase of the Nakata index from 112(49) to 226(108) mm/mm2 ($p<0.001$), without any significant change of the diameter ratio of the left pulmonary artery to the right pulmonary artery [from 1.01(0.46) to 1.19(1.07), p= NS]. Eleven patients have been followed-up without the need for any further corrective surgery due to spontaneous improvement, showing a percutaneous O2 saturation over 80% at the last assessment (**Fig. 4**). In this subset of patients, the arterial duct was small in 6 patients and closed uneventfully in 5 patients (45.5%), of whom 3 had pulmonary atresia with intact ventricular septum and 2 had Ebstein's anomaly during a mean follow-up of 4.1(2.2) months (range 3-7).

DISCUSSION

Post-natal patency of the arterial duct in congenital heart disease with duct-dependent pulmonary circulation is life-saving. [1][2][3] Maintaining the patency by stent implantation has been proposed as an effective alternative to a surgical systemic-to-pulmonary artery shunt in neonates who are unsuitable for primary repair or in whom there is anticipated spontaneous improvement of oxygen saturation as the pulmonary vascular resistance decreases. However, due to unsatisfactory technology in the past, the first neonatal series reported a need of vessel entry by cut-down of 24% resulting in a high rate of vessel damage, despite 100% success rate of stent implantation in the duct. [9] Further series enrolled only a small percentage of neonates [10] or reported multi-centre experiences selecting only arterial ducts with favourable anatomy. [11] Ours is one of the largest series enrolling neonates and small infants treated by a single operator in a tertiary referral centre. As in the only other intention-to-treat series published so far, [12] the stenting procedure was successful in a high percentage of cases without significant technical problems, morbidity or mortality. Ductal tortuosity was the major cause of procedural failure in other series, [10] although in our population most of the tortuous arterial ducts underwent successful stent implantation. The stenting procedure was abandoned whenever multiple, sharp bends in different planes were imaged, in the belief that multiple bends in a single plane could still be reasonable straightened once the stiffer part of a coronary guide-wire was passed across the vessel, but this would not be

the case in different planes. After successful deployment, no early stent occlusion occurred and the overall rate of sub-acute stent thrombosis was very low despite the fact that the stent diameter had been chosen smaller than the proposed surgical shunt to avoid any pulmonary overflow and/or competition with other sources of blood flow. However, the stented arterial duct tended to be less durable than a conventional surgical shunt due to ductal tissue prolapse through the stent struts and intra-stent endotelial hyperplasia, as already reported. [6] Indeed, also in our series, the mid-term fate of the stented duct was that of spontaneous, slow and progressive closure within a few months, although stent re-dilatation was usually performed successfully whenever the clinical conditions warranted this. Newer technologies, such as drug-eluting or more flexible, covered stents might broaden the application of this therapeutic strategy and improve long-term patency of the stented duct. However, the short durability of the stented duct should not be a significant issue even in certain surgical candidates in this era of early corrective surgery. Thus, this option should be used in patients in whom the stented duct may be needed for a short period of time for palliation allowing physiologic improvement or proceeding to an early corrective surgery. It may be the ideal therapeutic option in pulmonary atresia with intact ventricular septum submitted to right ventricular decompression or in severe Ebstein's malformation, in which only a short-term pulmonary blood flow support is often necessary to achieve a biventricular physiology. Indeed, in our series, almost ½ of such patients underwent uneventful spontaneous ductal closure within a few months from stent implantation. Stenting of the duct could be advisable in complex cardiac malformations with uni-ventricular physiology destined to the Fontan operation, in which the stented duct could act just as a bridge toward an early cavo-pulmonary anastomosis procedure, at the same time supporting an adequate and balanced pulmonary artery growth. Indeed, despite the use of smaller stent diameters with respect to other studies, [9][10][11][12] the stented duct promoted significant pulmonary artery growth over a mid-term follow-up. It was possibly due to an optimal angle between the ductus and the main pulmonary artery branches that did not show neither distortion nor discrepant growth at control angiographic examination, as already reported in other series. [12]

In conclusion, arterial duct stenting using low-profile, high-flexibility, pre-mounted coronary stents is a technically feasible palliation in a high percentage of neonates and small infants. It is a safe and effective option both in surgically high-risk neonates and in low-risk patients whenever a short-term pulmonary blood flow support is anticipated. Indeed, the stented arterial duct either supports the spontaneous physiologic improvement process or promotes a significant and balanced growth of the pulmonary artery in view of an early corrective surgery. However, this procedure is still not a standard approach to patients with duct-dependent pulmonary circulation and its use should be restricted to single centres with special expertise and experience.

