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32.1 ± 5.4 minutes vs 56.3 ± 8 minutes

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Abstract
Smoking increases the risk of abdominal aortic aneurysm (AAA) in both humans and mice, although the underlying mechanisms are not completely understood. An adventitial aortic antigen, AAAP-40, has been partially sequenced. It has motifs with similarities to all three fibrinogen chains and appears to be connected in evolution to a large family of proteins called fibrinogen-related proteins. Fibrinogen may undergo non-enzymatic nitration, which may result from exposure to nitric oxide in cigarette smoke. Nitration of proteins renders them more immunogenic. It has recently been reported that anti-fibrinogen antibody promotes AAA development in mice. Also, anti-fibrinogen antibodies are present in patients with AAA. These matters are reviewed in the overall context of autoimmunity in AAA. The evidence suggests that smoking amplifies an auto-immune reaction that is critical to the pathogenesis of AAA.

Introduction
Compared with the relatively small effects of genetic mutations or polymorphisms on the risk for abdominal aortic aneurysm (AAA), smoking presents a much greater risk by as much as an order of magnitude. For example, the risk-odds ratio for another polymorphism on 9p21 is 1.3 [2]. By contrast, the risk-odds ratio for heavy smoking is 12.0 [3], comparable only to the risks of age and male sex. Smoking also promotes aneurysm formation in laboratory mice [4, 5]. A molecular explanation for the effect of smoking has been proposed [6]. The purpose of this communication is to explain the hypothesis that nitric oxide (NO) in tobacco smoke nitrates a protein related to the fibrinogen superfamily in the aortic adventitia and thus enhances its antigenicity. In particular, I discuss four factors that are often associated with diseases of autoimmunity [7, 8]: genetic susceptibility, inflammation, matrix metalloproteinases (MMPs), and antibodies and autoantigens.

Human Genetics of AAA
Clifton reported three brothers affected with AAA in 1977 [9]. In 1978, the author operated on a friend and colleague to repair an AAA and bilateral popliteal artery aneurysms on separate occasions. The patient was otherwise healthy, fit, normotensive, and normcholesterolemic. His angiographic studies were unremarkable except for his aneurysms. There was no detectable atherosclerosis. His mother had died of a ruptured AAA, raising the question of whether a genetic predisposition was at work. In 1980, we reported on numerous differences between groups of patients undergoing aortic surgery for AAA versus occlusive (OCC) disease [10]. These differences (age,
sex, other features) provided a basis for questioning the notion that atherosclerosis causes AAA. These anecdotes are just a few factors that drew me into a career-long interest in the human genetics of AAA and the pathobiology of the disease.

Our first effort at clinical genetics in 1984 was a small study of patterns of inheritance in 14 families with a total of 41 affected members [11]. The conclusion from this analysis was that there might be X-linked and autosomal dominant forms of the disease. Extending this study to include a total of 50 families, we concluded that if there was only a single locus explaining the inheritance of AAA disease, it was likely to be autosomal dominant [12].

Many confirmations of the hypothesis of a genetic association followed. The first study with a proper control group was performed by Johansen and Koepsell [13], who reported on the family histories of 250 AAA patients and 250 control patients. Whereas 19.2% of AAA patients reported an affected first-order relative, only 2.4% of control patients were aware of an affected relative. The possibility that being born into a smoking family might have a “paragenetic” effect was not considered in the early studies. I use the neologism “paragenetic” to suggest that a phenotype may run in families without a genetic basis. For example, if both parents are non-smokers and disapprove of smoking, it seems less likely that their children will take up the habit.

Initial efforts to root the genetic hypothesis in a molecular basis involved the candidate gene approach [14]. Our first contribution implicated the TIMP-1 gene [15], which was subsequently confirmed by a larger study [16]. Another interesting candidate was the major histocompatibility complex molecular locus DR-15 (originally protein DR-2) [17, 18]. Other investigators also showed interest in the major histocompatibility complex [19]. In addition, we found an identical amino acid substitution in the ferritin light chain gene in 2 of 19 AAA patients [14].

Collagen XI-alpha 1 was of special interest to our laboratory for multiple reasons. It was overexpressed 38-fold in a AAA-derived fibroblast cell line (a clear outlier) relative to a cell line from normal aortic fibroblasts. It was subject to alternative slicing, with cartilage- and aorta-specific variants in exon 6. Furthermore, it was selectively expressed in the adventitia of the normal aorta. Sequencing of exon 6 revealed a heterozygous G>T signal 70 bp upstream from exon 6 in 14 of 19 consecutive AAA samples [14].

A plethora of additional genes were proposed by others, and the situation became more complicated. In 2007, Sandford et al. summarized a decade of effort [20], concluding that “while the candidate gene approach has led to significant advances in understanding the pathogenesis of AAA, it is unlikely that a single gene polymorphism will hold the key to aneurysm formation. Whole gene studies are likely to be required…”. These studies are now referred to as genome wide association studies (GWAS).

An advantage of GWAS is that no knowledge of AAA pathobiology is required, as it is a brute force approach. A disadvantage is that it is inherently large-scale and resource-intensive. A recent meta-analysis of six GWAS datasets with a total of 10,204 AAA patients and 107,766 control patients had 116 multinational co-authors [21]. Four novel single nucleotide polymorphisms (SNPs) were identified and added to a list of five others identified from previous studies. The pathobiological roles of all nine SNPs in AAA disease remain unknown. The summary situation is mostly unchanged since the review by Saratzis et al. in 2015 [22], which concludes that AAA represents a “multifactorial disease, with the likelihood that there are multiple variants of very low effect contributing to the overall genetic disease risk.” Thus, the genetic approaches that seemed so promising 25 years ago have failed to uncover a “smoking gun.”

This discussion would be incomplete without mentioning that we are now entering a “post-GWAS” era [23]. Another problem with GWAS is that the variations detected so far occur in non-coding DNA sequences, so their significance is not obvious. An alternative has been adoption of the epigenetic approach. Epigenetics refers to stable differences in gene expression that are “not attributable to DNA sequence variation” [24]. Joehanes et al. [25] report that the “epigenetic signatures of cigarette smoking” reflect “a broad impact on genome-wide methylation.” In addition to methylation, the study of microRNAs is another example of an epigenetic modification. No doubt there will be interesting developments in these areas in the future.
The Role of Inflammation

1986, Beckman proposed that autoimmunity plays a role in the pathogenesis of AAA [26]. Beckman observed an infiltration of plasma cells in 31 of 156 AAA specimens from patients who were not thought on clinical grounds to be examples of the "inflammatory variant" of aneurysms. He speculated that there was an immune reaction against atherosclerotic elements in the AAA wall, consistent with the view at that time that atherosclerosis causes non-specific aneurysms (the term "non-specific" is used because the Joint Committee on Reporting Standards, sponsored by the Society of Vascular Surgery and International Society for Cardiovascular Surgery, recommended in 1991 that this terminology replace the conventional usage "atherosclerotic aneurysm" due to insufficient evidence that atherosclerosis actually caused the disease [27]).

