Advances in the management and surveillance of patients with aortic coarctation
Walhout, R.J.

Citation for published version (APA):
Walhout, R. J. (2009). Advances in the management and surveillance of patients with aortic coarctation

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Chapter 7

Long-term outcome after balloon angioplasty of coarctation of the aorta in adolescents and adults: is aneurysm formation an issue?

R.J. Walhout¹,
M.J. Suttorp¹,
G.J. Mackaij²,
J.M.P.G. Ernst¹,
H.W.M. Plokker¹

¹ Department of Cardiology, St. Antonius Hospital, Nieuwegein, the Netherlands
² Interuniversity Cardiology Institute of the Netherlands, Utrecht, the Netherlands

Catheter Cardiovasc Interv 2009;73:549-56
Abstract

Background:
Balloon angioplasty for native coarctation of the aorta in adults has shown favourable short-term results, but long-term results remain incomplete, especially concerning the occurrence of aneurysm formation.

Methods:
Long-term follow-up data were collected in consecutive patients retrospectively. Results of balloon angioplasty (29 patients, age 15-71 years, during 1995-2005) for discrete, native coarctation were evaluated, including both clinical evaluation and MRI or CT.

Results:
Mean follow-up ranged from 2.2 to 13 years (mean 8.5 +/- 3.2). Immediate success was obtained in all patients. Early mortality or complications were not encountered. Peak systolic pressure gradient decreased from 52 +/- 21 to 7.2 +/- 7.6 mmHg (p < 0.001). Intima tear was detected in eight procedures angiographically, without signs of aortic dissection. Three-month follow-up angiography in these patients showed unchanged (4/8 patients) or diminished abnormalities (4/8 patients). One asymptomatic patient, known with left ventricular dysfunction due to significant aortic valve insufficiency, died suddenly five years after balloon angioplasty. Recoarctation occurred in one patient (3%). Late aneurysm formation was excluded by MR in 24/29 and CT in remaining 5/29 patients during follow-up, including those patients in whom intima tear was encountered immediately postangioplasty. In three of seven patients an irregular aortic contour persisted, without indication of progression or aneurysm formation. Hypertension was completely relieved in 67% (14/21 patients) and improved in 33% (7/21 patients).

Conclusions:
Balloon angioplasty for native coarctation yields low reintervention probability in adult patients. Despite occurrence of angiographically established intimal tearing, aortic dissection and aneurysm formation were not encountered.
Introduction

The role of balloon angioplasty in the management of native coarctation in adolescents and adults is less clear than in children. Although promising, reported experience in series of patients is limited. Reviewing the literature, we could found results of no more than one Asian, one Arabian, seven European, three North-American and one South-American institution. Only two of these institutions have reported results with a follow-up of more than five years. Recoarctation and aneurysm formation are two adverse outcomes that require reinterventions in these patients during follow-up. Despite encouraging initial and intermediate follow-up results of plain balloon angioplasty in adults, stenting has recently been advocated instead of plain angioplasty to improve reintervention rates. A potential advantage of stenting is prevention of residual gradient by immediate vessel recoil. This complication has been reported in almost 50% of cases of balloon angioplasty incidentally. Another, probably more important concern following angioplasty, is the occurrence of dissection, involving “false” aneurysm in short-term, and “true” aneurysm in long-term follow-up. The reapplication of the torn intima to the media by the use of aortic balloon- or self-expandable stents has been claimed to minimalize the extension of wall tears and subsequent dissection or aneurysm formation, a well known complication of balloon angioplasty alone. Although it may be expected to be superior based on these considerations, that was not apparent when these modalities were compared in a review of 16 series of patients with endovascular management. The mean duration of follow-up for these patients was 36 ± 23 months. Short-term advantage appeared to be counterbalanced by the occurrence of intimal hyperplasia during long-term follow-up, with reintervention rates up to 31%. Furthermore, it has to be recognized that the occurrence of recoarctation appears not to be an important clinical issue in adult patients with isolated coarctation, in contrast to patients of younger age and patients with aortic hypoplasia. The application of aortic stenting of long-segment coarctation probably just indicates a new indication of percutaneous management of patients that previously were not considered appropriate for balloon angioplasty, because of high recoarctation rates associated with this condition. As aneurysm formation is concerned, this outcome has been found in 0%-13% on medium-term follow-up after balloon angioplasty in adults. This figure does not compare unfavourable to most reported intermediate-term results following surgical repair in the adult population, whereas the same incidence has been reported following stenting in intermediate-term follow-up. However, excellent long-term results after surgical repair of adult coarctation have been reported, with no reinterventions during 18 years of follow-up. Since these long-term results are unique with respect to the excellent outcome and the duration of follow-up, more long-term data of different treatment modalities and different institutions are needed to determine whether any of these is superior with respect to efficacy and safety. We therefore evaluated our long-term results for balloon angioplasty of native coarctation in adults, with particular reference to the occurrence of aneurysm formation.
Chapter 7