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Tab. 1. Demographic data of the patients submitted to the attempt of stenting of the arterial duct.

Age (days)	15.2(19.9)(range 1-120, median 9)	
Weight (kgs)	3.3(0.8)(range 1.6-4.5, median 3.1)	
Diagnosis		
	Pulmonary atresia with intact ventricular septum	(n= 11)
	Tetralogy of Fallot*	(n= 8)
	Ebstein's anomaly	(n= 4)
	Complex CHD with pulmonary atresia	(n= 3)
PDA	diameter (mm)	1.2(1.0)(range 0-3.5)
	length (mm)	12.4(2.8)(range 8-15)
	shape:	conical 37.5%
		tubular 43.5%
		tortuous 19.0%
Stent	diameter (mm)	3.1(0.3)(range 2.2-3.5)
	length (mm)	12.7(3.1)(range 8-18)

* in 3 cases with discontinuous pulmonary arteries due to the origin of the left pulmonary artery from the arterial duct and in 1 case with restrictive ventricular septal defect.

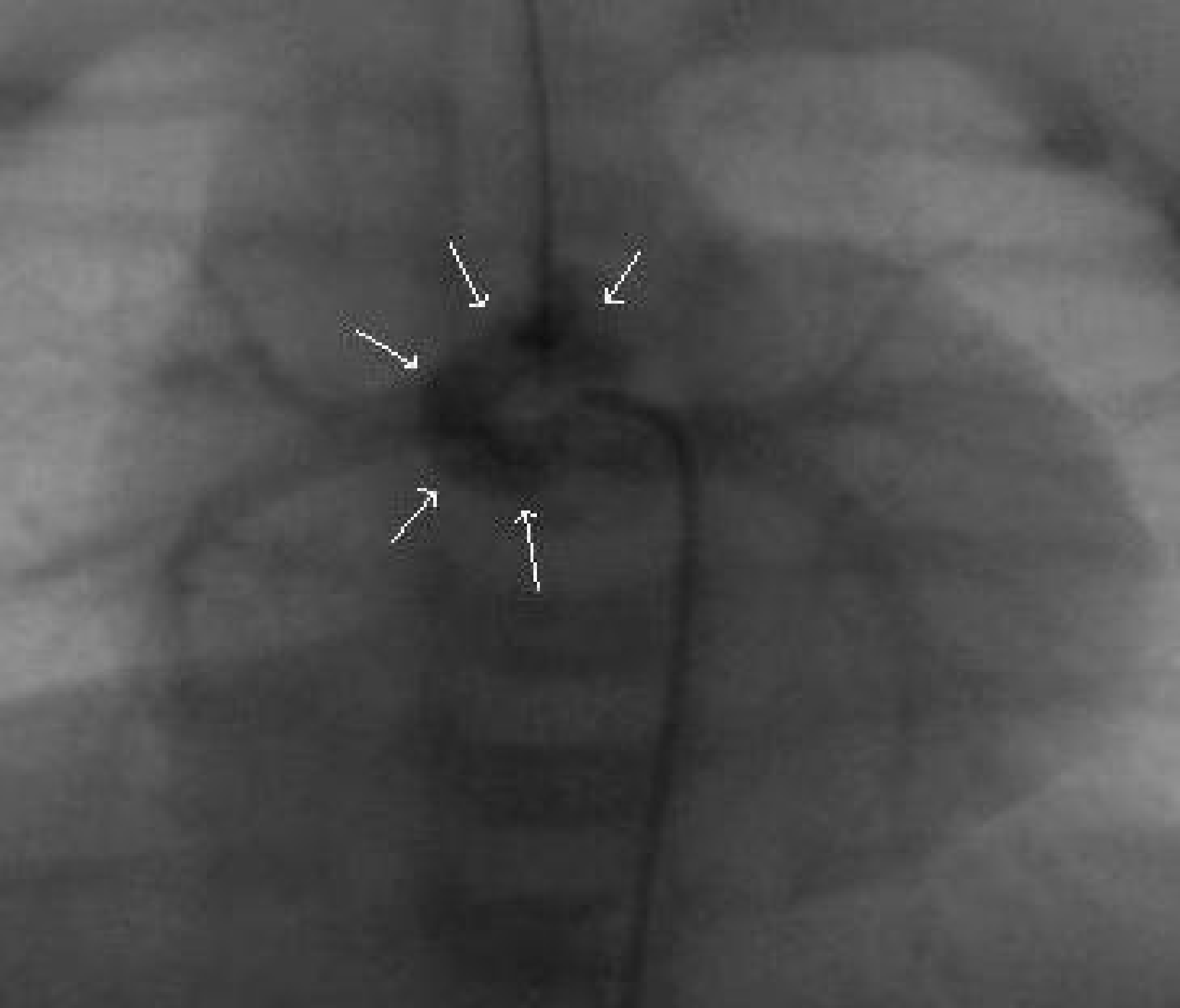
FIGURE LEGEND

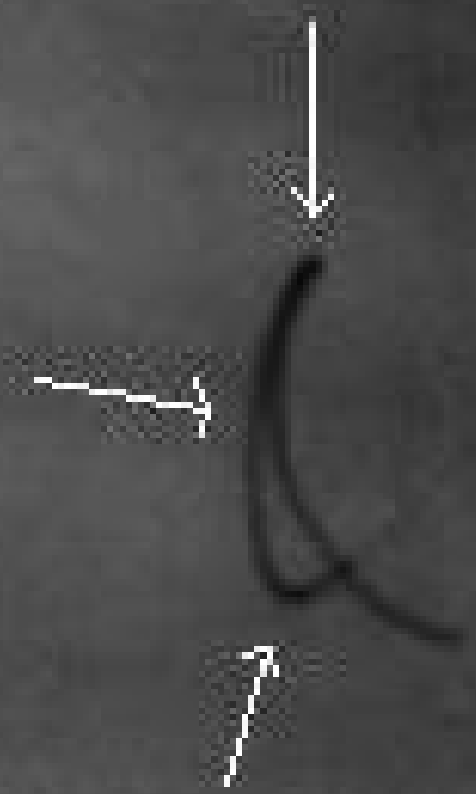
Fig. 1. Aortogram showing extreme ductal tortuosity deemed unsuitable for stent implantation in a neonate with severe Ebstein's anomaly. As imaged in postero-anterior (**A**) and lateral (**B**) views, the arterial duct showed a first sharp bend on the sagittal plane before forming a 360° loop on the frontal plane.
Abbreviations: arrows, coronary guide-wire; **Ao**, aorta; **PA**, pulmonary artery; **PDA**, patent ductus arteriosus