Another example of a Th2 (allergic or autoimmune) response appeared in 1990 [28], when I was invited to write a book chapter on the pathology of AAA. The assistance of a pathologist at Yale University School of Medicine was enlisted (G. J. W. Smith), and a "séance" was arranged to compare a tray of AAA slides with a tray of atherosclerotic aortic slides. One of the most conspicuous findings was the virtual absence of iron-hematoxylin-reactive elastin in the media of AAA specimens. Another finding was that there was inflammatory infiltrate in AAA at the junction of the outer media with the adventitia. In some cases, this infiltrate was so impressive that our pathologist remarked that it was reminiscent of that seen when syphilis was common. The infiltrate was primarily plasmacytic, and there were Russell bodies within areas of inflammation.

Russell bodies are eosinophilic aggregates of immunoglobulin G (IgG) seen in plasma cells undergoing excessive synthesis of antibodies in autoimmune conditions. They reflect an overstuffed endoplasmic reticulum. The role of inflammation in the etiology of AAA was further elaborated by Brophy et al. in 1991 [29]. A conspicuous mononuclear infiltrate was present in 8 of 10 specimens, primarily located at the adventitial/medial junction. The presence of Russell bodies was confirmed. In addition, large quantities of immunoglobulins were extractable from AAA tissue by affinity to protein A.

Evidence for a Th-1 (cytotoxic) response appeared in 1990, when Koch et al. formally proposed that "immunophenotypic analysis suggested an immune-mediated response" in non-specific AAA [30]. The analysis was based on 32 specimens: 4 normal aortas (NLs), 6 OCC aortas, 17 AAAs, and 5 inflammatory AAAs (IAA). Monoclonal antibodies were used to identify the various cell types. The extent of inflammatory infiltrate was IAA > AAA > OCC > NL. The authors interpreted these findings as a spectrum, suggesting that a single disease progressed from OCC to AAA. I advanced the notion that AAA and OCC are two separate disease processes with common risk factors like smoking and hypertension. The aneurysm might actually initiate atherosclerotic degeneration of the subendothelium [31, 32]. A study in mice suggests that aortic dissections precede the onset of atherosclerosis [33]. Other investigators have suggested that the two processes may be "running in parallel" [34].

More recent studies have significantly expanded the evidence for a Th-1 response in AAA [35, 36]. Amplification of beta-chain T-cell receptor transcripts from AAA lesions suggests that 9 of 10 patients have substantial proportions of identical polymerase chain reaction products. The authors conclude that "AAA is a specific antigen-driven T-cell disease."

MMPs

MMP activation or deregulation is a typical feature of autoimmune diseases. Loss of elastin is a sentinel histochemical feature of AAA, and Reilly et al. were the first to report that the "killer elastase" is a metalloproteinase with a molecular weight of ~80 kDa [37]. We subsequently identified it as gelatinase B or MMP-9 [38]. Mammalian collagenase (MMP-1) [39] and stromelysin (MMP-3) [40] are also present. Immunohistochemically, MMP-9 is co-distributed with macrophages, whereas MMP-1 is associated with endothelial cells of neovascularizing vessels and mesenchymal-like cells in the infiltrate [41]. MMP-2 is expressed by a fibroblast cell line cultured from a human AAA explant but not by a normal aortic cell line. The MMP-2 cell line is stable in its expression of MMP-2 over multiple passages (unpublished observations). Cytokines that regulate these MMPs are also elevated in AAA [42].
These observations are interesting, but they are phenomenological and do not establish causal relationships. The development of gene knockout (KO) technology in inbred mice has led to a new era in AAA experimentation. For example, Pyo et al. [43] report that AAA does not develop in MMP-9 null/null mice in the elastase-perfusion model. The AAA-susceptible phenotype is “rescued” by bone marrow transplantation (macrophages) from wild-type mice. These studies show that MMP-9 is a necessary condition for AAA. A similar strategy was employed by Longo et al. [44] in the abluminal (peri-adventitial) calcium chloride model. No aneurysms occurred in MMP-9 or MMP-2 KO mice, suggesting that both macrophage- and mesenchymal-derived MMPs are required and may work in concert to produce AAA.

It is possible that the nicotine in burning tobacco (and not some other component of the smoke) initiates or promotes the smoking/AAA association. Nicotine exposure equivalent to plasma levels in smokers augments MMP-9 and MMP-2 expression by macrophage and vascular smooth muscle cell lines in vitro [45]. Of course, in vitro findings do not always translate smoothly to the situation in vivo. Bergoeing et al. [4] found that cigarette smoking increases aortic dilatation in vivo without affecting the expression of MMP-9 or MMP-12. Wang et al. [46] report that acute infusions of nicotine produce aneurysms in Apo-E-deficient mice, but the aneurysms that occur in this model resemble those induced by angiotensin (Ang) II. In our experience, these AAAs begin as aortic dissections and not as a typical fusiform AAAs. Guo et al. [47] report that the JNK inhibitor, SP600125, attenuates the nicotine plus Ang II model of AAA formation, but again, these AAAs are false aneurysms.

Maegdefessel et al. [48] report that nicotine pellets (versus placebo) augment aneurysmal expansion in the elastase-perfusion model. This model avoids some of the difficulties of the Ang II model. It also avoids the problem of "smoker's hypertension" that develops in chronically smoke-exposed mice [49], which may independently promote AAA formation. Blood pressure measurements at 14 days showed no difference between nicotine and placebo groups, but more extensive observations might be useful to rule out this potentially misleading possibility. Of course, a direct effect of nicotine in pellets and enhancement of autoimmunity by smoke are not mutually exclusive as valid explanations of the smoking/AAA association.

**Antibodies and Autoantigens**

Capella et al. [50] carried out experiments to determine whether increases in IgG in AAA tissue are subclass-specific (by enzyme-linked immunosorbent assay (ELISA) with monoclonal antibodies) and whether the IgG complex is associated with increases in complement C3. Seven AAA, four OCC, and two NL aortic specimens were evaluated. Comparing by subclass, IgGs were elevated in AAA over NL by 193× for IgG1, 160× for IgG2, 389× for IgG3, and 627× for IgG4. Increases in IgGs in AAA specimens over NL and OCC specimens by subtype were statistically significant (p < 0.01). ELISA showed a 125× increase in immunoreactive C3 in soluble extracts of AAA, and Western immunoblots revealed multiple C3 immunoreactive isoforms or degradation products.

With evidence that immunoglobulins are recoverable from AAA tissue, interest intensified to find the aortic autoantigen(s). Gregory et al. [51] purified Ig from serial AAA specimens and found that it was immunoreactive with a protein of ~80 kDa in Western blots of 11 of 14 (79%) AAA patients versus 1 of 9 (11%) control patients (p = 0.002, Fisher's exact test). By immunohistochemistry, antibodies extracted from AAA specimens were immunoreactive with a microfibrillar protein in the matrix of the adventitia of the normal aorta.

