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Official Journal of the Aortic Institute at Yale-New Haven Hospital


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**PROVEN TO REDUCE BLOOD TRANSFUSIONS**

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  32.1 ± 5.4 minutes vs 56.3 ± 8 minutes

*In a prospective, randomized, controlled trial for cardiovascular surgery of 209 patients and compared to 206 control patients, a cohort of patients with intraoperative bleeding was treated with FLOSEAL Matrix (n=110) or control (n=104), with either SURGICEL hemostat (oxidized regenerated cellulose) or GELFOAM® sponge (purified porcine skin gelatin). In addition to the above outcomes, no difference in major complications (stroke, shock, sepsis, or myocardial infarction) or ICU stay was observed between groups during the study.*

**FLOSEAL Hemostatic Matrix Indication**

FLOSEAL Matrix is indicated in surgical procedures (other than ophthalmic) as an adjunct to hemostasis when control of bleeding by ligature or conventional procedures is ineffective or impractical.

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Do not inject or compress FLOSEAL Matrix into blood vessels. Do not apply FLOSEAL Matrix in the absence of active blood flow, e.g., while the vessel is clamped or bypassed, as extensive intravascular clotting and even death may result.

Do not use FLOSEAL Matrix in patients with known allergies to materials of bovine origin. Do not use FLOSEAL Matrix in the closure of skin incisions because it may interfere with the healing of the skin edges.

FLOSEAL Matrix contains Thrombin made from human plasma. It may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

FLOSEAL Matrix is not intended as a substitute for meticulous surgical technique and the proper application of ligatures or other conventional procedures for hemostasis.

Excess FLOSEAL Matrix (material not incorporated in the hemostatic clot) should always be removed by gentle irrigation from the site of application. FLOSEAL Matrix swells by approximately 10% to 20% after product is applied. Maximum swell volume is achieved within about 10 minutes.

The safety and effectiveness of FLOSEAL Matrix has not been established in children under 2 years of age and pregnant women.

Do not use air to remove residual FLOSEAL Matrix from Applicator tip. The Applicator tips should not be cut. Do not use FLOSEAL Matrix on bone surfaces where adhesives, such as methylmethacrylate or other acrylic adhesives, will be required to attach a prosthetic device.

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- Distal fixation length of ≥ 15 mm
- Aortic neck diameters with a range of 19 to 32 mm
- Iliac diameters with a range of 8 to 25 mm
- Morphology suitable for aneurysm repair

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- Patients experiencing reduced blood flow through the graft limb, aneurysm expansion, and persistent endoleaks may be required to undergo secondary interventions or surgical procedures.
- The Endurant II Stent Graft System is not recommended in patients unable to undergo or who will not be compliant with the necessary preoperative and postoperative imaging and implantation studies as described in the Instructions for Use.
- Renal complications may occur: 1) From an excess use of contrast agents. 2) As a result of emboli or a misplaced stent graft. The radiopaque marker along the edge of the stent graft should be aligned immediately below the lower-most renal arterial origin.
- Studies indicate that the danger of micro-embolization increases with increased duration of the procedure.
- The safety and effectiveness of the Endurant II Stent Graft System has not been evaluated in some patient populations. Please refer to the product Instructions for Use for details.

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Please reference product Instructions for Use for more information regarding indications, warnings, precautions, contraindications and adverse events.

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Asymmetric Dimethylarginine in Patients with Ascending Aortic Aneurysms

Natalia D. Gavriliuk, MD1*, Tatiana A. Druzhkova, MD1, Olga B. Irtyuga, MD, PhD1, Alexandr A. Zhloba, PhD1,2, Tatiana F. Subbotina, PhD1,2, Vladimir E. Uspenskiy, MD, PhD1, Nina P. Alexeyeva, MD3, Olga M. Moiseeva, MD, PhD1

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Abstract

Background: Ascending thoracic aortic aneurysm (aTAA) is a heterogeneous group of disorders that involve impaired endothelial function. The nitric oxide (NO) synthase inhibitor asymmetric dimethylarginine (ADMA) serves as an endothelial dysfunction marker. Thus, we investigated ADMA levels in patients with aTAA.

Methods: Eighty-six patients with aTAA and 18 healthy individuals were enrolled. All patients underwent echocardiography. Plasma ADMA levels were measured using high-performance liquid chromatography.

Results: ADMA levels were higher in aTAA patients than in control patients (p = 0.034). According to the multivariable regression model, higher ADMA levels were associated with ascending aortic diameter (p = 0.017), smoking (p = 0.016), and log-transformed estimated glomerular filtration rate (eGFR, p = 0.005).

Conclusion: This pilot study demonstrates an association of ADMA with ascending aortic dilatation; however, further studies are needed to investigate whether increased ADMA levels underlie aTAA development.

Key Words:
Asymmetric dimethylarginine • Thoracic aortic aneurysm • Endothelial dysfunction

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with different cardiovascular disorders [9, 10]. Although information on the role of ADMA in the pathology of cardiovascular disorders is continuously expanding, data regarding ADMA metabolism in patients with aTAA is limited. Thus, the aim of this study was to evaluate the relationship between ADMA levels and aTAA.

**Materials and Methods**

**Ethics**

The study protocol was approved by the local ethics committee of Federal Almazov North-West Medical Research Centre (15.05.2012, No. 0094). This study was performed according to the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

**Study Subjects**

From May 2012 to December 2014, 104 patients were recruited from the Federal Almazov North-West Medical Research Centre inpatient department, and those who provided informed consent were included in the current study. Patients with aTAA caused by thoracic trauma or previous aortic surgery and those with heritable connective tissue disorders (Marfan syndrome and others) and inflammatory diseases of the thoracic aorta were excluded. Other exclusion criteria were aortic dissection, abdominal aortic aneurysms, malignancy, hepatic or renal failure, and class IV heart failure. In total, we included 86 patients with ascending aortic aneurysms: 62 patients with tricuspid aortic valve (TAV)- and 24 patients with bicuspid aortic valve (BAV)-associated aneurysms. The control group consisted of 18 age-matched individuals with normal TAVs and similar risk factors for cardiovascular diseases (CVDs). The control group patients were selected from patients admitted to the outpatient unit with one or more CVD risk factors. The groups were comparable in terms of baseline characteristics but differed with regard to ascending aortic diameter, according to the inclusion criteria.

**Imaging**

All patients underwent two-dimensional and Doppler echocardiography using the Vivid 7.0 system (GE Healthcare, Chicago, IL USA) according to current ECHO guidelines. Diagnosis of BAV was based on the presence of only two commissures, delimiting only two aortic valve cusps, as observed on short-axis imaging of the aortic valve. For quantification of the ascending aortic diameter, contrast-enhanced multi-sliced computed tomography (CT; Somatom Definition 128, Siemens, Munich, Germany) was performed for all patients with aTAA. The inclusion criteria for the aTAA group were ascending aortic diameter (maximal dimension) of ≥4.5 cm for patients with TAV and ≥4.0 cm for patients with BAV.

**Blood Samples**

Blood samples were collected in tubes containing 3.8% sodium citrate as the anticoagulant and centrifuged at 3,000 rpm for 15 min at 4°C immediately after collection. Plasma samples were frozen and stored at -80°C until analysis. Plasma ADMA levels were measured using high-performance liquid chromatography after solid-phase extraction using the cation-exchange cartridges Oasis MCX 1 cc/30 mg (Waters Corp., Milford, MA, USA), followed by derivatization with orthophthalaldehyde [11]. The concentration of total serum homocysteine (tHcy) was determined using the chemiluminescent micro-particle method (Abbott Clinical Chemistry, Abbott Park, IL, USA).

**Statistics**

All statistical analyses were performed using Statistica for Windows 10.0 (StatSoft Inc., Tulsa, OK, USA). Normally distributed data were presented as average ± standard deviation (SD), while non-normally distributed data are presented as median (Q25, Q75). All p values < 0.05 were considered statistically significant. Variables with skewed distribution (estimated glomerular filtration rate [eGFR] and tHcy) were analyzed after logarithmic (log) transformation. The differences between normally distributed continuous values were assessed using an unpaired two-tailed t-test or one-way analysis of variance (ANOVA) with post-hoc Bonferroni test. Description of the qualitative variables (number and percentage) was carried out using the χ² test. Box plots were used to display a statistical summary of the median, quartiles, and extreme values. Spearman’s rank correlation was used to determine correlations with continuous variables. Univariate and multivariate linear regression were performed to investigate the association of ADMA with different variables.

**Results**

Eighty-six patients had aTAA, and 18 had CVD risk factors but did not present with ascending aortic dilatation. The clinical parameters of the groups are presented in Table 1. ADMA plasma levels were higher in the aneurysm group than in the control (p = 0.034, Figure 1). In addition, a positive correlation between ADMA plasma levels and ascending aortic diameter was found (corrected $R^2 = 0.047$, $\beta = 0.239$, p = 0.004; Figure 2). The ADMA plasma levels, however, did not differ between patients with TAV (0.49 ± 0.1 μmol/L) and those with BAV (0.5 ± 0.12 μmol/L, p = 0.6).