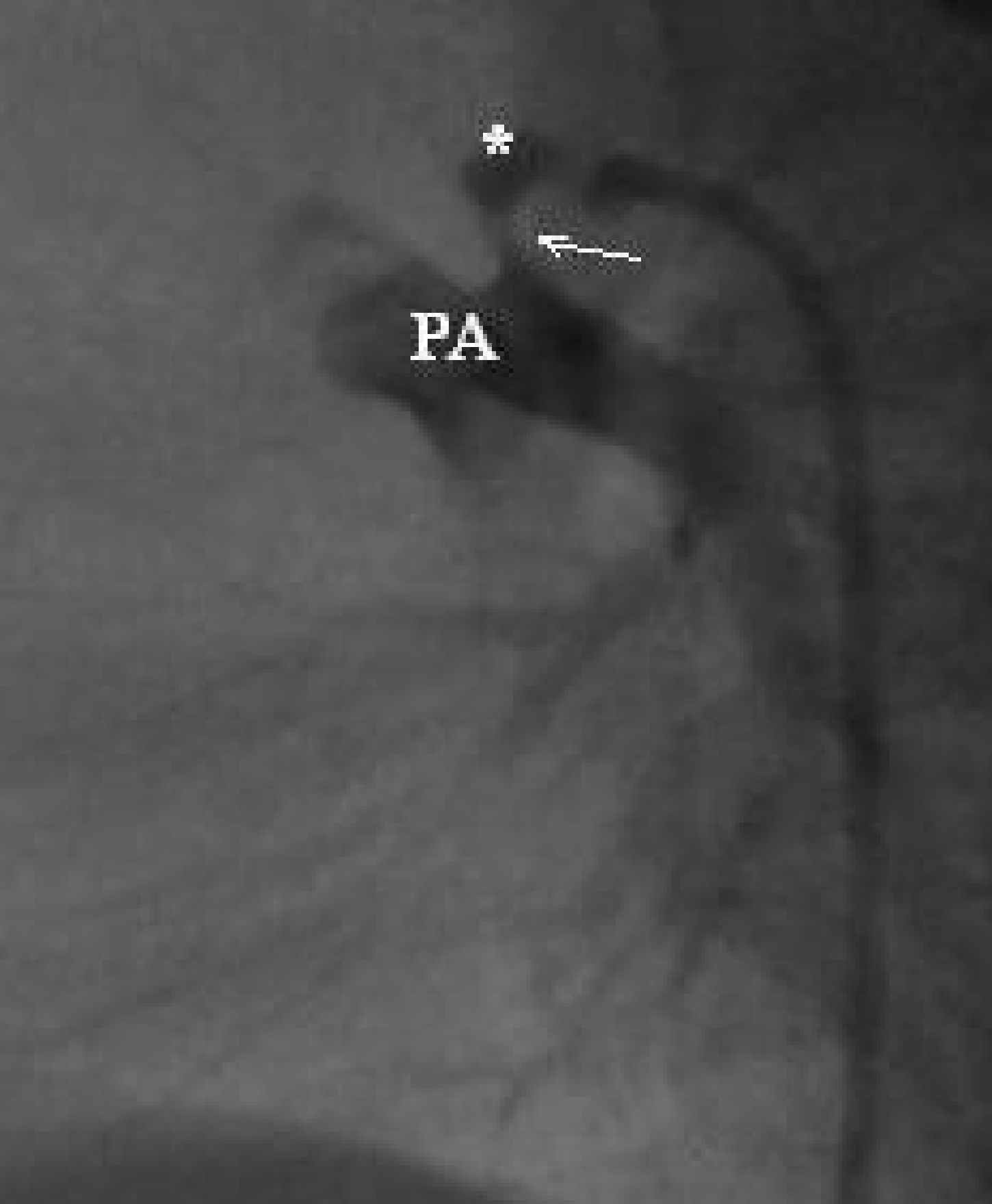
Fig. 2. Arterial duct stenting in a low-weight neonate with criss-cross heart, ventricular septal defect, double outlet right ventricle and pulmonary valve atresia. **A**, aortogram in lateral view imaging a tortuous arterial duct (*****), critically stenosed at its pulmonary end (**arrow**). **B**, aortogram in right oblique view showing the ductal stenosis completely relieved by the stent implantation.
Abbreviations: Ao, aorta; **PA**, pulmonary artery; *****, patent ductus arteriosus

Fig. 3. Hybrid palliative approach in a low-weight neonate with critical tetralogy of Fallot, right aortic arch with mirror-image of the epi-aortic vessels and discontinuous pulmonary arteries. The right, hypoplastic pulmonary artery (*****) was retrogradely fed by a huge aorto-pulmonary collateral (**arrow**)(**A**), while the left pulmonary artery was in continuity with a long, tubular arterial duct (**arrows**)(**B**). The stenting procedure (**C**) stabilized the ductus arteriosus thereby recruiting the left PA as well as made possible to perform via right thoracotomy a modified right Blalock-Taussig shunt after unifocalization of the major aorto-pulmonary collateral.
Abbreviations: Ao, aorta; **PA**, left pulmonary artery

Fig. 4. Mid-term course of percutaneous O2 saturation after arterial duct stenting.