This experiment was repeated by Chew et al. [52], who confirmed that AAA immunoglobulins are immunoreactive with a matrix protein of ~80 kDa, extractable from aneurysmal aortas by high concentrations of guanidinium hydrochloride. We inferred that this was a dimeric form of an AAA antigenic protein with molecular weight of ~40 kDa, which had been affinity-purified with antibodies from AAA specimens [53]. This protein was named AAAP-40 for aneurysm-associated antigenic protein 40 kDa.

The partial amino acid sequence of AAAP-40 was determined. It had homology to a protein in pig with an aorta-specific tissue distribution. The porcine protein had been discovered and named microfibril-associated glycoprotein 36 KDa by Kobayashi et al. [54]. AAAP-40 has seven tyrosine residues, including one...
tyrosine doublet, which are prime sites for nitration [55]. AAAP-40 also has short homologies with all three chains of fibrinogen, suggesting that its evolutionary history placed it close to the common ancestor of the three modern chains. We calculated the evolutionary distance of AAAP-40 from fibrinogen-beta (measured in point-accepted mutation rates [PAMs]; among fibrinogen-related proteins [FRePs], a PAM unit is about a million years). Only 30 PAMs separated AAAP-40 from fibrinogen-beta [56]. These results agreed with a neighbor-joining tree computing the relatedness of MAGP-36, AAAP-40, MFAP-4, and a “fibrinogen-like protein of the sea cucumber” [57].

Antibody against a unique amino acid sequence of AAAP-40 (not found in any other mammalian protein) was immunoreactive with adventitial microfibril of the human aorta and selected other vessels [58, 59]. This antibody was also immunoreactive with a microfibrillar protein in mouse aortic adventitia [60]. Figure 1 illustrates that a commercial antibody against fibrinogen-beta is immunoreactive with a microfibrillar protein in the human aortic adventitia. Figure 2 shows that AAAP-40 is site-specifically expressed in the human arterial tree. It is abundant in the aorta, common iliac, internal iliac, and popliteal arteries but is barely detectable in the external iliac artery. This distribution corresponds to the susceptibility of the different vessels to aneurysm formation [10, 61]. Taken together, these observations suggest that the AAA autoantigen is a normal constituent of the aortic adventitia and not a product of atheromatous degeneration.

Smoking Promotes AAA in Mouse Models

Stolle et al. [5] report that cigarette smoke promotes AAA in an Ang II/Apo-E-deficient mouse model. Although it is notable that smoke exerts effects in this model, we found that APO-E deficiency is not required for AAA formation. We had success in inducing AAA in normal C57/Bl6 mice that were selected only for advanced age (i.e., retired breeders) [62, 63].

Bergoeing et al. [4] adapted the elastase perfusion mouse model to determine whether tobacco smoke lowers the threshold of aortic injury required for AAA development. The adaptation involved changing the concentration of elastase in the perfusate, resulting in high-dose, standard-dose, and low-dose regimens. Exposure to tobacco smoke began 2 weeks before perfusion and continued until sacrifice 2 weeks after

![Figure 1](image1.png)

**Figure 1.** Tissue sections from the adventitia of a normal human (cadaver donor) aorta photographed at 400×. An immunohistochemical stain (Gomori’s aldehyde fuchsian) was used for microfibrill-associated glycoprotein (MAGP). Verhoeff’s elastic stain (EVT) was used for collagen (pink) and elastin (black). Immunohistochemistry employed rabbit anti-human fibrinogen as a primary antibody and goat anti-rabbit Ig as a secondary antibody. No primary antibody was used as a control. MAGP and fibrinogen co-distributed with collagen (pink) in EVG staining. The elastin of the adventitia did not have the lamellar organization characteristic of the arterial media.

![Figure 2](image2.png)

**Figure 2.** Immunohistochemical studies of human arterial segments from the autopsy of a patient with no abdominal aortic aneurysm (AAA) and minimal occlusive disease. The antibody was rabbit anti-human AAAP-40, raised against a synthetic peptide, based on a unique sequence not found in any other mammalian protein (-GMAKEYDGFQYT). Staining was performed in one batch for all sections. Immunoreactive protein stained blue in the adventitia of the aorta and the aneurysm-prone popliteal, internal, and common iliac arteries. The aneurysm-resistant external iliac artery exhibited minimal staining. We were surprised to note staining of the carotid artery, but this finding may explain the elongation often seen in AAA patients.
perfusion. Smoking resulted in larger aneurysms in low-dose mice (aortic diameter increased by 134%) compared with non-smoking low-dose mice. There was no difference in MMP-9 expression between smoking and non-smoking mice.

In parallel with human AAA disease, after a mouse model has been initiated by smoke exposure, enhanced expression of the aneurysm phenotype persists even after a smoke-free interval. Jin et al. [64] found that after smoke exposure for 6 weeks followed by no smoke exposure for another 6 weeks, the promoting effect was still in force. They proposed three possible explanations for the smoking effect: 1) a persistent increase in MMP activity; 2) a persistent direct injury to the aorta; or 3) promotion of an immune response. They found that smoking overrode MMP effects, as the smoking effect persisted even in doxycycline-treated mice or those with null/null elastolytic deficiencies. Injury to the aorta was ruled out by direct electron microscopic studies. Thus, the promotion of an immune response was favored because leukocytes from smoke-exposed mice localized to the aneurysms of smoke-free mice and increased their aortic diameters. Apparently, after leukocytes are initiated, possibly by exposure to nitro-tyrosine in aortic FRePs, they acquire memory for promoting an autoimmune response.

Zhao et al. [65] identified a natural IgG antibody in mice that binds to fibrinogen and initiates the inflammatory response that culminates in AAA development. They found that a mouse anti-fibrinogen antibody enhances AAA formation. Also, they reported that AAA patients have circulating antibodies against “fibrinogen or fibrinogen-associated epitopes in human aneurysmal tissue”. This finding confirms the rationale for the use of ELISA to detect antibodies as a screening test for the disease as proposed by Knoetgen et al. in 1997 [66].

Smoking-Induced Nitration of Plasma and Tissue Proteins

Tyrosine nitration is a modification that may change the rate of proteolytic degradation of nitrated proteins. Protein nitration in cardiovascular diseases has been extensively reviewed by Turko and Murad [67]. The authors note that the process is selective (e.g., residue-, protein-, and tissue-specific). Not all tyrosine residues of a protein are nitrated, and not all proteins are targets for nitration. Typically, one or two tyrosine residues are site-specifically nitrated. The product of nitration is 3-nitro-tyrosine, which has been established as a biomarker of “nitro-oxidative stress” [68].

Nitrotyrosine in plasma proteins is increased in smokers with chronic obstructive pulmonary disease, consistent with “increased nitration associated with inflammatory processes” [69]. Nitrated plasma proteins are also increased in lung cancer patients [70]. Fibrinogen is among the plasma proteins that are nitrated.

Our interest in this subject matter arose in the context that cigarette smoke contains substantial amounts of NO [71]. We found that the nitrite content of AAA tissue is comparable to levels that were once considered possibly carcinogenic in smoked sausage [72]. This concentration of nitrite (but not nitrate) damages the aortic matrix in vitro [73] and leads to tyrosine depletion in a solution of collagen [74]. Immunogenicity of tyrosine-nitrated self-proteins has been reviewed in the context of understanding the mechanisms leading to autoantibody production [55]. Structurally modified self-proteins give rise to new epitopes to which T and B lymphocytes are not tolerant. These nitrated proteins elicit cellular and humoral responses in mice.