ADMA levels were also correlated with log-transformed tHcy level (rs=0.23, p = 0.025) and eGFR ($\beta=0.29$, p = 0.004; Figure 3); however, the Hcy levels did not differ between patients with aTAA and controls (p = 0.79). Smoking was strongly associated with higher ADMA levels (0.52 ± 0.11 μmol/L in smokers with aTAA vs. 0.46 ± 0.11 μmol/L in nonsmokers with aTAA; p = 0.002). According to linear regression analysis adjusted for smoking, smokers exhibited a stronger cor-
Table 1. Characteristics of enrolled subjects.

<table>
<thead>
<tr>
<th></th>
<th>aTAA</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>57.6 ± 8.6</td>
<td>55.1 ± 11.3</td>
<td>0.29</td>
</tr>
<tr>
<td>Obesity, n (%)</td>
<td>39 (45%)</td>
<td>10 (55%)</td>
<td>0.44</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.7 ± 4.7</td>
<td>30.6 ± 6.0</td>
<td>0.14</td>
</tr>
<tr>
<td>Smokers, n (%)</td>
<td>42 (48%)</td>
<td>8 (44%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Smoking history (y)</td>
<td>25.8 ±11.9</td>
<td>18.6 ± 12.9</td>
<td>0.11</td>
</tr>
<tr>
<td>Cigarettes/day, n</td>
<td>19.17 ±10.91</td>
<td>15.5 ± 7.98</td>
<td>0.31</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>73 (84%)</td>
<td>14 (78%)</td>
<td>0.54</td>
</tr>
<tr>
<td>Office systolic BP (mm Hg)</td>
<td>129 ± 14</td>
<td>134 ± 27</td>
<td>0.26</td>
</tr>
<tr>
<td>Office diastolic BP (mm Hg)</td>
<td>80 ± 11</td>
<td>85 ± 13</td>
<td>0.09</td>
</tr>
<tr>
<td>Coronary artery disease, n (%)</td>
<td>47 (55%)</td>
<td>9 (50%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Lower extremity arterial occlusive disease, n (%)</td>
<td>4 (3%)</td>
<td>1 (6%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Cerebrovascular disease, n (%)</td>
<td>11 (13%)</td>
<td>2 (11%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus, n (%)</td>
<td>8 (9%)</td>
<td>2 (11%)</td>
<td>0.79</td>
</tr>
<tr>
<td><strong>Echocardiography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic diameter in the sinuses of Valsalva (mm)</td>
<td>43.3 ± 5.6*</td>
<td>34.7 ± 3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diameter of ascending aorta in sinotubular junction (mm)</td>
<td>47.1 ± 6.2*</td>
<td>34.0 ± 3.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximal aortic diameter (mm)</td>
<td>49.1 ± 7.1*</td>
<td>35.3 ± 3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak aortic gradient (mm Hg)</td>
<td>14 ± 17</td>
<td>8 ± 3</td>
<td>0.14</td>
</tr>
</tbody>
</table>

*(table continues)*
The relation between ADMA levels and aortic diameter (r = 0.31, p = 0.03) than nonsmokers (r = 0.23, p = 0.13; Figure 4). Furthermore, multiple regression analysis revealed that ascending aortic diameter, smoking, and eGFR were associated with ADMA levels (Table 2).

**Discussion**

It is known that aTAA is a multi-etiologic disease. Strong evidence supports endothelial dysfunction in patients with aTAA, particularly in cases with BAV [12, 13]. NO plays a pivotal role in the regulation of vessel wall homeostasis by influencing endothelial cell function [14, 15], and the NO pathway may also be involved in BAV development [16]. Patients with BAV are believed to have low expression levels of endothelial NO synthase [17]. ADMA is a NO synthase inhibitor and a marker of endothelial dysfunction. Extensive clinical evidence suggests that CVD are associated with increased ADMA levels [17, 18]. Toker et al. [19] studied the development of atherosclerosis and dilatation of the abdominal aorta induced by acrylamide exposure in rats and found an association between these processes and increased ADMA levels. Based on this information, we speculated that high ADMA levels play a role in TAA formation. Yet, few studies on this topic have been performed in patients with aTAA [20, 21]. Most investigators compared ADMA levels in

<table>
<thead>
<tr>
<th>Table 1. (Continued)</th>
<th>aTAA n = 86</th>
<th>Control n = 18</th>
<th>p</th>
</tr>
</thead>
</table>

**Contrast-enhanced multi-sliced computed tomography**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>aTAA</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic sinuses of Valsalva (mm)</td>
<td>44.9 ± 7.3</td>
<td>97.2 ± 28.8</td>
<td>0.23</td>
</tr>
<tr>
<td>Mid ascending aorta (mm)</td>
<td>49.5 ± 8.0</td>
<td>59.4 ± 25.2</td>
<td>0.36</td>
</tr>
<tr>
<td>Mid descending aorta (mm)</td>
<td>29.5 ± 6.7</td>
<td>102.1 ± 34.8</td>
<td>0.35</td>
</tr>
<tr>
<td>Abdominal aorta at the celiac axis origin (mm)</td>
<td>22.2 ± 7.3</td>
<td>4.02 ± 0.1</td>
<td>0.034</td>
</tr>
</tbody>
</table>

**Laboratory data**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>aTAA</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>90.0 ± 21.6</td>
<td>97.2 ± 28.8</td>
<td>0.23</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>54.8 ± 18.0</td>
<td>59.4 ± 25.2</td>
<td>0.36</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>95.06 ± 27.9</td>
<td>102.1 ± 34.8</td>
<td>0.35</td>
</tr>
<tr>
<td>ADMA (μmol/L)</td>
<td>0.49 ± 0.11*</td>
<td>0.42 ± 0.1</td>
<td>0.034</td>
</tr>
<tr>
<td>C-reactive protein (mmol/L)</td>
<td>7.92 (0.78-9.57)*</td>
<td>2.64 (1.3-3.1)</td>
<td>0.22</td>
</tr>
<tr>
<td>tHcy (μmol/L)</td>
<td>13.8 ± 3.5</td>
<td>13.5 ± 7.1</td>
<td>0.79</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.5 ± 0.4</td>
<td>3.6 ± 0.6</td>
<td>0.3</td>
</tr>
</tbody>
</table>

**Medication**

<table>
<thead>
<tr>
<th>Medication</th>
<th>aTAA</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihypertensive medications, n (%)</td>
<td>68 (79%)</td>
<td>14 (78%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors, n (%)</td>
<td>30 (35%)</td>
<td>5 (33%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Angiotensin II receptor blockers, n (%)</td>
<td>11 (13%)</td>
<td>3 (17%)</td>
<td>0.3</td>
</tr>
<tr>
<td>Calcium channel blockers, n (%)</td>
<td>10 (12%)</td>
<td>4 (22%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Beta-blockers, n (%)</td>
<td>46 (53%)</td>
<td>9 (50%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Diuretics, n (%)</td>
<td>28 (32%)</td>
<td>6 (33%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Statins, n (%)</td>
<td>24 (28%)</td>
<td>6 (33%)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

ADMA = asymmetric dimethylarginine; aTAA = ascending thoracic aortic aneurysm; BMI = body mass index; BP = blood pressure; eGFR = estimated glomerular filtration rate (by CKD-EPI formula); LDL = low-density lipoprotein; tHcy = total homocysteine.

*Data presented as mean ± standard deviation and median (Q25:Q75).
patients with aTAA with healthy individuals without CVD risk factors. Thus, these studies did not assess the influence of commonly known risk factors on ADMA levels in patients with aTAA. Therefore, we compared ADMA plasma levels in patients with aTAA to those in individuals with common CVD risk factors.

Our data revealed significant differences in ADMA levels between patients with aTAA and control subjects with similar CVD risk factors. The results of this study are consistent with previous results. Drapisz et al. [21] noted that ADMA levels were associated with size of the aortic annulus, peak aortic velocity, aortic distensibility, aortic stiffness index, and aortic strain in patients with non-stenotic BAV; however, in contrast to our study, the study by Drapisz and colleagues included younger patients (range 24-33 years) and only patients with BAV. Intriguingly, in our study, we did not find any differences in ADMA levels between TAV and BAV patients, but our results disclosed a positive correlation between ADMA plasma levels and in-

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**Figure 3.** Correlation between log-transformed estimated glomerular filtration rate and plasma asymmetric dimethylarginine levels (corrected R² = 0.073; β = -0.29; p = 0.004).

**Figure 4.** Adjusted linear regression of asymmetric dimethylarginine levels (μmol/L) and ascending aortic diameter according to smoking status (r = 0.23, p = 0.13 in nonsmokers; r = 0.31, p = 0.03 in smokers).