Methods

Between 1995 and 2005 29 consecutive adult patients with native, discrete type of coarctation underwent angiography with the intention to perform angioplasty. Informed consent was obtained from all patients. Data were analysed retrospectively, using data of the CONCOR national registry on congenital heart disease in the Netherlands for our institution. Coarctation was considered to require intervention in case of 1) systolic blood pressure gradients between upper and lower extremities exceeding 20 mmHg and/or 2) direct visualization of collateral vessels by MRI or CT and/or 3) increase in flow from proximal to distal descending thoracic aorta as measured by velocity-encoded cine MRI. 18 Isthmus hypoplasia, defined as isthmus diameter less than 40% of diameter of ascending aorta, and arch hypoplasia, defined as proximal or distal transverse arch diameter less than 60% or 50% respectively of the diameter of the ascending aorta, determined angiographically, were considered relative contra-indication for balloon angioplasty and such patients were referred for surgical management consequently. Stenting was not performed, except in one patient. This subject, being physician, explicitly requested stenting, which was acknowledged despite another clinical routine. Data of this successful and uneventful procedure have not been included in our results.

Technique

The technique of percutaneous balloon angioplasty for coarctation was described previously. 19 There were no important differences in technique or equipment over the 10-year period. Invasive measurement of the peak systolic gradient and biplane angiography were performed before and immediately after angioplasty. Aortic diameters of the ascendens, arch, isthmus, coarctation and at the level of diaphragm were measured. The balloon catheter was advanced up to the aortic arch and then retracted until the balloon crossed the coarctation. Inflation with diluted contrast was performed until the waist in the balloon disappeared. This procedure was performed three times, to optimize the final result. To measure aortic pressures and perform an angiogram, a catheter was passed over the guidewire, with special precaution to avoid manipulating the tip of the guide wire over the area of the freshly dilated aortic segment. This procedure was repeated using a larger balloon diameter when the result was unsatisfactory. The size of the balloon was chosen depending on the aortic diameter as measured at the level of the diaphragm, in such a way that the balloon would not exceed that diameter initially, and not by more than two mm in a secondary stage, performed when necessary.

The immediate result of angioplasty was considered successful if angiography showed no residual stenosis or indented vessel walls and the intra-vascular pressure gradient was reduced to less than 20 mmHg. In those cases in which the angiographic result was satisfactory but pressure gradient lower than 20 mmHg could not be reached, procedures were considered successful consequently.
Follow-up
Follow-up included clinical evaluation every three months in the first year after intervention and yearly thereafter. Arm and leg cuff pressures were registered. Follow-up included echocardiographic Doppler ultrasound studies, to assess the aortic flow and morphology directly, and cardiac magnetic resonance acquisition and imaging using a 1.5 Tesla MRI scanner (Intera, Philips Medical Systems, Best, the Netherlands). The MR protocol applied has been advocated for follow-up of repaired coarctation.\textsuperscript{20} In case of a (relative) contraindication against MR-study, CT was performed. Recoarctation requiring reintervention was defined in the same way as coarctation. In case of indication of intima tear follow-up angiography was scheduled and performed within three months following angioplasty. An aneurysm was defined as an aortic ratio of greater than 1.5, measuring aortic diameters at the coarctation repair site and thoracic aorta at the level of the diaphragm.