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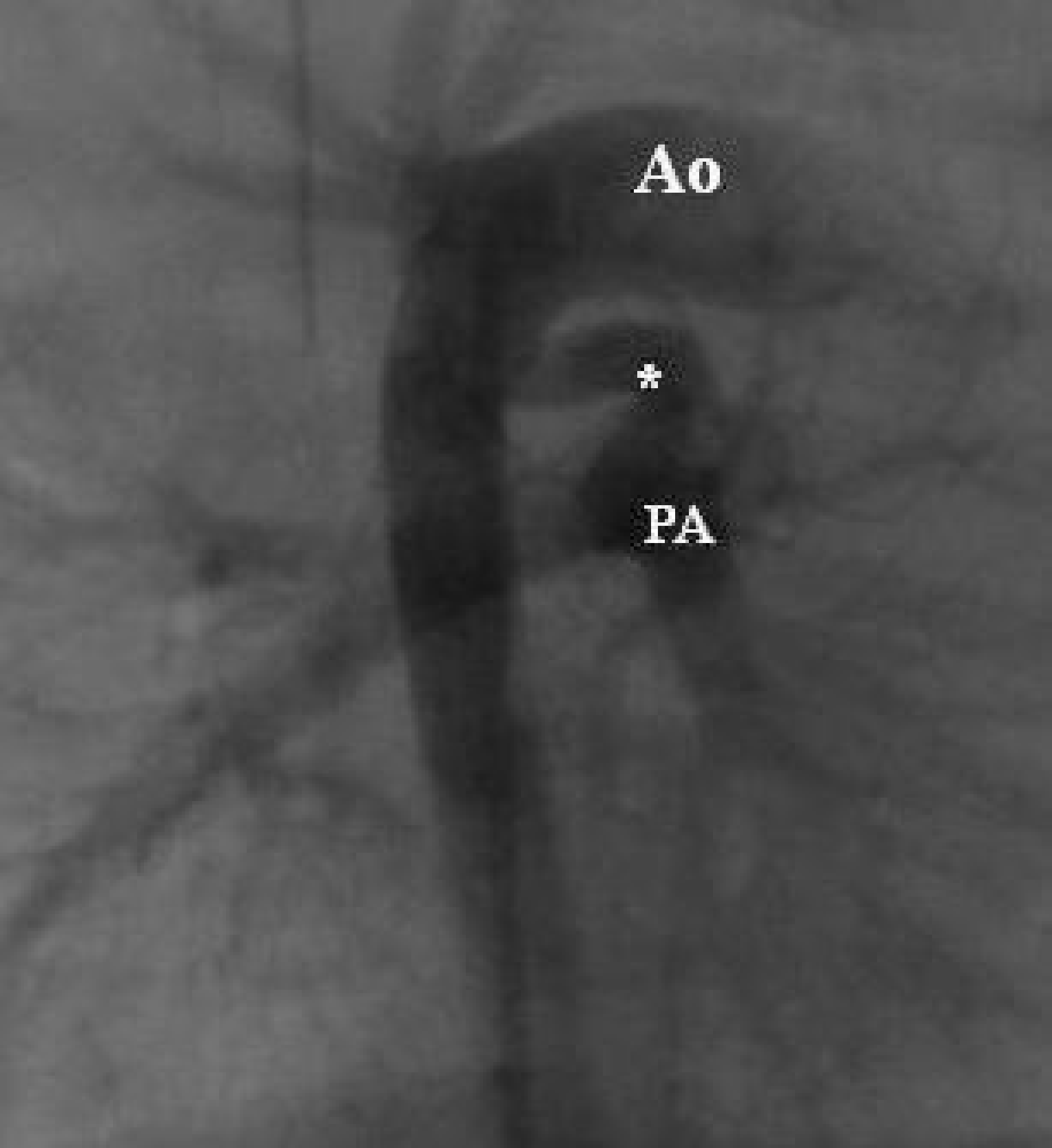