The Smoking/Autoimmune Hypothesis

AAA has features of an autoimmune disease. Inflammation is rampant, and autoantigens are identifiable with purified auto-antibodies. The principal auto-antigen appears to be a microfibrillar protein with similarities to fibrinogen localizing to adventitia of the aorta. It has seven loci for potential tyrosine nitration. NO in tobacco smoke may nitrate this protein, which would be expected to enhance its immunogenicity. Anti-fibrinogen antibodies promote AAA in mouse models. Finally, antibodies against fibrinogen are detectable in humans with AAA. These findings suggest that smoking heightens autoimmunity in AAA in humans and mice. The autoimmune hypothesis does not exclude other possible explanations for the smoking/AAA association.
Conflict of Interest

The author has no conflict of interest relevant to this publication.

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Diagnostic Utility of Chest Radiography in Predicting Long-Standing Systemic Arterial Hypertension

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Abstract

Purpose: To investigate the association between aortic arch width on frontal chest radiography and systemic hypertension.

Methods: A total of 200 consecutive patients were included. Relationships between aortic arch width measurement on chest radiography and blood pressure measurement were investigated using Student’s t-tests and Fisher’s exact tests.

Results: Twenty-five patients were normotensive (< 130/90 mmHg), and 175 were hypertensive. Using cut-off values, 136 patients had an aortic arch width ≥ 3.5 cm, and 65 had an aortic arch width ≥ 4 cm. We found a significant relationship between aortic arch width and hypertension (p < 0.001) as well between aortic arch width cut-off values of 3.5 cm and 4 cm and hypertension (p < 0.001 and p < 0.005, respectively). An aortic arch width ≥ 3.5 cm was associated with a positive likelihood ratio (LR) of 2.3, negative LR of 0.39, sensitivity of 73, specificity of 68, positive predictive value of 94, negative predictive value of 0.36, pretest odds of 7, posttest odds of 16, and posttest probability of 94%. An aortic arch width ≥ 4 cm was associated with a positive LR of 4.50, negative LR of 0.70, sensitivity of 36, specificity of 92, positive predictive value of 97, negative predictive value of 17, pretest odds of 7, posttest odds of 31.5, and posttest probability of 97%.

Conclusions: Aortic arch width measurement on chest radiography can be used to predict the presence of long-standing systemic arterial hypertension.

Key Words: Aortic arch width • Chest radiography • Hypertension

Introduction

Systemic hypertension affects 25% of the adult population, including 78 million persons in the United States and more than 1 billion persons worldwide. Its prevalence increases with age. Hypertension is the most common cause for an outpatient visit to a physician and the most important preventable risk factor for stroke, myocardial infarction, heart failure, peripheral vascular disease, aortic dissection, atrial fibrillation, end-stage renal disease, and premature death worldwide. In the United States, it has surpassed smoking as a cause of preventable death. At least 20% of affected persons are initially unaware of their condition. Chest radiography is arguably the most commonly performed radiographic examination, with at least 70 million radiographs performed each year in the United States. Aortic arch width is a landmark identified on every chest radiograph and can easily be used for screening purposes. To our knowledge, no scientific study has been performed in a United States population to determine the predictive value of aortic arch width on frontal chest radiography for the diagnosis of systemic hypertension. Therefore, we investigated the association between aortic arch width and systemic hypertension.
Aortic Arch Measurement

The width of the aortic arch was measured prospectively. Aortic arch width was measured from the point of the left lateral edge of the trachea to the left lateral wall of the aortic arch (Figure 1).

Blood Pressure Measurement

Blood pressure measurements were obtained retrospectively through medical record review. Measurements were performed using standard medical office sphygmomanometers and recorded in electronic medical records as part of routine physician visit procedures. A blood pressure measurement of < 130/90 mmHg was considered normal.

Statistical Analysis

The relationship between aortic arch width measurement on chest radiography and blood pressure measurement was investigated using Student’s t-tests. Aortic arch width measurements were also categorized using cut-off values of 3.5 cm and 4 cm, and their correlations with blood pressure were investigated using Fisher’s exact tests (two-sided). A p < 0.05 was considered statistically significant. Likelihood ratios (LRs) were calculated to determine the predictive value of aortic arch width measurement for long-standing arterial systolic hypertension.

Results

Of the included patients, 25 (12.5%) were normotensive (< 130/90 mmHg), and 175 (87.5%) were hypertensive (≥ 130/90 mmHg) (Table 1.) Mean systolic

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Table 1. Demographic data of the study population. A clear majority of the patients were male due to nature of the patient population where the study was conducted.

<table>
<thead>
<tr>
<th></th>
<th>Age (Mean, Range)</th>
<th>Obesity (%)</th>
<th>Hyperlipidemia (%)</th>
<th>Tobacco (%)</th>
<th>DM (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main population</td>
<td>57.7 (23-96)</td>
<td>77 (38.5)</td>
<td>102 (51)</td>
<td>10 (5)</td>
<td>50 (25)</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>60.4 (24-95)</td>
<td>70 (35)</td>
<td>100 (50)</td>
<td>9 (4.5)</td>
<td>49 (23)</td>
</tr>
<tr>
<td>Normotensive</td>
<td>39.4 (23-80)</td>
<td>7 (3.5)</td>
<td>2 (1)</td>
<td>1 (0.5)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

DM = diabetes mellitus
blood pressure was 146 mmHg (standard deviation (SD): 14.7; range: 96-178; median: 145). Mean diastolic blood pressure was 85 mmHg (SD: 11.5; range: 48-117; median: 84.5).

One hundred thirty-six (68%) patients had an aortic arch width ≥ 3.5 cm, and 65 (33%) patients had an aortic arch width ≥ 4 cm. Mean aortic arch width was 38 mm (SD: 5.8; range: 24.9-57.8 mm; median: 36.8).

We found a significant relationship between aortic arch width on chest radiography and blood pressure measurement (p < 0.0001) as well as also significant relationships between aortic arch width cut-off values of 3.5 cm and 4 cm and the presence of hypertension (p < 0.0001 and p < 0.005, respectively).

An aortic arch width ≥ 3.5 cm was associated with a positive LR of 2.3 (95% confidence interval (CI): 1.28, 4.08), negative LR of 0.39 (95% CI: 0.27, 0.57), sensitivity of 73, specificity of 68, positive predictive value of 94, negative predictive value of 26.6, pretest odds of 7, posttest odds of 16, and posttest probability of 94%.

An aortic arch width ≥ 4 cm was associated with a positive LR of 4.50 (95% CI: 1.17, 17), negative LR of 0.70 (95% CI: 0.59, 0.82), sensitivity of 36, specificity of 92, positive predictive value of 97, negative predictive value of 17, pretest odds of 7, posttest odds of 31.5, and posttest probability of 97%.