Statistical analysis
All of the statistical analyses were performed using SPSS software package (SPSS for Windows, 14.0, SPSS Inc, Chicago IL, USA). Data are expressed as mean ± standard deviation or range (minimal-maximal) as appropriate. Decreases in pressure gradients and aortic diameters of the dilated segments before and after balloon dilatation were compared using independent-samples T-test (two-tail, unequal variances). A p-value < 0.05 was considered significant.

Results
Balloon angioplasty of native coarctation of the aorta was performed in 29 consecutive adolescents and adults, aged 16 to 71 years (median 29 years). Seventeen of 29 patients (59%) had associated heart defects, involving bicuspid aortic valve, with or without valvular dysfunction (12 patients, 41%), ventricular septal defect (two patients, 7%), mitral valve insufficiency (two patients, 7%) and atrial septal defect, type secundum (one patient, 3%). Associated structural heart defects were managed surgically in four patients before, and two patients after balloon angioplasty. These procedures comprised aortic valve replacement by mechanical prosthesis or pulmonary autograft, composite graft replacement of the aortic valve, aortic root and ascending aorta (Bentall procedure), mitral valve repair and closure of a ventricular septal defect.

Immediate results
The peak systolic pressure gradient decreased from 52 +/- 21 to 7.2 +/- 7.6 mm Hg (p < 0.001) (see Figure 1).
The mean coarctation diameter increased from 7.5 +/- 3.5 to 15.5 +/- 3.5 mm (p < 0.001) immediately after angioplasty (Figure 2).
The procedure was considered successful in all patients. No procedure-related
complications or mortality occurred. Vascular access was not acquired in one patient with a unilateral peripheral vascular occlusion. Consequently, the procedure was performed via both the contralateral femoral artery and brachial artery. An intima tear was detected angiographically in eight of 29 procedures, without indication of acute aortic dissection in any of these cases. A saccular aneurysm distal of the coarctation was encountered before a subsequently performed angioplasty. Hospital stay varied from 12 to 48 hours for all patients.

**Figure 1.** Box and Whisker plots of pre- and postprocedural peak pressure gradient across coarctation segment in 29 patients, managed by balloon angioplasty for native, discrete type coarctation.

**Figure 2.** Box and Whisker plots of pre- and postprocedural aortic diameters, evaluated angiographically in 29 patients, managed by balloon angioplasty for native, discrete type coarctation.
Long-term follow-up of angioplasty in adolescents and adults

Clinical evaluation and imaging during follow-up
One sudden death occurred, not related to the angioplasty procedure after five years following dilatation. Left ventricular systolic function was severely reduced in this asymptomatic 25-year-old male patient. Aortic valve replacement had been proposed but was rejected because of the lack of symptoms. MR-study performed 11 months before his sudden death, demonstrated only a slight indentation at the site of the coarctation. Q-flow measurements at the coarctation site and level of diaphragm revealed stroke volumes of 88 and 82 mL, corresponding with the absence of collateral circulation and of a hemodynamically significant recoarctation. After 2.2 to 13 years of follow-up (mean 8.5 +/- 3.2 years), all patients showed continued clinical improvement. Blood pressure control had been successful by medication before angioplasty in eight patients. Hypertension was completely relieved in 67% (14 of 21 patients) and improved in 33% (seven of 21 patients). Systolic blood pressure at the right brachial artery ranged from 167 +/- 28 mmHg before balloon angioplasty to 132 +/- 17 mmHg at long-term follow-up. All patients had ultrasound investigations. Twenty-four patients (83%) had MR and five patients (28%) CT as primary imaging modality. Seven of these patients (24%) had additional conventional angiographic studies, combined with either MR or CT in follow-up. Four patients (14%) had MR combined with CT.

Recoarctation
Recoarctation occurred in one patient (3%), in whom flow increase from coarctation segment to the segment at the diaphragm was found, compatible with a significantly indentated coarctation segment angiographically (see Figure 3).