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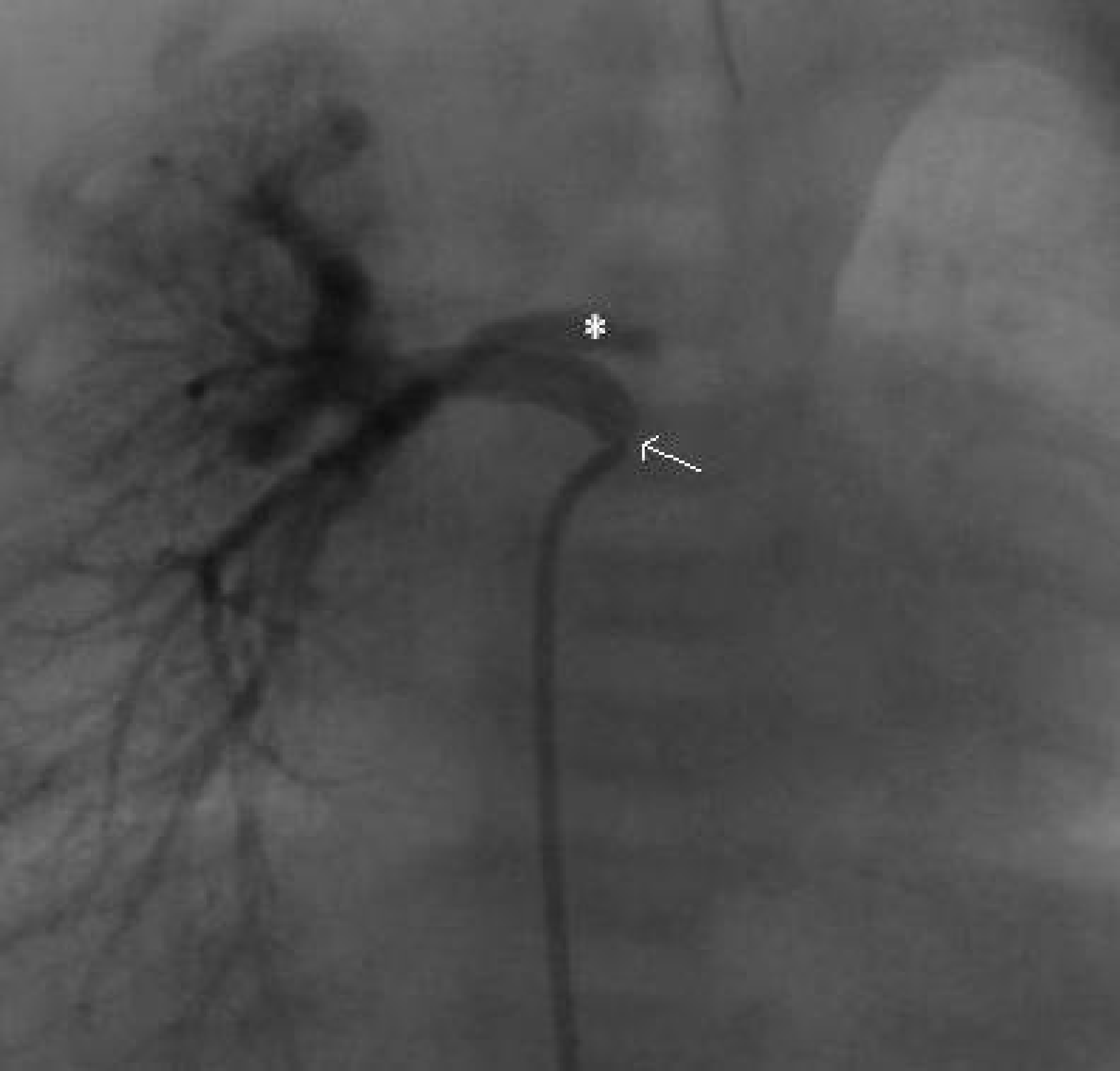