**Table 2.** Multivariate regression model of plasma ADMA level predictors.

<table>
<thead>
<tr>
<th>Model</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>SE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>0.685</td>
<td>0.282</td>
<td>2.425</td>
<td>0.018*</td>
</tr>
<tr>
<td>Age</td>
<td>0.0013</td>
<td>0.0016</td>
<td>0.096</td>
<td>0.833</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.040047</td>
<td>0.024940</td>
<td>-0.169</td>
<td>-1.606</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.055</td>
<td>0.022</td>
<td>0.258</td>
<td>2.473</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.0008</td>
<td>0.0025</td>
<td>0.036</td>
<td>0.336</td>
</tr>
<tr>
<td>Diameter of ascending aorta</td>
<td>0.0044</td>
<td>0.0018</td>
<td>0.284</td>
<td>2.430</td>
</tr>
<tr>
<td>Log eGFR</td>
<td>-0.120</td>
<td>0.042</td>
<td>-0.323</td>
<td>-2.865</td>
</tr>
<tr>
<td>Log total homocysteine</td>
<td>-0.0004</td>
<td>0.0463</td>
<td>-0.001</td>
<td>-0.009</td>
</tr>
<tr>
<td>Aortic valve morphology</td>
<td>0.006</td>
<td>0.019</td>
<td>0.041</td>
<td>0.334</td>
</tr>
</tbody>
</table>

ADMA = asymmetric dimethylarginine; eGFR = estimated glomerular filtration rate (by CKD-EPI formula); Log = logarithm; Regression summary: r = 0.510; adjusted R² = 0.186; F(8,79) = 3.4791, p < 0.017. *indicates significant p < 0.05.
increased ascending aortic diameter. Another previous study of only patients with BAV demonstrated that inflammation and endothelial dysfunction played a more important role in BAV with aortic stenosis than in aortopathy [20]. That study also reported an association between ascending aortic diameter and ADMA levels, albeit with borderline significance. Differences between the results of the previous studies and those of the present study may be partly explained by the younger age and the inclusion of very few smokers (2%) in the previous study as compared to the number of smokers (48%) included in the present study.

We also found a significant association between smoking and ADMA plasma levels, consistent with previous data [22, 23]. Regular cigarette smoking increases ADMA levels, as previously reported by Campesi et al. [22] and confirmed in our study. In the case of patients with common CVD risk factors, this correlation is stronger as a result of the initially higher ADMA levels caused by aTAA. In the present study, we found significant differences in the ADMA levels between nonsmoker aTAA patients and nonsmoker controls and comparable ADMA levels between smoker aTAA patients and smoker controls. No randomized prospective trials have investigated the effect of smoking cessation on TAA [24]; however, among patients with aTAA who smoke, the rate of aneurysm expansion is higher than that in nonsmokers [25].

Surprisingly, the multivariable model described a strong positive correlation between ADMA levels and ascending aortic diameter. Our study data correspond to those of a previous study by Ali et al. [20]. Nevertheless, our findings directly lead to the question of whether increased ADMA levels cause dilation of the ascending aorta or merely reflect other pathologic processes in the vascular wall.

While our results are interesting, some limitations of this study should be acknowledged. This study did not include long-term prospective observation with repeated examinations and therefore, did not document a predictive value of ADMA levels as a biomarker of aTAA progression.

Conclusion

In the present study, a strong association between ascending aortic diameter and plasma ADMA levels was observed. Interestingly, the levels of ADMA did not differ between BAV and TAV patients, and the main risk factors that influenced the ADMA levels were smoking and eGFR.

Acknowledgments

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Conflict of Interest

The authors have no conflict of interest relevant to this publication.

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Gavriliuk, N.D. et al.             ADMA in Ascending Aortic Aneurysm


16. Lee TC, Zhao YD, Courtman DW, Stewart DJ, Abildgaard NL. Abnormal vascular remodeling in mice lacking endothelial nitric oxide synthase. Circulation. 2000;101:2345-2348. DOI: 10.1161/01.CIR.101.20.2345


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Abstract
A 74-year-old woman was admitted for right coronary angioplasty. During the procedure, she complained about chest pain, and contrast injection showed an iatrogenic dissection of the ascending aorta. A contrast computed tomography (CT) scan confirmed the diagnosis via visualization of a large non-circulating false lumen, which involved nearly the entire ascending aorta. The patient remained hemodynamically stable and asymptomatic while receiving medical therapy alone. Another CT scan performed 3 days later showed complete regression of the false lumen. This case suggests that uncomplicated iatrogenic dissection of the ascending aorta, even when large, may be managed successfully by medical therapy.

Key Words:
Iatrogenic Dissection • Intramural hematoma • Coronarography • Aortic root • Aorta • Coronary artery

Introduction
The last two decades have seen a growing trend towards more frequent coronary angiography (CA) and percutaneous coronary intervention (PCI). As a consequence, procedure-related complications have been observed more frequently. Iatrogenic aortic dissection (IAD) results from a catheter-induced lesion of the intima, creating bleeding inside the aortic wall. Although the intimal tear is typically very small (leading to non-circulating blood flow in the false lumen), IAD should be distinguished from intramural hematoma, as the latter is generally due to primary vasa vasorum bleeding that results from a pathologic aortic wall without intimal lesion [1].

Case Presentation
In the present case, a 74-year-old woman was admitted for elective coronary angioplasty in connection with a positive exertion test. Her medical history was only relevant for hypercholesterolemia. After drug-eluted stent implantation in the mid-right coronary artery, the patient complained of chest pain. Direct aortography by contrast injection showed an IAD arising from the right coronary sinus (Figure 1A) and stagnation of the contrast agent in the false lumen (Figure 1B), suggesting that the intimal tear was very small and was probably sealed spontaneously. Thus, no additional stent was implanted. A contrast computed tomography (CT) scan confirmed that an IAD with a non-circulating false lumen involved nearly the entire ascending aorta (Figure 2A). Because the patient remained hemodynamically stable and totally asymptomatic, we initiated medical therapy alone, which was composed of blood pressure control by beta-blockers in combination with calcium channel inhibitors. A control CT was performed 3 days later and showed complete regression of the false lumen of the dissection (Figure 2B) without any related complication. The patient was discharged after 10 days and presented with an uneventful follow-up after 1 year.
IADs induced by catheter manipulations are very rare, as procedure-related incidences of 0.006% and 0.1% have been reported for CA and PCI, respectively [2]. In some cases, the intimal tear may originate from a lesion localized in the ascending aorta or in the aortic arch, but most of the time, the dissection progresses from nearby coronary ostia injuries [3]. IAD of the ascending aorta (Type A) may be life-threatening, requiring surgical replacement of the diseased vessel to avoid pericardial effusion, coronary artery dissection, or acute aortic regurgitation, particularly if the extension reaches more than 40 mm [4, 5]. Occasionally, emergency stent implantation actually seals a minor intimal tear that originated from coronary ostia [5]. Spontaneous regression under medical therapy alone has also been observed in case of limited IAD, probably due to spontaneous sealing and stagnation of blood flow in the false lumen [2, 3].

Conclusion
This case illustrates the successful management of an uncomplicated ascending iatrogenic AD with
a minimal intimal tear and a non-circulating false lum-
men using medical therapy alone.

Conflict of Interest
The authors have no conflict of interest relevant to this publication.

References

Abstract
Iatrogenic aortic dissection (IAD) is a rare complication of percutaneous coronary interventions (PCI). There are no clear guidelines for IAD management, and limited data are available. Registry data and case series combined with extrapolations from our experience with spontaneous Type-A dissections suggest that very limited dissections are often managed conservatively with coronary stenting of the entry tear when possible, while more extensive dissections are managed surgically. We present a case report of a 50-year-old woman who underwent PCI for an ST-elevation myocardial infarction that resulted in an extensive IAD from the ostium of the right coronary artery to the aortic root, ascending aorta, and aortic arch. While the current evidence strongly supports surgical management of such extensive dissection, our patient was successfully managed conservatively with complete resolution according to short-term computed tomography imaging. This case suggests that conservative management may be a reasonable approach for select patients with extensive IAD.

Key Words:
iatrogenic aortic dissection • Percutaneous coronary intervention

Introduction
Iatrogenic aortic dissection (IAD) is a rare complication of percutaneous coronary intervention (PCI) [1-4]. In contrast to spontaneous Type-A aortic dissection (AD), where emergent surgical intervention is recommended to avoid devastating sequelae, the optimal management for IAD is less clear. While initial studies reported a 50% early mortality following surgical management of IAD, recent registry data suggest that mortality is comparable to that of spontaneous ADs (16% for IAD vs. 17% for spontaneous AD) [3, 4]. Patients with IAD are typically older compared to patients with spontaneous AD but are usually diagnosed immediately and thus require less extensive surgery. Herein, we present a case of successful conservative management of IAD following PCI extending from the right coronary artery (RCA) into the aortic root and arch.