Figure 3. Sagittal oblique contrast-enhanced MR angiogram of a 41-year-old male, four years following an initially successful balloon angioplasty of a severe coarctation. Recoarctation was diagnosed, based on both flow measurement in proximal and distal segments of the descending aorta and the indicated, local indentation (arrow). Of notice is the ascending aorta, which was known previously to be dilated.
On velocity-encoded cine MR studies at five months to 12 years (mean 5.3 +/- 4.2 years) after angioplasty, there was no increase in flow at the level of diaphragm, compared to measurement distal of the coarctation in 23 of 24 patients (96%), thus excluding significant recoarctation in these patients. Although two of these 23 patients demonstrated diameter reduction of 27% and 29% with reference to measurements postangioplasty, normal flow measurements excluded recoarctation. Also, the five patients in whom long-term result was assessed by CT did not demonstrate a recoarctation. Average aortic diameter at the dilated segment at follow-up did not differ significantly from the immediate post-angioplasty results (15.9 +/- 2.9 versus 15.6 +/- 3.2 mm, p = 0.67).

**Late aneurysm formation**

In those patients in whom intima tear was encountered immediately postangioplasty, disappearance thereof occurred in four of seven patients angiographically at three-month follow-up. In the remaining three of seven patients an irregular aortic contour persisted, without indication of progression or aneurysm formation in any of these patients. MRI and CT were performed in seven of seven and four of seven patients.
during follow-up respectively and did demonstrate either disappearance or stable presence of aortic abnormalities that resulted from vessel disruption. The images of one of these patients are depicted in Figure 4.

**Discussion**

Our experience suggests that balloon angioplasty of native aortic coarctation in adolescents and young adults is safe and highly effective with sustained improvement on long-term follow-up. Pressure gradient drops across the coarctation segment were significant in all cases immediately and proved durable in all but one case of recoarctation. Persistent hypertension was improved or even relieved completely in the majority of patients.

**Aneurysm formation & intima tear**

Despite occurrence of angiographically detectable internal vessel disruption in eight of 29 patients, acute dissection or late aneurysm formation did not occur in our series. These complications have been reported in several cases and retrospective series of angioplasty in children and adults. Although some early experience was not encouraging with respect to true aneurysm with an incidence of 43% (three of seven patients) at one to two years follow-up in children, more recently this figure lowered to 10-20% at one-year follow-up, with aneurysm formation at the previously dilated aortic segment. The majority of reports, including more recently published series, describe aneurysm incidence below 10% during intermediate- and long-term follow-up. Most aneurysms in these reports include small abnormalities without progression over time, for which no intervention was indicated. Only one of 940 patients died within three weeks following balloon angioplasty in the registry reported by Tynan et al. Two early and six late aneurysms occurred on intermediate follow-up in this series, predominantly comprising children. Reported occasionally in adults, these outcomes seem not to be encountered frequently in (large) retrospective series in the adult population. Three recent series of balloon angioplasty were included in a review of endovascular management of coarctation in adults. Referral to surgery, based on aneurysm formation or dissection, occurred in one patient in each of these series. Disappointingly, equal rates of aneurysm formation were reported following stenting or a combined approach. Our findings accord to those in several series without any dissection or aneurysm formation. The strict anatomic criteria for balloon angioplasty probably influenced these satisfactory results. Due to its increased use and higher volumes per institution, we consider differences in the technique of angioplasty less likely to cause different morbidity between institutions.

**Imaging of vessel disruption**

An intima tear was diagnosed angiographically in eight of 29 procedures immediately. It is now recognized that balloon angioplasty for native coarctation
is invariably associated with disruption of the inner vascular layer of the aorta. The first experience with balloon angioplasty for experimental coarctation, using a lamb model, indicated intimal and medial tears by cross pathologic inspection in the first three days after successful dilation. Intravascular ultrasound imaging has shown prominent dissections of the inner vascular layers that are often not detected by angiography after angioplasty. Sohn et al. reported intimal tear or flap to be noted by intravascular ultrasound in 12 of 12 angioplasty procedures for native coarctations in patients ranging from 0 to 19 years of age, of which just the half was detected by angiography. Other false-negative results of aortography have been documented previously. Computed tomography, although highly specific, has also limited sensitivity for this indication. MRI has developed as routine non-invasive imaging tool in the surveillance of patients and was applied in the surveillance of our patients consequently. It should be performed regularly for it is the gold standard procedure for detection of a hypoplastic aortic arch, aortic aneurysms (ascending aorta, aortic arch and descending aorta) and recoarctation. It provides detailed composite views of the aortic arch and coarctation. A comparitative study with transesophageal imaging indicated that both techniques provide comparable details of the isthmus and coarctation site, but only MR imaging adequately demonstrated the aortic arch. Additionally, collateral flow can be visualized and quantified. MRI has been described to be sensitive for detection of localized dissection. It was able to demonstrate intima tear in a case in which CT and a two dimensional echocardiogram failed in this respect. We therefore consider our follow-up protocol, including routine MRI and CT in case of a (relative) contra-indication, to be appropriate.