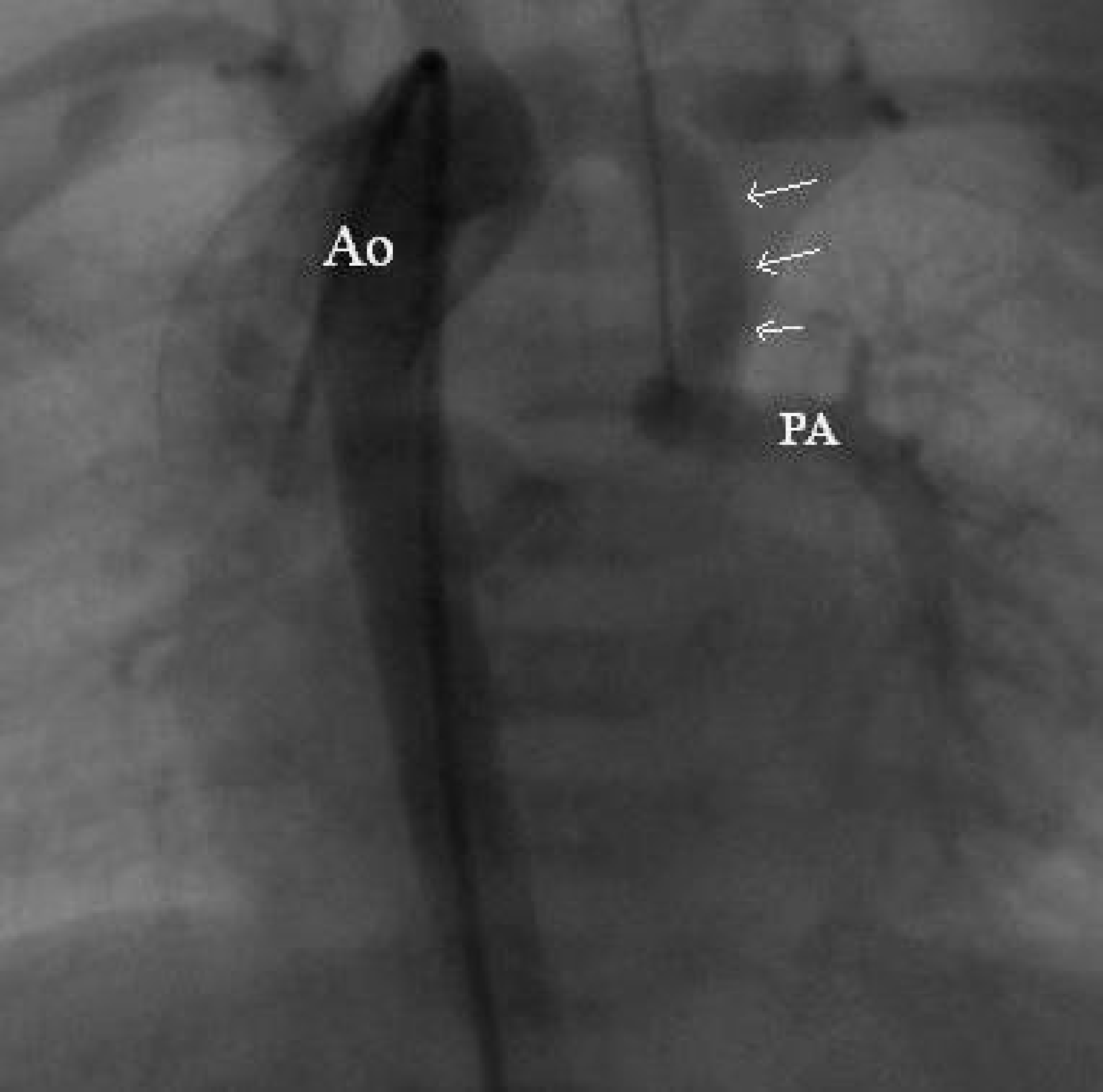
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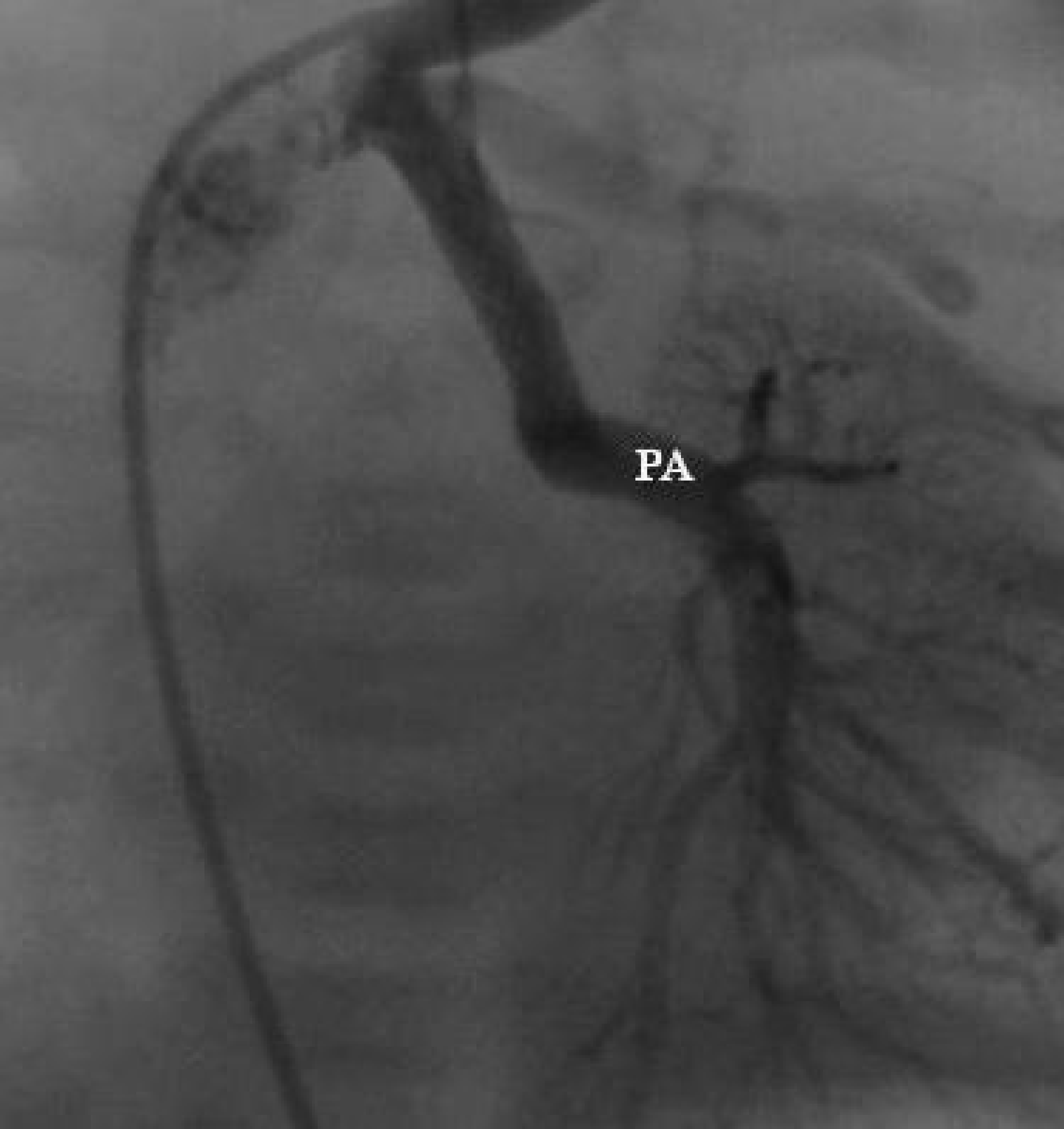