Case Presentation
A 50-year-old otherwise healthy female smoker presented at the emergency department with a 2-day history of gastric reflux-like symptoms. An electrocardiogram revealed ST segment elevation in the inferior leads. The patient was therefore transferred immediately for a coronary angiogram. A right radial approach was utilized and showed normal left main and left anterior descending arteries and a circumflex with a 70% obtuse marginal...
lesion. The RCA had a 99% occlusive thrombus with distal TIMI (Thrombolysis in Myocardial Infarction) 2 flow. A wire was passed to yield a proximal RCA dissection that involved the entire length of the vessel. Three drug-eluting stents were deployed, resulting in TIMI 3 flow; however, the dissection had extended retrogradely into the aortic root and arch (Figure 1A, B, C). Furthermore, the dissection flap itself was not covered, demonstrating persistent communication with the false lumen. Emergent computed tomography (CT) confirmed the diagnosis of IAD, and the patient was then transferred to our hospital for further management. She remained pain-free and hemodynamically stable throughout the assessment and transfer.

On arrival, repeat CT scan demonstrated a stable dissection with no active extravasation into the false lumen, no pericardial effusion, and no aortic insufficiency (Figure 1D, E). The patient received a labetalol infusion to target a systolic blood pressure <120 mm Hg, and aspirin and ticagrelor therapy was continued. Another CT scan the following morning demonstrated a decrease in the size of the false lumen from 11 mm to 7 mm at the sinus of Valsalva and no evidence of contrast enhancement in the false lumen. A dissection flap was noted to extend across the RCA ostium, but the flap did not limit blood flow. The patient was discharged on day 3 with orders for ramipril, bisoprolol, and clonidine, as well as dual antiplatelet therapy. At the 2- and 4-month clinical follow-up visits, the patient remained asymptomatic. The 4-month CT scan showed complete resolution of the dissection with a patent RCA (Figure 2).

**Discussion**

IAD is a rare complication of PCI with an estimated incidence of 0.02% to 0.06% [1]. Patients with IAD are often older than those with spontaneous AD [1-3]. The RCA is commonly the site of IAD. Dunning et al. classified IAD based on extent of dissection: Class I dissections involve the ipsilateral aortic cusp, Class II dissections involve the ipsilateral cusp with extension of <40 mm up the aorta, and Class III dissections involve the ipsilateral cusp with extension of >40 mm up the aorta. These authors advocated for coronary stent therapy for Class I and II IAD, and surgery for Class III IAD [2]; however, these recommendations were based on a limited series of patients,
and the outcome of conservative management for Class III IAD was not evaluated. More recently, data from the Registry on Aortic Iatrogenic Dissection (RAID) was found to support conservative management of IAD, although the majority (77%) of cases had limited dissections (Dunning I and II), and more than half (35 of 74 patients) used stents to cover the intimal tear [1].

Our patient had an extensive dissection (Dunning class III) that extended into the aortic arch with a coronary dissection tear that was not covered. While there are no clear guidelines for IAD management, Dunning et al. advocated for surgical management for such class III dissections [2]. Nonetheless, we elected to pursue conservative management due to the absence of evidence of active contrast extravasation into the false lumen on a CT scan hours after the dissection occurred, as well as some resolution on the predischarge CT. Importantly, considerable dissection into the aortic root, aortic insufficiency, and hemopericardium are general indications for urgent surgical intervention; however, none of these conditions were observed in our patient. Furthermore, persistent active extravasation of blood into the false lumen on serial imaging would also prompt urgent surgery, but this condition was not observed in our patient. This case suggests that conservative management with serial imaging, aggressive blood pressure control, and close follow-up may be a reasonable approach for select IAD cases.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

References


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Abstract
Acute aortic intramural hematoma, which is a variant of acute aortic syndromes, most frequently occurs spontaneously and typically is treated similar to classic aortic dissection. Here, we describe a case in which an iatrogenic aortic intramural hematoma occurs shortly after transaortic valve replacement. The patient was managed conservatively, and the hematoma quickly resolved as demonstrated by serial imaging.

Key Words
Aortic intramural hematoma • Latrogenic injury • TAVR

Introduction
Complications after transcatheter aortic valve replacement (TAVR) occur in 9.3% of patients and involve the aorta in 1.8% of patients [1]. Iatrogenic aortic dissection has been reported after coronary [2] and cardiac surgical procedures [3]. Because TAVR is utilized primarily in patients with higher surgical risk, acute aortic injuries that occur following TAVR create uncertainty for the ideal management of these conditions.

Case Presentation
An 83-year-old woman presented with severe symptomatic aortic stenosis with New York Heart Association class III symptoms of congestive heart failure. Patient history was significant for cardiomyopathy (ejection fraction of 45-50%) and coronary artery disease. As a frail, high-risk patient with a Society of Thoracic Surgeons score of 4.6 and combined morbidity/mortality risk of 20.1%, she was determined to be best suited for TAVR.

Preoperative computed tomography revealed normal aortic diameter and 2-3+ left ventricular outflow tract (LVOT) calcification. Transesophageal echocardiographic (TEE) images revealed an ascending aorta with a 3.5-cm diameter. A 26-mm SAPIEN 3 TAVR was implanted through a transfemoral artery approach using a 23-mm balloon for predilation, and this valve appeared well-seated. Immediately post-TAVR, intraoperative TEE showed development of an aortic intramural hematoma (IMH) with 9-10-mm crescentic thickening of the wall. This IMH extended from the aortic annulus to 2-3 cm above the valve (Figure 1A and Video 1; see supplemental Video 1 at http://dx.doi.org/10.12945/j.aorta.2016.16.029.vid.01) and was new based on preoperative imaging. Given the stability of the patient and her advanced age, aggressive management of her blood pressure and surveillance imaging were deemed the most appropriate treatment strategy. TEE performed the following day revealed that the IMH rim had markedly decreased to a maximum wall thickness of 3-4 mm (Figure 1B and Video 2; see supplemental Video 2 at http://dx.doi.org/10.12945/j.aorta.2016.16.029.vid.02). Follow-up computed tomography angiography (CTA)
performed 2 days post-TAVR confirmed an aortic IMH with wall thicknesses of 4 mm and 2 mm in the greater and lesser curvatures, respectively. This IMH extended up to the distal ascending aorta and was new compared with the pre-operative CT. It was considered stable compared to the TEE.

The patient was discharged 6 days post-TAVR. CTA performed 2 months post-TAVR revealed complete resolution of the IMH. The patient remained stable 12 months after discharge.

Discussion

This patient suffered an acute iatrogenic aortic injury related to a TAVR procedure. Prior to the advent of TAVR, risk factors for iatrogenic dissection included advanced age; history of atherosclerosis, diabetes, or systemic arterial hypertension; and prior coronary artery bypass surgery [3]. Patients with iatrogenic dissection related to cardiac surgical procedures generally have involvement of ascending aorta, absence of pain and the intramural hematoma variant of dissection [3]. Recent data for TAVR revealed that patients with LVOT calcification and aggressive annular oversizing may be at risk for aortic root rupture and peri-aortic hematomas [4], although it is uncertain whether risks for these aortic complications similarly predispose individuals to other forms of aortic injury. The patient in this case report had LVOT calcification that may have contributed to the aortic injury during annular expansion, although the valve was not oversized. A spectrum of aortic injuries can occur post-TAVR and include those contained to the aortic wall and those in the periaortic space to rupture. In this case, the aortic injury was an IMH, which is distinguished from a classic dissection via imaging by crescentic or circumferential thickening of the aortic wall related to bleeding within the wall without any evidence of an entry point or intimal flap [5].

The American College of Cardiology/American Heart Association aortic guidelines do not delineate different management strategies for dissection that is iatrogenic in etiology [6]. The European Society guidelines discuss iatrogenic catheter injuries, and although the management for these cases is not standardized, a conservative strategy is frequently applied [7]. These iatrogenic injuries related to percutaneous coronary procedures are frequently managed conservatively and may be sealed with stent placement in cases that originate in the coronary arteries [2]. Patients with iatrogenic aortic syndromes (dissection/hematoma) have similar outcomes to patients with spontaneous dissections, including those who undergo surgical repair [3, 8]. In general, spontaneous IMH is usually treated similarly to typical dissection with emergent surgery as these lesions may evolve and have outcomes similar to those for patients with typical dissections [6]; however, the appropriate treat-

Figure 1. Transesophageal echo (TEE) image acquired immediately post-transcatheter aortic valve replacement (TAVR) indicates crescentic thickening of the ascending aortic wall consistent with intramural hematoma (Panel A). TEE image acquired on first day post-TAVR shows marked reduction in the degree of aortic wall thickening (Panel B).
may be managed conservatively, but if the dissection extends into the sinuses of Valsalva or if the coronary arteries are involved, then surgery is more clearly indicated [1]. In the case presented, conservative management was deemed most appropriate given the lack of pericardial effusion, the involvement of sinus of Valsalva or coronary arteries and the lack of significant aortic dilation.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question

References


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Early Spontaneous Resolution of an Iatrogenic Acute Type A Aortic Dissection

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Abstract

Acute aortic dissection is a rare but devastating complication during cardiac catheterization. We present the case of an elderly female who incurred a Stanford Type A/DeBakey Type I acute aortic dissection extending into the arch vessels and descending aorta likely occurring during right coronary artery engagement for angioplasty. The patient was treated successfully by immediately sealing the entrance of the dissection via the placement of a stent and anti-impulse therapy. Follow-up computed tomography scan showed complete resolution of the dissection within one month.