**Clinical significance of vessel disruption**

Although vascular disruption by balloon angioplasty may be evident in some patients, its significance remains undetermined. Diminution or disappearance of intimal tears within months has been described in the majority of lesions in both experimental and clinical studies, as was found in four of seven patients in this series. Furthermore, late persistence of an intimal tear not necessarily results in any clinical consequence. Even significant intimal tears after dilation have not been associated with aneurysm formation at short-term to midterm follow-up in the series of 12 patients, described by Sohn et al. Even when small aneurysms are found, measuring 2.0-2.3 cm in a series of Fawzy et al., no change in size was noted on follow-up MRI up to 10 years later, thus warranting a non-invasive approach. The only independent risk factors for aortic complication, including aneurysm formation and dissection, found in 235 adults with repaired, dilated or non-repaired coarctation were identical: advanced age and bicuspid aortic valve. False aneurysm formation in the descending aorta was encountered in this series in patients following surgical repair and without previous intervention, but not in patients following balloon angioplasty. In conclusion, vascular wall injury seems unavoidable, although the “ideal” extend thereof has not been determined, lacking data to correlate exact mural changes that occur immediately after angioplasty with follow-up observations.
Comparison to surgical repair

Reports on the results of surgical repair for the adult patient group are limited and rather conflicting. Surgical repair of coarctation in adults has been considered obviously more hazardous than in children, with higher mortality rates of surgical repair in adults over 40 years of age. Nevertheless, an excellent reintervention rate of just 2% has been reported in 45 adults in 2005, without aneurysm formation during 18 years of mean follow-up. Aneurysms are found following all types of surgical repair, but especially after Dacron patch aortoplasty, with incidence as high as 90%. Beside aortic aneurysm, complications of surgical management include bleeding, paraplegia, recurrent laryngeal injury, phrenic nerve injury, chylothorax, wound infection and paradoxical postoperative hypertension. Recoarctation is another well-known late-term outcome of various types of surgical repair. Hager et al. recently reported results of 273 patients following surgical repair at a single institution and found a reintervention rate of 11%, all involving recoarctation. Patient selection for surgical repair has changed since the introduction of percutaneous management and available long-term follow-up results of surgical repair are not based on contemporary surgical technique. Nevertheless, we think the aforementioned findings and outcome of our study and others suggest that balloon angioplasty offers a safe and effective alternative for surgery in adults with discrete type of coarctation.

Conclusions

Balloon angioplasty for native coarctation yields a low long-term reintervention probability in adult patients. These results compare favourably with those of surgical repair. Results of aortic stenting, another alternative for plain angioplasty, are awaited. Intermediate-term risks of restenosis and aneurysm formation following aortic stenting do not appear to be lower than for angioplasty. Despite occurrence of angiographically established vessel disruption, clinically significant aortic dissection and aneurysm formation were not encountered in this series. Our experience suggests that balloon angioplasty of native aortic coarctation in adolescents and adults can be performed safely and effectively with good immediate outcome. Furthermore, it offers satisfactory long-term results with low incidence of persisting hypertension, recoarctation and aneurysm formation. As long as superior long-term follow-up results of aortic stenting are to be awaited, it thus may be considered as first-line therapy in adolescents and adults with native and discrete coarctation. Similar to alternatives for angioplasty, life-time surveillance using contemporary imaging techniques is warranted to detect poor outcome in time.
References

17. Duke C, Qureshi SA. Aortic coarctation and recoarctation: to stent or not to stent? J Interv Cardiol 2001;14:283–98
Long-term follow-up of angioplasty in adolescents and adults

40. Longe TF, Lesser JR, Schwartz RS. Early aortic intimal tear without haematoma or dissection: early diagnosis by cardiac magnetic resonance imaging. Heart 2005;91:416