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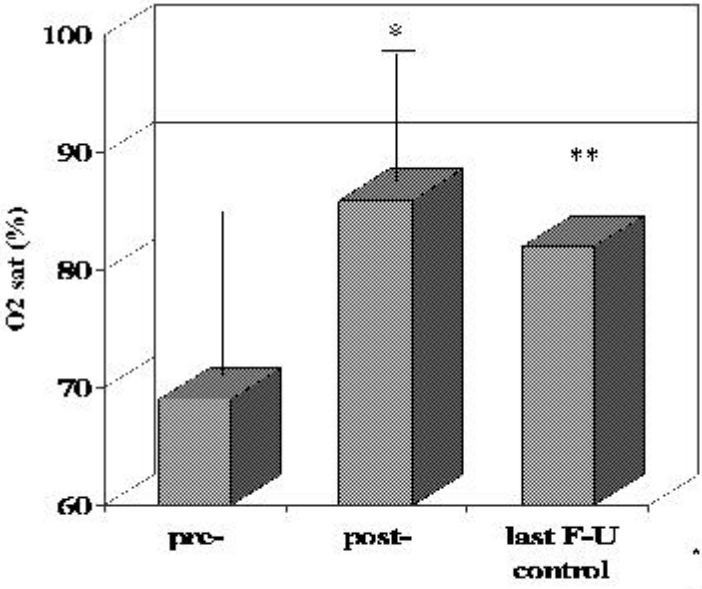

*p <0.0001 vs pre-

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