Discussion

Hypertension affects more than 1 billion persons worldwide. In the United States alone, 78 million individuals have hypertension. High blood pressure may not cause symptoms until end organ damage manifests clinically. For this reason, hypertension has been called the “silent killer” [1]. Subclinical organ damage has been considered an intermediate stage in the spectrum of vascular disease and is a strong determinant of total cardiovascular risk [2]. Chest radiography has been shown to predict associated target organ damage in hypertensive patients [3]. Specifically, aortic arch width is positively correlated with both systolic and diastolic blood pressure and was found to be a reliable marker of target organ damage due to its correlation with blood creatinine values, retinal fundoscopic changes, cardiothoracic ratio, and left ventricular mass on echocardiography [3]. Left ventricular hypertrophy is considered the most powerful determinant of cardiovascular outcome in hypertensive patients [4], and an aortic arch width of > 3.6 cm is suggested as a marker of target organ damage [3]. Subsequent studies demonstrated a significant and independent association between aortic arch width and cardio-ankle vascular index [5], which is considered to reflect arteriosclerosis of the aorta and is a novel parameter of arterial stiffness and surrogate marker of subclinical atherosclerosis [6]. Based on this association, an aortic arch width of 4.1 cm has been suggested as a cut-off value for the presence of subclinical atherosclerosis with modest sensitivity and specificity [5]. In our study, an aortic arch width ≥ 3.5 cm demonstrated a positive LR of 2.3 (95% CI: 1.28, 4.08) with modest sensitivity and specificity but a very high positive predictive value of 94 for hypertension. On the other hand, an aortic arch width ≥ 4 cm demonstrated a positive LR of 4.50 (95% CI: 1.17, 17.00) with relatively low sensitivity of 36, very high specificity of 92, and very high positive predictive value of 97 for hypertension.

Aortic arch width does not exceed 3 cm in most adult chest radiographs in the United States [7], whereas a recent study among an Asian-Indian population reports a width of 3.04 cm in healthy adults [8]. Felson [7] analyzed the width of the aortic “knob” in 500 normal persons from the left border of the trachea transversely to the lateral margin of the aorta and found an age-related increase in the width of the aortic “knob”. That is, 95% of persons under 30 years of age had a width < 3 cm, 91% of persons between 30 and 40 years of age had a width < 3 cm, and 69% of persons over 40 years of age had a width < 3 cm. In no case did the aortic “knob” width measure > 4 cm. However, these studies were not focused on the “size and pressure” association. Permanent changes in the size of the aorta happen gradually and progressively as part of the aging process and are probably exacerbated by systemic arterial hypertension [3]. Dilation is most likely related to degradation of elastic fibers in the aortic wall. When monitored over years, especially in high-risk populations, systemic arterial blood pressure often demonstrates dramatic variability, with short-term episodic spikes reaching or exceeding 200
mmHg and sustained undulations of longer duration between 100 to 200 mmHg triggered by emotional states, exercise, medications, life style, habits, diet, or other disease processes. The literature about aortic arch width on chest radiographs in relation to systemic arterial blood pressure primarily consists of cross-sectional studies evaluating populations at one point in time without taking into account the wall-damaging impact of short-term and long-term fluctuations in blood pressure over time. This can explain some inconsistent results among studies attempting to assess the correlation of “size and pressure”, which yield a variety of suggested cut-off values for the width of the aortic arch as a predictor of systemic hypertension. This challenge is also reflected in variable guidelines for protective target blood pressures.

Our study was conducted in a high-risk patient population for cardiovascular disease including systemic hypertension. Most patients were monitored over a long period of time, which allowed us to more accurately assess their blood pressure status. Most of our patients had recurrent visits to our healthcare system over several months to several years, which allowed for multiple blood pressure measurements. We decided to select a representative blood pressure measurement among multiple blood pressure measurements from the time period preceding the date of the optimal posteroanterior chest radiograph used for measurement of the aortic arch width.

Higaki et al. [9] reported a strong correlation between aortic arch width and age, central systolic blood pressure, and central pulse pressure in a study population with known or suspected coronary artery disease. They showed that larger aortic arch widths were associated with not only dilation but also stiffening of the aorta. Rayner et al. [3] demonstrated a significant difference in aortic arch width between normotensive and hypertensive populations (3.28 vs. 3.69 cm, respectively) using standard mercury sphygmomanometer measurements in a hypertension clinic. These results are comparable to our findings (3.31 vs. 3.87 cm, respectively).

One limitation of our study is that we did not perform multivariate linear regression analysis of variables to determine independent predictors of progressive aortic arch widening, such as aging. However, studies show that in a healthy aging population, cardiovascular dimensions in frontal chest radiographs show only modest age-related changes [10]. The other limitation of our study is the relatively high frequency of multiple confounding cardiovascular disease processes in our patient population, which made isolation of systemic hypertension as the only factor determining the aortic arch width more difficult.

In conclusion, aortic arch width measurements on chest radiography can be used to predict the presence of long-standing systemic arterial hypertension.

Conflict of Interest

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

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EDITOR QUESTION

1. How do you feel we should incorporate your findings into clinical practice? How should we “act” on your findings?

   The increase in aortic arch width on chest radiograph may be the first indication of long-standing systemic hypertension and should thus trigger further work-up with subsequent appropriate therapy, including lifestyle changes and medication. We mention suspected long standing systemic hypertension on all our reports when we find an aortic arch width of 4cm or higher.
Persistent Buttock Claudication after Endovascular Abdominal Aortic Aneurysm Repair: A Surgical Solution

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Abstract
We describe the successful surgical treatment of a 71-year-old man affected by right buttock claudication after a right internal iliac artery (IIA) coil embolization as an adjunct to endovascular iliac artery aneurysm repair. Computed tomography angiography revealed extensive aortoiliac calcifications and thrombus in the vessel walls. Despite patency of the contralateral IIA and preservation of right distal collateral flow through ipsilateral hypogastric branches, the symptom was persistent and disabling. The high-risk patient underwent an “open” repair of the infrarenal abdominal aneurysm with removal of the entire stent-graft and concomitant revascularization of the right IIA. Post-operative recovery was uneventful, and the patient remained asymptomatic during a 30-month follow-up. This case underscores the importance of considering all potential solutions, including open surgery, to preserve pelvic inflow after aortoiliac stent grafting, particularly for high-risk patients with vulnerable plaque and higher risk of thrombus embolization.

Key Words:
Buttock claudication • Coil embolization • Internal iliac artery • Endovascular abdominal aortic aneurysm repair

Introduction
Buttock claudication is the most frequent ischemic complication after hypogastric artery occlusion prior to endovascular abdominal aortic aneurysm repair. The English literature contains conflicting reports of the incidence and severity of symptoms. While many authors find internal iliac artery (IIA) coil embolization a relatively trouble-free procedure, there are reports of devastating sequelae and mortality associated with the technique [1, 2]. A variety of new endovascular devices and surgical procedures have been proposed for situations in which the hypogastric artery must be covered by the iliac limb endograft [3, 4]. The aim of this report is to present a successful surgical technique of hypogastric artery bypass to treat persistent buttock claudication occurring after endovascular common IIA repair with unilateral IIA interruption.