Key Words

Iatrogenic aortic dissection • Angioplasty • Percutaneous coronary intervention • Complication

Introduction

Acute Stanford Type A aortic dissection (AAD) is a catastrophic medical emergency associated with a high (57%) early mortality without surgical intervention [1]. Iatrogenic AAD (IAAD) may rarely present as a complication during coronary angioplasty [2-3]. We present the case of an IAAD complicating right coronary artery (RCA) angioplasty, for which the entry site of the dissection was stented successfully. Aggressive anti-impulse therapy was instituted, resulting in near complete resolution of the IAAD within 5 days and complete healing within one month.

Case Presentation

A 71-year-old female with hypertension and hyperlipidemia was investigated for symptoms of worsening exertional dyspnea and chest discomfort. A nuclear cardiac stress test revealed moderate focal inferobasal ischemia. Subsequent diagnostic coronary angiography via the right radial artery revealed a chronic total occlusion of the distal right coronary artery (RCA), with left to right collaterals to the posterior descending artery and posterolateral branches. There was no significant coronary artery disease affecting the left coronary system. Percutaneous coronary intervention (PCI) was then attempted on the distal RCA using an Amplatz (AL1) guide catheter but it was too large and the RCA was not engaged. A Judkins (JR4) guide catheter was then employed to engage the RCA and a FineCross and Fielder FC guidewire was passed to the distal RCA. At this point a large aortocoronary dissection was noted on angiography.
Coronary angiography (Figure 1). The dissection involved the RCA ostium and proximal RCA, extending to the thoracic aorta. Upon recognition of this severe complication, a coronary stent was promptly placed across the entry site of the dissection, traversing the RCA ostium and proximal RCA with a small protrusion into the aorta. Subsequent contrast injections were minimized and a Guidezilla™ was inserted to be sure that all contrast injections were well past any possible entry point of the dissection. Intravascular ultrasound showed good stent apposition, complete coverage through the RCA ostium and no evidence of flow outside of the stent. The patient’s hemodynamics remained stable throughout the procedure.

An urgent transthoracic echocardiogram showed no pericardial effusion, normal left ventricular ejection fraction, mild central aortic insufficiency and evidence of ascending aortic hematoma. Computed tomographic angiography (CTA) of the chest confirmed the diagnosis of a Stanford Type A aortic dissection starting at the origin of the RCA, extending to the proximal descending thoracic aorta, at the level of the right pulmonary artery. The false lumen extended to the non-coronary cusp but spared the

Figure 1. Coronary angiography. Panel A. Dissection of the right coronary artery (RCA) ostium causing retrograde dissection and retention of contrast media within the false lumen of the ascending aorta (arrow). Panel B. The entry site of the dissection was sealed successfully by stenting across the proximal RCA into the ostium.

Figure 2. Computed tomographic scan of the chest on Day 1. Panel A. Transverse view at the level of the left coronary ostium showing the false lumen (asterisk) involving the right and non-coronary sinuses but sparing the left coronary sinus. Panel B. Transverse view at the level of the main pulmonary arteries showing the dissection extending to the descending thoracic aorta (arrow). Panel C. Transverse view of the aortic arch showing extensive aortic dissection and calcifications within the aortic wall (arrows).
left coronary cusp (Figure 2). The dissection also extended into the right brachiocephalic and right common carotid arteries, with non-critical stenosis of the proximal right common carotid artery. The ascending aorta was aneurysmal, measuring 4.4 cm maximally in the mid-ascending portion. The descending thoracic aorta measured 3.3 cm at its widest in the proximal descending portion distal to the left subclavian artery. A very heavily calcified ring in the aortic wall, just above the RCA ostium, likely increased the risk of aortic dissection during angioplasty substantially.

On examination, the patient was in no acute pain or distress. She was hemodynamically stable with no neurological deficit. She was admitted to our intensive care unit for aggressive anti-impulse therapy and close monitoring [4]. Conservative management was favored over surgical intervention on the aortic root because of several technical considerations. Firstly, the proximal aortic anastomosis in the vicinity of the large calcified ring would be very difficult and precarious. Secondly, it would be dangerous handling the RCA with the stent extending through the ostium. Thirdly, the significant amount of calcium in the aortic arch would pose a very high embolic risk. We were hoping that intensive anti-impulse therapy would limit the progression of this dissection and promote thrombosis of the false lumen.

Serial transthoracic echocardiograms performed during her hospital stay showed interval stability without evidence of pericardial effusion. CTA performed 4 days after her initial scan demonstrated interval resolution of the aortic dissection (Figure 3A-C), with minimal intramural hematoma extending from the aortic root to the mid descending thoracic aorta. The maximal ascending aortic diameter had decreased to 4.2 cm and the maximal descending thoracic aortic diameter had decreased to 3.1 cm. She remained pain-free throughout her hospital stay and was discharged in stable condition after 6 days. A follow-up CTA one month later showed complete resolution of the dissection (Figure 3D-F). She was asymptomatic with normal effort tolerance and her physical examination was unremarkable.

**Figure 3.** Computed tomographic scan of the chest on Day 5 (Panels A-C) and 1-month post-dissection (Panels D-F). Transverse views at the level of the left coronary ostium (Panel A), main pulmonary arteries (Panel B) and aortic arch (Panel C), showing near-complete resolution of aortic dissection with minimal residual intramural hematoma (arrows). Axial views at the level of the left coronary ostia (Panel D), main pulmonary arteries (Panel E) and aortic arch (Panel F) showing complete resolution of the dissection.
Discussion

The incidence of IAAD arising as a complication of coronary catheterization ranges from 0.02% to 0.06% [2, 3]. In challenging cases involving PCI to chronically occluded vessels, the risk of IAAD has been reported to be 1.9% [5]. Despite the potentially devastating nature of this complication, no clear guidelines exist regarding its optimal management. Dunning et al. [2] previously described a classification system for these dissections based on the degree of aortic involvement: Class 1 included dissections limited to the coronary cusp; Class 2 included dissections extending less than 40 mm up the ascending aorta whereas Class 3 included those extending distally for more than 40 mm. The authors recommended treating Class 1 and 2 lesions with stenting and/or medical therapy, and Class 3 surgically. Surgical management is the treatment of choice for spontaneous AAD [1]. However, emergent surgical correction of IAAD following PCI is particularly challenging due to concomitant anticoagulation used during PCI and varying degrees of myocardial ischemia resulting from co-existing coronary artery disease.

Various reports have described the merits of treating even extensive PCI-related IAADs non-surgically, with coronary stenting and/or conservative management [3, 6, 7]. In a series of 74 patients with cardiac catheterization induced aortocoronary dissections (20% with Dunning Class 3 dissections), Núñez-Gil et al. [3] demonstrated good results of stenting and/or conservative therapy, with 69 patients (93%) remaining complication-free at a median follow-up of 5 years. Only 3 patients (4%) required cardiac surgery and 2 (3%) succumbed to sequelae of aortic dissection during early follow-up. Follow-up imaging revealed a completely healed aorta, similar to our case, in 5 patients (7%).

The importance of abrogating the propagation of the dissection by sealing its entry point in the coronary artery via stenting have been highlighted in previous reviews of catheter-induced aortocoronary dissections [6, 7]. Shah et al. [6] described a series of 86 patients, of whom 65 patients (76%) underwent stenting and/or conservative therapy with 3 deaths (3%). The remaining 21 patients (24%) underwent aortic repair with or without coronary artery bypass grafting. Amongst those who received surgical treatment, 3 patients (14%) died. Carstensen et al. [7] reported a series of 67 patients, of whom 55 (82%) underwent stenting and/or conservative therapy. Two deaths (4%) occurred in the group treated non-surgically and 3 deaths (25%) occurred within the surgically treated group.

The majority of patients with spontaneous AAD have inherently diseased aortic walls. In contrast, apart from age-related changes, patients with IAAD may have relatively normal aortic walls, which could possibly permit better healing once the entry site of the aortic dissection is sealed. Also, the presence of advanced atherosclerosis could limit the dissection plane. This may explain the tendency for patients with catheter-induced IAAD to respond well to stenting and/or conservative therapy.

This case highlights the role of non-surgical management of IAAD, especially in the setting of high-risk surgical candidates with unfavorable anatomy or severe comorbidities. Despite the impressive nature of our patient’s dissection, there was no compromised perfusion, significant aortic insufficiency, or evolving pericardial effusion allowing meticulous observation and aggressive medical management thereby avoiding a very high risk surgery. There was a rapid recovery with spontaneous improvement beginning within days and complete resolution by CT at one month.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.
References


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Iatrogenic Aortic Dissection: Review of the Literature

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Key Words
Iatrogenic aortic dissection • Dissection

AORTA received almost simultaneously the four separate reports (included in this issue) of iatrogenic aortic dissection following coronary angioplasty [1-3] and transaortic aortic valve replacement [4]. Medical management was successful in all these cases. In an ad hoc review of the literature, we have tabulated the currently available case series of iatrogenic aortic dissection (Table 1). The thrust of these case reports [1-4] and literature review (Table 1) points toward the adequacy of medical management in most cases. For dissections induced by coronary angioplasty, immediate sealing of the inciting proximal coronary tear by stenting appears important in securing safe medical outcome.