Case Presentation
A 71-year-old man with a history of heart failure, hypertension, peripheral arterial disease, and hypercholesterolemia presented to our department for persistent and disabling right buttock claudication. The symptom occurred subsequent to ipsilateral IIA coil embolization performed 24 h prior to endograft limb extension to the external iliac artery (EIA) as an adjunct to endovascular repair of a common iliac artery aneurysm. No antecedent back trauma or history of prolapsed lumbar discs was reported.

Abdominal duplex scan showed complete occlusion of the right IIA with stent-graft exclusion prior to endovascular common iliac artery aneurysm. Patency of the contralateral IIA was detected. No
other aneurysm sites or aortoiliac stenotic lesions were recognized. Continuous wave Doppler revealed a signal at the right buttock level with a lower intensity than that of the contralateral side. Contrast-enhanced multidetector computed tomography angiography confirmed the diagnosis and showed patency of the distal portion of the right IIA and its branches, with preserved distal collateral flow (Figure 1). Additional findings included severe aortic and iliac calcifications and mural thrombus. Preoperative cardiac testing did not detect atrial fibrillation and the patient was considered to have grade III preoperative risk according to American Society of Anesthesiologists classification.

Under general anesthesia, through median transperitoneal access and infrarenal clamping, the stent-graft and IIA coil were removed. After retrograde right hypogastric blood flow was assessed, revascularization was performed in two steps. First, a bifurcated Dacron graft was anastomosed in an end-to-end fashion from the infrarenal aorta to the left common iliac artery and the distal part of the right IIA, respectively. Second, a separate graft, proximally anastomosed end-to-side with the corresponding anterior aspect of the main body of the aorto iliac graft, was jumped to the right EIA (Figure 2).

Post-operative recovery was uneventful. The patient was discharged in good general condition with complete pain relief on life-long mono-antiplatelet treatment (acetylsalicylic acid 300 mg). At 30-month follow-up, there was no buttock claudication, pelvic ischemia, or complaint of paresthesias, pain, discomfort, or walking limitation. Computed tomography angiography showed patency of both grafts with no anastomotic stenosis/pseudoaneurysms. The right IIA at the level of its first branch was well perfused (Figure 3).

Discussion

Pooled data from different studies reveal that the incidence of buttock claudication after coil embolization of one or both IIAs ranges from 11% to 50%, with
differences in type and severity [1]. Persistent buttock claudication represents approximately 13% of all of IIA coil embolization procedures, with no statistically significant difference between unilateral and bilateral IIA interruption [2]. Although some studies report that IIA embolization is a well-tolerated procedure with a small chance of severe morbidity, recent literature appears to support the notion that every effort must be made to preserve one or both hypogastric arteries during endovascular aneurysm repair [3, 4].

This report demonstrates the potentially problematic nature of the management of the disabling sequelae of this complication. Despite the fact that the IIA embolization was performed in a staged fashion and the coil placement was proximal to the internal iliac bifurcation with evidence of distal patent collateral vessels and consequent time to develop a collateral pelvic circulation with blood flow from the contralateral IIA and ipsilateral EIA, the patient experienced constant and painful buttock claudication. Likely, periprocedural distal embolization or a hypotension episode may have contributed to the onset of the early buttock claudication [5].

Different surgical solutions have been designed to restore hypogastric perfusion. Many surgeons prefer a retrograde IIA revascularization with relocation of the IIA to the external iliac or femoral arteries via a retroperitoneal approach to avoid extensive pelvic dissection, reduce trauma to the abdominal wall musculature, and achieve less postoperative patient discomfort [6]. However, in our case, we believe the best choice to restore buttock circulation was to perform direct revascularization. In fact, retrograde perfusion may be inadequate for many reasons. First, the short available segment of the EIA due to extension of the endograft limb and the deep location of the patent IIA vessel branches can make the surgical area uncomfortable and the entire procedure technically complicated, with a risk of injury to large veins. Second, perfusion may

Figure 2. The left image shows the removed stent-graft and embolization coil placed on a schematic design of the previous implant. The right images show intraoperative surgical direct aortoiliac revascularization of the right internal iliac artery and both common iliac arteries via a transperitoneal approach.

Figure 3. Follow-up computed tomography angiography at 6 months showed a good result of the procedures with patency of all branches of the graft without further complications.
be not achieved in case of severe atherosclerotic external deterioration of the iliac-femoral junction. Finally, prolonged clamping of the EIA associated with difficult control of intraoperative activated clotting time during performance of the anastomosis can cause potential peri-postoperative limb thrombosis.

Based on these considerations, whenever possible and reasonable according to American Society of Anesthesiologists score, our choice has been to perform direct bypass from the aorta to the IIA with an end-to-end anastomosis between a branch of a bifurcated Dacron graft and the residual distal part of the hypogastric artery via a transperitoneal approach. We believe that this offers better exposure of distal IIA branches. From a technical point of view, to perform an “octopus” trifurcated graft, as described above, with a separate jump to the EIA from the main body graft shows some advantages. First, unless a poor run-off or quality of the artery wall were intraoperatively detected, this configuration can result in an optimal perfusion pressure of each target vessel without any risk of steal syndromes. Moreover, in case of occlusion of the IIA branch, there is reduced risk of thrombotic involvement of the anastomosed branch to the EIA. Finally, the anastomosis achieved on the anterior aspect of the main body is technically easier and provides better perioperative control of bleeding when compared with an end-to-side proximal anastomosis of a separate IIA graft to the corresponding posterior or side of an aorto-iliac prosthesis branch. Although treatment should be individualized, we recommend this surgical approach in cases of persistent buttock claudication to restore hypogastric artery circulation after IIA coil embolization.

**Conflict of Interest**

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

**References**


Single-stage Endovascular Treatment of a Penetrating Aortic Ulcer with a Concomitant “Isolated” Iliac Aneurysm

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Abstract
Penetrating aortic ulcer (PAU) is an acute aortic syndrome that can proceed to life-threatening aortic dissection or even aortic rupture. Isolated iliac aneurysms are relatively rare and often asymptomatic due to their deep pelvic location but are frequently associated with high mortality with rupture. We report a case of a 68-year-old man with a symptomatic penetrating ulcer in the descending aorta and an asymptomatic right iliac aneurysm involving the common and internal iliac arteries. The patient was successfully treated by endovascular repair in a single-stage manner using stent grafts in the descending aorta and right common iliac artery after coil embolization of the right internal iliac artery. Follow-up imaging showed complete resolution of the PAU and exclusion of the right iliac aneurysm without endoleak. Aggressive endovascular treatment for a symptomatic PAU with an asymptomatic isolated iliac aneurysm is feasible and allows complete treatment of vascular pathology at a single time.

Key Words:
Penetrating aortic ulcer • Iliac aneurysm • Endovascular

Introduction
Penetrating aortic ulcers (PAUs) are aortic atherosclerotic lesions that ulcerate through the internal elastic lamina into the media, allowing hematoma formation in the media [1]. PAU is one of three types of acute aortic syndrome that accounts for 2–11% of all acute aortic syndromes [2]. Elefteriades’ group recognized the aggressive nature of PAUs and differentiated their early behavior from that of classic type A and B dissections, showing that the rupture rate of symptomatic PAUs is as high as 38% [3]. Isolated internal iliac aneurysms (IIAs), in absence of a concomitant abdominal aortic aneurysm, are unusual. Many IIAs are asymptomatic and are found incidentally, as their deep location in the pelvis precludes routine detection; however, patients with IIA frequently present with multiple aneurysms (43–67%) [4]. The incidence of IIA rupture in Western and Asian patients is approximately 30% [4]; however, IIA rupture is associated with high mortality (30–50%) [5], and the threshold for elective repair is generally considered to be 30 mm in maximal transverse diameter [4, 5].

Here, we report a case of symptomatic PAU associated with an asymptomatic right “isolated” IIA that was diagnosed incidentally during work-up for the PAU. Both the PAU and right IIA were successfully treated using a single-stage endovascular approach.

Case Presentation
A 68-year-old Chinese man with a history of smoking (45 years) and hypertension was admitted
with acute severe chest and back pain. Electrocardiography showed nonspecific ST-T changes and normal ventricular function without pericardial effusion. His physical examination was unremarkable other than an elevated blood pressure of 185/106 mmHg; laboratory tests showed normal troponin levels, and D-dimer was 510 ng/ml (normal range < 500 ng/ml). The patient was suspected to suffer from an acute aortic syndrome and was treated with β-blockade and morphine. Three-dimensional computed tomography angiography showed a proximal descending penetrating aortic ulcer with associated intramural hematoma (Figure 1A, 1B, and 1C); there was also an aneurysm of the right common iliac artery (maximum diameter 36 mm) involving the origin of the right IIA (Figure 2A). There were no other aneurysms.

After 4 days of medical treatment, his systolic blood pressure was no longer elevated, but he experienced only partial relief of chest pain; accordingly, repair of the symptomatic PAU and right IIA (> 30 mm) was planned using a single-stage endovascular approach. Under general anesthesia, the bilateral common femoral arteries were exposed; a 6-F sheath was placed in the left femoral artery, demonstrating the PAU (Figure 1D) and right IIA (Figure 2B). An 8-F sheath was used to place a Lunderquist extra-stiff guidewire (145 cm, Cook Medical, Bloomington, Indiana, USA) and catheter into the ascending aorta. The PAU was covered with a stent graft (diameter 36 mm; length 150 mm; Endurant, Medtronic Inc., Minneapolis, Minnesota, USA) starting immediately distal to the origin of the left subclavian artery; intraoperative angiography demonstrated no endoleak (Figure 3A). A 0.035” guidewire (TERUMO, Fujinomiya, Japan) was used to access the right IIA from the left femoral artery, and coil embolization was performed using two coils (diameter 15 mm, MWCE-
35-8-15, Cook Medical) to exclude the IIA (Figure 3B). The IIA was covered with a stent graft (diameter 16 mm, length 120 mm, Endurant, Medtronic Inc.) placed from the right common iliac artery into the right external iliac artery. Completion angiography demonstrated no endoleak with good flow to the lower extremities (Figure 3C). The operation time was 1.5 h. The patient’s chest pain was completely relieved, and he recovered well. He was discharged on postoperative day 7.

Six months after discharge, computed tomography angiography showed good patency of both stent grafts without endoleak; there was no buttock claudication.

Discussion

PAUs frequently present as an acute aortic syndrome, with risk of intramural hematoma, pseudoaneurysm, rupture, or dissection [2]. PAUs often occur in elderly patients with extensive comorbidities, severe atherosclerosis, and a high incidence of abdominal aortic aneurysms (42.1%) [3, 6]. Elefteriades’ group showed that symptomatic PAUs must be treated emergently, as the PAU reaches the adventitia and rupture is expected [3, 7, 8]; the rupture rate of symptomatic PAUs is as high as 38% [3]. As with acute aortic dissection, PAU is classified according to the aortic site affected; type A PAU involves the ascending aorta, and type B involves the descending thoracic aorta [9]. Type B PAU progression, persistent pain despite medical therapy, increasing pleural effusion, and coexistence of intramural hematoma are indications for repair [8, 9]. In this case, the patient had persistent chest pain despite β-blockade and pain treatment as well as an intramural hematoma, mandating treatment to prevent rupture. As type B PAUs are frequently localized, open surgical repair shows excellent results [3, 8] and is considered the gold standard treatment. However, endovascular repair offers a less invasive approach in high-risk patients, showing good perioperative results with low 30-day mortality (4.8 –7%) [10].

IIAs are frequently asymptomatic and not easily detected due to their deep pelvic location; accordingly, they are frequently repaired electively. In this case, the IIA was above established treatment thresholds [4, 5]. Cambria et al. reported a series of 18 patients with spontaneous aortic dissection in the presence of coexistent or previously repaired aneurysms and showed that concomitant aortic pathologies increase the risk of aortic rupture in both proximal and distal aortic segments [11]. Chaer et al. reported a more contemporary series of synchronous and metachronous thoracic aneurysms in patients with abdominal aortic aneurysms and confirmed the high incidence of rupture with associated mortality in both abdominal and thoracic locations [12]. We believe that predisposing factors for acute aortic syndromes and degenerative aneurysms may overlap, increasing the risk of concomitant presenting entities. Accordingly, as the iliac artery is a first-order aortic branch, the rupture risk of the IIA in our patient was likely higher than that of an IIA without a thoracic aortic lesion, leading us to treat both the PAU and IIA in single-stage manner. Over the past decade, endovascular repair for IIAs has been established to be safe and effective in patients with appropriate anatomy, especially in the common iliac artery [5]. The different locations of the two entities in this patient (i.e., chest and pelvis) suggests that an endovascular approach may be preferable to the surgical trauma of two open procedures; in addition, this patient’s left IIA was patent, minimizing the risk of pelvic ischemia and buttock claudication after coil embolization of the right IIA.

In summary, a symptomatic PAU associated with an asymptomatic IIA are synchronous aortoiliac lesions associated with a high risk of rupture of either lesion but can be treated in a single-stage manner using an endovascular approach. Despite lack of endoleak, continued surveillance is important, although the frequency of surveillance is not well established [10, 13]. In addition, patients with IIA frequently develop multiple aneurysms, suggesting that surveillance and screening remains a life-long concern.
Conflict of Interest

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

References


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Use of Iliac Branch Device for Endovascular Treatment for Abdominal Aorta Aneurysm with Small Diameter Neck

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Abstract

We present the case of a 78-year-old woman with a 4.5-cm symptomatic abdominal aortic aneurysm with a small diameter (13-mm diameter) infrarenal aortic neck who underwent endovascular treatment using an iliac branch device as a bifurcated aortic stent-graft.