Conflict of Interest
The authors have no conflict of interest relevant to this publication.

Table 1. Summary of available case series on iatrogenic aortic dissection.

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<tr>
<th>Authors &amp; Year</th>
<th># Patients with IAAD*</th>
<th>Case of Dissection</th>
<th>Type/Extent of Dissection</th>
<th>Treatment &amp; Outcomes</th>
<th>Authors’ Recommendations</th>
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<td>Dunning et al. 2000 [5]</td>
<td>9, Incidence= 0.02% in patients with acute MI = 0.19%</td>
<td>In all 9 cases a RCA dissection extended retrograde to the aortic root. - In 44% of cases Amplatz guide catheters were employed.</td>
<td>Proposed a classification system for IAAD: Class 1: (n= 4) Focal dissection restricted to the ipsilateral cusp. Class 2: (n=3) Involving the cusp and extending up the ascending aorta &lt; 40mm. Class 3: (n=2) Involving the cusp and extending up the ascending aorta &gt; 40mm.</td>
<td>- All 4 Class 1 cases were successfully treated with coronary stenting and medical management. - Class 2: 1 patient successfully treated with emergency CABG, the other 2 with coronary stenting and medical management. - Class 3: Both underwent emergency surgery and died. Both had presented originally with an acute MI.</td>
<td>- Class 1 and Class 2 dissections are best treated by sealing the entry point in the coronary artery by means of stenting. - Surgical intervention is usually warranted for Class 3 dissections.</td>
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* IAAD = iatrogenic (specifically cardiac catheterization induced) acute Type A dissection.
Table 1. (Continued)

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<th>Authors &amp; Year</th>
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<td>Yip et al. 2001 [6]</td>
<td>7, Incidence= 0.05%</td>
<td>- 6 patients had a retrograde IAAD from the RCA to the coronary sinus and 1 from the LAD to the coronary sinus - Caused by balloon inflation in 5 cases, guiding catheter (6 Fr) in 1 and thrombectomy system in 1.</td>
<td>- IAAD localized (Group L) to the coronary sinus in 5 patients and extended into the ascending aorta (Group AA) in 2.</td>
<td>- All 5 cases in Group L managed successfully by coronary stenting. A 6-month follow-up Thallium scan showed a perfusion defect in 2 patients who also had angina and restenosis of the RCA on coronary angiography. The other 3 were asymptomatic and had normal scans. - Stenting was unsuccessful in 1 patient in Group AA who then refused emergency surgery and died. The other patient (LAD aortocoronary dissection) underwent successful emergency surgery.</td>
<td>- Immediate coronary stenting to seal the entry site of the aortocoronary dissection and prevent its expansion should be performed. - Surgical intervention is necessary for patients with severe IAAD and complications. Coronary stenting is still beneficial in stabilizing these patients prior to surgery.</td>
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<td>Carstensen and Ward 2008 [7]</td>
<td>4 cases by the authors and a review of 63 cases reported in literature.</td>
<td>Authors’ Cases: - 2 due to the guide catheter, 1 due to balloon and 1 due to wire. RCA was PCI target in 3 cases, LCX in 1. Literature Review: - Guide catheter in the majority, unclear in several others.</td>
<td>Authors’ Cases: - 2 extended to the mid-ascending aorta, 2 limited to the coronary sinuses. Literature Review: - In 37 (59%) cases the dissection was limited (Group L) to the coronary sinus. - In 26 (41%) cases there was rapid extension (Group RE) above the annulus or aortic valve involvement.</td>
<td>Authors’ Cases: - Immediate ostial stenting upon recognition of the dissection. - 10-32 month follow-up. Repeat CT/TEE showed resolution of the dissection in all cases with no complications. Literature Review: - Overall: Conservative Therapy n=15 (2 deaths); Stenting n=36 (0 deaths); Surgery n=12 (3 deaths). - 11 cases of Group L were managed conservatively, 25 by stenting (1 had dissection progression despite stenting so had surgery) and 1 underwent immediate surgery. - 4 of 26 cases in Group RE were managed conservatively; 2 died suddenly. In 13 cases stenting was done but this failed in 2 and they had surgery. 9 underwent surgery; of these 3 died all of whom were having PCI for an acute MI.</td>
<td>- Ostial stenting should be performed promptly upon recognition of an aortocoronary dissection so as to seal and check the expansion of the dissection.</td>
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* IAAD = iatrogenic (specifically cardiac catheterization induced) acute Type A dissection.
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<th>Authors’ Recommendations</th>
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<td>Núñez-Gil et al. 2015 [8]</td>
<td>74, Incidence = 0.06%</td>
<td>- Catheter in 68 patients (91.8%) [6F size in 65 (87.8%), 0.035-in wire in 4.</td>
<td>- Dunning Class 1 in 45 patients (60.8%); Class 2 in 12 (16.2%) and Class 3 in 15 (20.3%).</td>
<td>- 36 patients managed conservatively, 35 underwent stent placement and 3 referred for surgery.</td>
<td>- After stabilization of the early critical phase of the IAAD, complete healing of the aorta occurs and no complications are observed in the long term.</td>
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<td>- RCA was engaged in 42 patients (56.8%), the LCA in 30 (40.5%).</td>
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<td>- 2 early deaths due to cardiogenic shock.</td>
<td>- The entrance of the dissection in the coronary artery should be closed by placing a stent.</td>
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<td>- Dunning Class 1 in 45 patients (60.8%); Class 2 in 12 (16.2%) and Class 3 in 15 (20.3%).</td>
<td></td>
<td>- During long-term follow-up (median = 51.2 months), no patient suffered any sequelae of IAAD.</td>
<td>- Retrograde IAAD not involving a coronary may be treated conservatively and monitored closely via serial imaging.</td>
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<td>- 36 patients managed conservatively, 35 underwent stent placement and 3 referred for surgery.</td>
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<td>- The entrance of the dissection in the coronary artery should be closed by placing a stent.</td>
<td>- Patients with major symptoms, expanding dissections and coronary flow obstruction may need surgical intervention.</td>
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<td>- Confined to the root in 33 (38.8%) patients, extending to the ascending aorta in 35 (41.1%), the aortic arch in 11 (12.9%) and the descending aorta in 6 (7.1%).</td>
<td></td>
<td></td>
<td>- The majority of patients, including those with more extensive dissections (Dunning Class 3) can be managed conservatively or by the placement of a stent.</td>
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<td>Shah et al. 2016 [9]</td>
<td>2 cases by the authors and a review of 86 cases reported in literature.</td>
<td>- Catheter trauma in 34 (54%) [sizes specified in 23: 5 cases occurred due to 6F, 12 due to 7F and 6 due to 8F], balloon inflation in 15 (23.8%) and contrast injection in 13 (20.6%).</td>
<td>- 46 (53.5%) patients treated by stenting only, 26 (33.8%) surgically and 19 (22.1%) conservatively.</td>
<td>- The majority of patients, including those with more extensive dissections (Dunning Class 3) can be managed conservatively or by the placement of a stent.</td>
<td>- The patient’s hemodynamic status and how quickly the entry point of the dissection is closed by stenting to prevent its progression, determine treatment measures.</td>
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<td>- RCA was intervention target in 66 patients (76.7%), the LAD in 10 (11.6%), the LCx in 6 (7%), the LMCA in 3 (3.6%), and the obtuse marginal branch in 1 (1.2%).</td>
<td>- 6 patients (4 with DeBakey 2 and 2 with DeBakey 1 IAAD) died: 3 were conservatively treated (cause of death in 1 unknown, 1 refused surgery after unsuccessful stenting of dissection origin and suffered re-infarction and the 3rd had dissection extension into the descending aorta and died 4 months later of cardiogenic shock) and 3 were surgically treated (2 died due to post-op multi-organ failure and the 3rd could not be weaned off CPB).</td>
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* IAAD = iatrogenic (specifically cardiac catheterization induced) acute Type A dissection.

References

Elefteriades, J. A. et al.

Simplified Approach for Repair of Early Pseudoaneurysm of the Left Coronary Button Following Composite Graft Due to Acute Type A Aortic Dissection

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Abstract
We present a simplified surgical technique that was performed on a 37-year-old man who presented with a pseudoaneurysm of the left coronary ostium two months after repair of acute Type A aortic dissection with a composite graft. Intraoperatively, the surgical sites showed extreme adhesions. The leakage at the level of the coronary suture line was exposed from inside the aortic graft. Repair was performed using 7.0 polypropylene sutures, and the postoperative course was uneventful. The patient was discharged on postoperative day six without further complications.

Key Words
Aortic dissection • Composite graft • Coronary button • Pseudoaneurysm

Introduction
Pseudoaneurysm is a rare but challenging complication that occurs at the level of aortic anastomoses or coronary reimplantation suture lines following composite graft replacement [1]. The etiology of pseudoaneurysm includes weak tissue secondary to aortic dissection or connective tissue disease and technical failure during anastomosis construction [2, 3]. Pseudoaneurysm repair requires surgical intervention in the vast majority of cases, although exceptional cases can be treated via an interventional technique. The aim of this brief report is to present a simplified approach for the treatment of a pseudoaneurysm of the left coronary orifice presenting in the early postoperative period following composite graft replacement of the aortic root for Type A aortic dissection.

Case Presentation
The 37-year-old patient had undergone composite graft replacement for acute Type A aortic dissection 2 months earlier at another university hospital in Switzerland. At initial presentation, the patient suffered from pericardial tamponade, had to be intubated during transportation, and underwent emergency surgery due to unstable hemodynamics.

Initial repair was performed without complication and consisted of the implantation of a composite graft with a mechanical valve (St. Jude Medical, St. Paul, MN, USA). The distal anastomosis was performed with an open aortic arch technique during a brief period of moderate hypothermic circulatory arrest using selective antegrade cerebral perfusion, involving perfusion catheters in both carotid arteries, for brain protection. Re-institution of cardiopulmonary...
bypass was achieved via cannulation of the sidearm of the aortic graft (Vascutek© Anteflow, Renfreshire, UK). Coronary reimplantation was performed with a modified button technique using 6.0 polypropylene sutures and a pericardial strip as reinforcement. Intra-operative transesophageal echocardiography (TEE) performed at the conclusion of the procedure was normal.

The immediate postoperative evolution was uneventful, and the patient was discharged on postoperative day 8. An initial computed tomography (CT) scan was performed four weeks after discharge and revealed extravasation of contrast medium, indicating an 8 mm pseudoaneurysm behind the aorta and close to the left coronary artery origin. The initial decision was to treat conservatively by lowering the systolic blood pressure to values between 80 and 100 mm Hg; however, a second CT scan 4 weeks later revealed that the pseudoaneurysm had increased in size to 17 mm (Figure 1A), although the patient remained asymptomatic. At this point, correction of the pseudoaneurysm was planned as soon as possible.

Figure 1. Panel A. Computed tomography (CT) scan performed 2 months after initial surgery showing a pseudoaneurysm (arrow) close to the left coronary button anastomosis and posterior to the aortic root. Panel B. Preoperative echocardiography showing the perfused pseudoaneurysm (arrow) of the left coronary button anastomosis. Panel C. Intraoperative transesophageal echocardiography after repair of the pseudoaneurysm (red arrow = smaller pseudoaneurysm without perfusion; white arrow = left main coronary artery). Panel D. Postoperative CT scan 1 month after repair of the pseudoaneurysm showing normal anatomy at the level of the left main coronary artery (arrow).
Surgical Technique

Prior to reopening the sternotomy, the external iliac artery and vein were exposed. Preparation of the mediastinal and intrapericardial sites was very difficult due to the extremely strong adhesions between the vascular prosthesis and the adjacent structures (mainly the pulmonary artery but also the right atrium and the superior vena cava). For this reason, we decided to cannulate the femoral artery and vein using the Seldinger technique. The patient was cooled to a core temperature of 28°C. Shortly before hypothermic arrest, pentothal was administered, and then the cardiopulmonary bypass was interrupted without clamping the prosthesis, as mobilization of the prosthesis would have considerably prolonged the time of the bypass. The previous anastomosis between the arch prosthesis and the composite graft was opened (Figure 2A), and the ascending aortic graft was prepared from inside to facilitate dissection from the surrounding structures (e.g., pulmonary artery). Then, the graft was clamped, and cardiopulmonary bypass was reinstated. The patient was then rewarmed after only 5 min of hypothermic arrest. During this period, inspection of the left coronary orifice from inside the aortic prosthesis was performed. A small leak was identified at the lower part of the coronary button suture line. This leak was repaired with two separate U-stitches from inside of the coronary button anastomosis, and additionally, the previous suture line was tightened with an additional stitch (Figure 2B-D). Cross-clamp time was only 22 minutes.

Intraoperative TEE was performed before and after repair (Figure 1B and C). The patient’s immediate postoperative evolution was uneventful, and he was discharged on postoperative day six. A CT scan performed at four weeks did not show any perfusion into the pseudoaneurysm cavity, which had decreased in size (Figure 1D).

Discussion

Here, we describe a simplified technical approach to pseudoaneurysm of the left coronary orifice during the early recovery following composite graft replacement for Type A acute aortic dissection. This complication is a rare but challenging event that almost always requires surgical repair even though the dense adhesions behind the aorta likely prevent rupture. Another potential complication of the pseudoaneurysm is compression of the left main coronary artery due to expansion of the aneurysm.

The etiology of the pseudoaneurysm aneurysm in our patient was most probably weakening of the continuous polypropylene suture. Other potential causes like infection or tissue necrosis secondary to too gen-

Figure 2. Schematic illustration of the situation before re-exploration. Composite graft prosthesis and separate Vaskutek Anteflow for the distal ascending aorta (open arch technique) are shown. Pseudoaneurysm (arrow) is shown at the level of the left coronary button (Panel A). The repair technique involved opening of the previous anastomosis between the composite graft and the ascending-arch prosthesis, and the pseudoaneurysm was fixed from the inside. A small loop of the previous polypropylene suture was discovered to be loose (Panel B). First, a U-stitch was made close to the loop and tied. One end of the suture was cut and passed through the loop (Panel C). Finally, the loop was eliminated by tying both sutures together (Panel D).
The use of glue seemed unlikely since the coronary button looked completely normal.

Diagnosis of a pseudoaneurysm is made by echocardiography and/or CT scan, which should always be performed in the first three months following repair of acute Type A aortic dissection. TEE may help to localize the exact position of the leakage and to confirm intraoperatively that the problem has been solved.

In the present case, moderate hypothermic circulatory arrest helped to save time by greatly facilitating control of the aortic graft. After incision of the graft in its anterior region, the transection was performed under visual control, and circular preparation of the graft was possible without injury to the pulmonary artery or the superior vena cava. Once the cranial part of the prosthesis was clamped, the cardiopulmonary bypass was restarted, and aneurysm repair was performed from inside during rewarming.

Complete reconstruction of the anastomosis of the left coronary artery ostium to the composite graft is rarely necessary as small leakages can usually be repaired by just a few single stitches from inside the aortic graft. In the presence of larger defects in the suture continuity, particularly in case of late presentation, direct repair may not be feasible. In this case, internal inspection may be useful for circumferential dissection, and repair may require either xenopericardium to reinforce the tissue or complete removal and reconstruction of the anastomosis, either directly with interposition of a short venous graft or with a classical Cabrol modification if the coronary artery button cannot be sufficiently mobilized.

The technique we used in this case is safe because it does not require exposure of the coronary button from outside of the graft behind the aorta. Furthermore, this technique can be applied both early and late following composite graft repair of a dehiscence of the coronary artery button anastomosis.

**Conflict of Interest**

The authors have no conflict of interest relevant to this publication.

**References**


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Minimalist’ Trans-Aneurysmal Approach to Coronary Button Pseudoaneurysm

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Key Words
Iatrogenic aortic dissection • Coronary Button Pseudoaneurysm

The case report by Carrel and colleagues [1] should help surgeons approaching pseudoaneurysms of the coronary button anastomoses after composite graft replacement of the aortic root.

We find that such coronary button false aneurysms are uncommon. We have encountered one such false aneurysm among over 500 composite graft root replacements performed (Figure 1). This was in a patient later found to harbor a pathogenic mutation in the TGFBR2 gene (causative of Loeys-Dietz syndrome), which might have contributed to additional tissue weakness. We have repaired several such aneurysms referred from other centers. We believe that careful tightening of the coronary button suture line is of critical importance in avoiding such problems.

In our experience, these anastomotic pseudoaneurysms are seen more commonly at the right coronary artery button. These present a special problem, as there is often an accompanying large pseudoaneurysm located anteriorly under the breastbone and in front of the aorta.

Like Carrel and colleagues [1], we also expose the femoral artery and vein for safety prior to redo sternotomy. Once safely through the bone, we dissect just enough to permit spreading the retractor (Figure 2). We leave the pseudoaneurysm intact. We cannulate femorally and assume cardiopulmonary bypass. If we have been able to surround the upper aorta (scenario 1), we do not need deep hypothermic circulatory arrest (DHCA). We simply clamp the aorta and move on. If surrounding the upper aorta is not feasible (scenario 2), we go on to deep hypothermic circulatory arrest (we employ a low threshold for DHCA to avoid difficult to control hemorrhage). Either with the aorta clamped (scenario 1) or on DHCA (scenario 2), we open the false aneurysm (Figure 3). Once the clot is scooped away, the RCA button anastomosis is usually easily exposed and well-visible (Figure 4). Like Carrel...
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and colleagues [1], we find that tightening the anastomosis and placing one or two stitches suffices. In this case (RCA pseudoaneurysm) the sutures are all placed from outside the aortic graft, without ever opening it. We then rewarm and wean from cardiopulmonary bypass.