Key Words:
Abdominal aorta aneurysm • Iliac branch device • Endovascular treatment • Elderly patients

Introduction

Abdominal aorta aneurysm (AAA) with a small diameter infrarenal aortic neck is a challenge for endovascular treatment, as it requires careful pre-treatment planning and familiarity with multiple devices.

Case Presentation

A 78-year-old woman with a 4.5-cm symptomatic AAA was evaluated using multidetector computed tomography (Figure 1A). On post-processing measurement, the infrarenal aortic neck was 13 mm in diameter (Figure 1B), with a length from renal arteries to iliac bifurcation of 65.1 mm (Figure 1C). The patient was evaluated for endovascular aneurysm repair (EVAR). Due to the small diameter of the proximal neck and the short length of the abdominal aorta, we chose a Jotec E-iliac stent-graft system (proximal diameter, 16 mm; length of proximal stent from the contralateral left side branch, 65 mm) and a 10 × 57 mm Eventus covered stent as a left iliac limb.

With the patient under spinal anesthesia and with right femoral surgical accesses, the iliac branch device was introduced with its proximal stent below the left renal artery (Figure 2A) and deployed after abdominal aorta angiography. From percutaneous 7-F left femoral access, the left side branch was cannulated. Then, after angiographic confirmation, the covered stent was deployed. The proximal neck on both iliac limbs underwent molding-balloon dilatation. A final abdominal aorta angiogram confirmed correct positioning of the devices, complete exclusion of the AAA, and patency of renal arteries, abdominal aorta graft, and iliac arteries (Figure 2B). Clinical and imaging follow-up at 1 year demonstrated complete technical and clinical success (Figure 3).
Discussion

Small diameter aorta neck and iliac vessels are one of the most common anatomic reasons for exclusion of AAA from EVAR [1], especially for elderly atherosclerotic patients. In these patients, other endovascular techniques have been performed, such as single EVAR limb and femoro-femoral cross-over bypass, double-barrel-covered stent, aorta-covered stent associated with double-barrel-covered stent for iliac arteries, and custom small EVAR.

To our knowledge, the treatment of AAA with small diameters using an iliac branch device as a bifurcated endoprosthesis is a new technique in the literature [2]. Endovascular appliances and techniques continue to evolve, permitting treatment of previously prohibitive anatomies [3].

Conflict of Interest

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


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

**State-of-the-Art Review**

*David Tilson: “Autoimmunity in the Abdominal Aortic Aneurysm and the Association with Smoking”*

It is well known that smoking increases the risk of developing an abdominal aortic aneurysm, a dilatation of the body’s main artery in the abdomen, which can be life-threatening.

In his article, David Tilson discusses the mechanisms through which smoking causes aneurysm development, which are not yet fully understood. The hypothesis he discusses is that the destruction of the vessel wall is at least partly caused by an autoimmune process, which means that the body’s immune system destroys its own cells. The nitric oxide in tobacco smoke can make changes to a specific molecule in the vessel wall, making these molecules more recognizable for the body’s immune system, which causes inflammation and vessel wall destruction. Several scientific findings support this theory, but the author stresses that there might be other mechanisms by which smoking promotes aneurysm development as well.

**Original Research Article**

*Hakan Sahin et al.: “Diagnostic Utility of Chest Radiography in predicting long-standing systemic arterial hypertension”*

Long standing high blood pressure is an important risk factor for the development of an aortic aneurysm, a dilatation of the body’s main artery. Many people are unaware of their blood pressure problem. In this research project, Hakan Sahin et al. studied if the width of the aorta seen on an X-ray of the chest is associated with increased blood pressure in these patients. Their study confirmed a significant statistical relationship between aortic width above 4 cm measured on X-ray and high blood pressure. They therefore suggest that if an increased aortic width is detected on X-ray, the patient should undergo further tests to see if he or she has high blood pressure.

**Case Reports**

*Alessandro Robaldo et al.: “Persisten buttock claudication after EVAR: a Surgical Solution.”*

The authors describe a case of a patient who underwent repair of a dilated vessel in his pelvis using a stent graft, a tubed prosthesis inserted into the dilated vessel. During this procedure, a branch vessel had to be occluded. Since this vessel is one of those providing blood flow to the buttock, the patient developed disabling pains in his buttock. Therefore, an open surgery was performed in which the stent graft was taken out, the dilated vessel replaced with another graft and the occluded vessel re-connected to blood flow. The patient recovered well and had no further pains after the
procedure. The authors discuss different surgical options in this setting, explain the technique used and its advantages.

Haidi Hu et al.: “Single-stage endovascular treatment of a penetrating aortic ulcer with a concomitant "isolated" iliac aneurysm”

Haidi Hu et al. discuss a case of a patient who had a “penetrating ulcer”, a localized destruction of the vessel wall of her aorta, the body’s main vessel. Besides this ulcer, which was located in the aorta at the level of her chest, she also had a dilatation of an important vessel in her pelvis, the right iliac artery. The authors decided to treat both problems at the same time with stent grafts, tubed prostheses which are inserted into the vessel. The procedure went well and follow up imaging showed that the ulcer was resolved and the dilatation of the other vessel fully excluded by the stent graft. The authors therefore suggest to treat synchronous aneurysms or ulcers of the aorta and the iliac artery with stent grafts in a single procedure. Continued surveillance after the procedure is important.

Umberto Rossi et al.: “Iliac branch device used as endovascular treatment for an abdominal aorta aneurysm with small diameter neck”

When an aortic aneurysm, a dilatation of the body’s main vessel, is covered from the inside with a stent graft prosthesis, a sufficient “neck” of normally shaped vessel on both ends is necessary to anchor the device. Umberto Rossi et al. discuss a case of a patient whose aneurysm in the abdomen did have a “neck” with a very small diameter of only 13mm, which makes the procedure very challenging. Since in this case, the neck of the aneurysm had a size more typical for an iliac artery in the pelvis, they decided to treat this aneurysm with a device which was originally intended for the treatment of the iliac arteries. The procedure went well with the aneurysm being excluded and all vessels remaining patent.
List of Upcoming Meetings

April 2018

1. 14th International Congress of Update in Cardiology and Cardiovascular Surgery
   April 5, 2018 to April 8, 2018
   Antalya, Turkey
   www.uccvs2018.org

2. Vascular and Endovascular Controversies
   April 24, 2018 to April 27, 2018
   London, United Kingdom
   www.cxsymposium.com

3. AATS Aortic Symposium
   April 26, 2018 to April 27, 2018
   New York, NY, United States
   www.aats.org/aortic

4. AATS 98th Annual Meeting
   April 28, 2018 to May 1, 2018
   San Diego, CA, United States
   www.aats.org/annualmeeting

May 2018

1. Vascular Research Initiatives Conferences
   May 9, 2018
   San Francisco, California, United States
   vascular.org/meetings/2018-vric

June 2018

1. Aortic Valve Repair Summit
   June 18, 2018 to June 19, 2018
   Paris, France
   www.eacts.org

2. 2018 SVS Vascular Annual Meeting
   June 20, 2018 to June 23, 2018
   Boston, Massachusetts, USA
   vascular.org/meetings/2018-vascular-annual-meeting