The two anatomic lesions, LCA and RCA pseudoaneurysm, present different anatomic challenges. In LCA pseudoaneurysm, the accompanying clot-filled false aneurysm is posteriorly located and is not even exposed surgically. In RCA pseudoaneurysm, the clot-filled false aneurysm covers the aortic region and impairs aortic and cardiac access. The surgeon not only “sees” the clot-filled false aneurysm, but traverses it to accomplish the repair.

Performing RCA pseudoaneurysm repair through the pseudoaneurysm simplifies the procedure immensely, obviating tedious and dangerous dissection to access and dissect cardiac structures directly.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question
References


The following pages summarize and review this issue’s articles for an audience without a background in medicine or research.

Natalia D. Gavriliuk et al.: “Asymmetric Dimethylarginine in Patients with Ascending Aortic Aneurysms”

Ascending thoracic aortic aneurysm is a disease in which patients develop a potentially life-threatening dilatation of their body’s main vessel, the aorta, in their chest right at its origin at the heart. There probably is a variety of causes for ascending aortic aneurysm, many of them unclear. Natalia D. Gavriliuk et al. studied the level of a molecule called “Asymmetric dimethylarginine (ADMA)” in the blood of 86 patients with ascending aortic aneurysm and 18 healthy patients. ADMA might have impact on the function of the inner layer of the vessel wall. They concluded that ADMA was higher in patients with larger aortic diameters, in smokers, and was associated with kidney function. It is important to note that a statistical association does not mean that there is a causative relation between both facts. Since this small study was a pilot study, further investigations are necessary to understand the role of ADMA in aortic aneurysms.

Case Reports

Aurélien Roumy et al.: “Spontaneous Regression of a Large Iatrogenic Dissection of the Ascending Aorta”

Roumy et al. report a case of a patient who underwent a procedure to open up one of the vessels that supplies the heart muscle with blood. During this procedure, a wire was inserted into the heart. This wire caused a potentially life-threatening disruption (“dissection”) of the layers of the wall of the aorta, the body’s main vessel. The patient was stable and had no symptoms. Because the tear was very small and it was suspected that it might seal spontaneously, it was decided not to perform surgery. After three days, an imaging study showed regression of the dissection. There were no further complications during the following year. The authors therefore suggest that certain types of procedure-related aortic dissection can be treated medically without surgery.

Derrick Y. Tam et al.: “Conservative Management of Extensive Iatrogenic Aortic Dissection”

Tam et al. report a similar case to the case presented by Roumy et al. regarding the treatment of an aortic dissection, a disruption of the layers of the wall of the aorta, the body’s main artery, which has been caused by a procedure to treat calcifications of the coronary arteries. The coronary arteries supply the heart muscle with blood and their occlusion can cause a heart attack. To open the occlusion, a small tubed stent graft can be inserted in the vessel with the help of a wire that is introduced through a vessel in the groin or wrist and advanced through the aorta. In rare cases, this procedure can damage the wall of the aorta. Usually, aortic dissection is treated surgically to prevent rupture or other complications. In the presented case, it was decided to refrain from surgery and imaging studies during follow-up showed resolution of the dissection. Tam et al. therefore suggest, similar
to Roumy et al., that some procedure-related dissections can be treated without surgery.

Taylor Thomas et al.: “Transient Aortic Intramural Hematoma Complicating Transaortic Valve Replacement”

Thomas et al. report a case of a patient who underwent transaortic valve replacement, a technique in which a folded heart valve prosthesis is inserted through a puncture in a vessel in the groin and then expanded in the position of the aortic valve, which serves as the gate between the heart and the aorta. In this case, the patient developed a hematoma in his aortic wall (called “intramural hematoma”) shortly after the procedure. An intramural hematoma is usually treated surgically with aortic replacement, but in this case the surgeons decided to wait. A follow-up imaging study showed resolution of the hematoma, and no further operation was necessary. While this patient did well, the appropriate treatment strategy in intramural hematoma as a complication of a procedure is still unclear. It has to be decided on an individual basis depending on the patient’s stability, risk factors and the extent and location of the hematoma.

Mohammad A. Zafar et al.: “Early Spontaneous Resolution of an Iatrogenic Acute Type A Dissection”

Zafar et al. discuss a case similar to those reported by Tam et al. and Roumy et al. In the presented case, a patient developed an aortic dissection (a disruption of layers of the vessel wall of the body’s main artery, the aorta) after a minimally invasive procedure aiming to reopen an occluded coronary vessel. Coronary vessels supply the heart muscle with blood, and their occlusion can cause a heart attack. The entry point of the blood flow was inside the coronary vessel, which is why it was decided to occlude that tear with a small tubed stent prosthesis. The occlusion of the entry tear stopped further blood flow between the vessel layers and led to resolution of the aortic dissection on imaging after one month. This case similarly highlights the relevance of a non-surgical treatment of these patients, especially if they are high risk surgical candidates.

John A. Elefteriades et al.: Editoral Comment “Iatrogenic Aortic Dissection: Review of the Literature”

Since this issue contains four case reports on the treatment of “iatrogenic aortic dissections”, this editorial comment provides an overview of the literature that has been published on this subject so far. An “iatrogenic aortic dissection” is an aortic dissection (a potentially life threatening disruption of the layers of the vessel wall of the aorta, the body’s main artery), that has not occurred spontaneously but has been caused by another procedure performed on the patient. This can happen for example during cardiac surgery or during a procedure called “percutaneous coronary intervention (PCI)” which is a minimally invasive procedure to open up occluded coronary vessels in the heart to treat or prevent a heart attack. The majority of the studies and case reports suggest that these patients can often be treated without surgery. If the dissection is caused by an injury to a coronary vessel, it is important to try and seal the injury with a small tubed stent graft prosthesis (“aortic stent”) to stop blood flow to the dissection.

Thierry Carrel et al.: “Simplified Approach to Repair Early Pseudoaneurysm of the Left Coronary Button Following Composite Graft Because of Acute Type A Dissection.”

Carrel et al. describe a case of a young patient who had undergone surgery for acute Type A dissection, a potentially life threatening disease in which the wall layers of the body’s main artery, the aorta, disrupt. In this case, the dissection involved the origin of the aorta and the aortic valve, which constitutes the gate between the heart and the aorta. During the initial surgery, valve and aorta were replaced with a tubed graft prosthesis that is connected to a heart valve prosthesis. Since the coronary arteries, which supply the heart muscle with blood, arise from the aorta right after the aortic valve, they need to be connected to that tubed graft as well during surgery. In the presented case, the patient was found to have a leakage from one of the connections where a coronary artery was sewn into the graft two months after surgery. He had to undergo reoperation because the leakage could rupture or compress the coronary artery. This surgery is known to be very difficult. Carrel et al. report a technique in which they opened the prosthesis and repaired the leakage with stiches from the inside. The patient recovered well and developed no further leakage.

John A. Elefteriades et al.: Editorial Comment “Minimalist Trans-Aneurysmal Approach to Coronary
Button Pseudoaneurysm”

This editorial comments on the case report by Carrel et al. Carrel et al. who reported a case of a patient who had developed a leakage at the site where a coronary vessel, one of the vessels who supply blood flow to the heart, had been attached to a graft prosthesis replacing a diseased aorta (the body’s main vessel). This leakage can cause a pseudo-aneurysm, a blood-filled pocket, with potentially dangerous complications, and therefore usually needs surgical repair. In the case described by Carrel et al., the leakage concerned the left coronary button that is difficult to reach during surgery. They opened up the prosthesis and repaired the leakage with stitches from the inside. Elefteriades et al. describe and illustrate a technique for repair in case the leakage concerns the right coronary artery. The right coronary artery suture line is easier exposed and can be reached and repaired from the outside by opening the pseudo-aneurysm.
List of Upcoming Meetings

December 2016

1. International Conference for Innovations in Cardiovascular Systems
   December 4-6, 2016
   Tel Aviv, Israel
   Meeting information available at: 2016.icimeeting.com

2. 13th European Cardiology Congress
   December 5-6, 2016
   Madrid, Spain
   Meeting information available at: cardiology.conferenceseries.com/europe

January 2017

1. 35th Annual International Symposium: Clinical Update in Anesthesiology, Surgery and Perioperative Medicine
   January 15-20, 2017
   Cancun, Mexico
   Meeting information available at: www.clinicalupdateinanesthesiology.org

2. Controversies and Updates in Vascular Surgery
   January 19-21, 2017
   Paris, France
   Meeting information available at: cacvs.org

3. 53rd Annual Meeting of the Society of Thoracic Surgeons and STS/AATS Tech-Con 2017
   January 21-25, 2017
   Houston, Texas
   Meeting information available at: www.sts.org/education-meetings/sts-annual-meeting

4. STS/CTSNet Career Fair at the 53rd Annual Meeting
   January 22-24, 2017
   Houston, Texas
   Meeting information available at: www.ctsnet.org/events/2017-sts-and-ctsnet-career-fair