RESUMO

A periaortite crónica e a fibrose retroperitoneal são entidades relacionadas que cursam com inflamação periaortica e deposição de tecido fibroinflamatório no espaço retroperitoneal. Estas entidades clínicas podem ocorrer como complicação do tratamento endovascular (EVAR) do aneurisma da aorta abdominal ou após a implantação de stents ou endopróteses no tratamento de doença arterial oclusiva aortoiliaca.

Realizamos uma revisão sistemática da literatura na base de dados MEDLINE de artigos originais que documentassem o desenvolvimento de periaortite após tratamento endovascular aortoiliaco.

Incluímos um total de 12 artigos que descrevem 14 casos desta complicação, nomeadamente após EVAR no tratamento do aneurisma da aorta abdominal.

A maioria dos doentes são do sexo masculino numa faixa etária que varia dos 45 aos 78 anos. Esta complicação verificou-se com a utilização de diferentes dispositivos que incluíram stents de nitinol ou aço inoxidável bem como no caso das endopróteses, com revestimento de poliéster ou politetrafluoretileno. A gravidade do quadro clínico foi altamente variável sendo que alguns casos se apresentaram com hidronefrose consequente à obstrução uretral. O tratamento com corticoterapia, tamoxifeno ou uma combinação dos dois foi eficaz em todos os casos.

A periaortite é uma complicação extremamente rara do tratamento endovascular aortoiliaco. À semelhança dos casos idiopáticos, a corticoterapia apresenta elevada eficácia sendo fundamental a instituição precoce do tratamento de forma a evitar complicações.

Palavras-chave
Periaortite; Fibrose retroperitoneal; Stent; Endoprótese; Aneurisma da aorta abdominal; EVAR

ABSTRACT

Chronic periaortitis and retroperitoneal fibrosis are related entities that develop with periaortic inflammation and deposition of fibroinflammatory tissue in the retroperitoneal space. This pathological fibroinflammatory process may be associated with endovascular treatment of abdominal aortic aneurysms (EVAR) as well as the treatment of aortoiliac arterial occlusive disease with stent/stent-graft implantation.

We performed a systematic review of the literature in the MEDLINE database of original articles that documented the development of periaortitis after endovascular aortoiliac treatment for occlusive and aneurysmatic arterial disease.

We included a total of 12 articles describing 14 cases of this complication. Most of the reported cases are related to the development of periaortitis after EVAR in the treatment of abdominal aortic aneurysms (AAA).

The majority of patients are male, with ages ranging from 45 to 78 years. This complication was verified with the use of different devices that included nitinol or stainless-steel stents. In the case of stent-grafts this complication occurred with...
INTRODUCTION
Chronic periaortitis is a rare disease that includes a set of idiopathic disorders characterized by inflammation and fibrosis in the retroperitoneal space around the aorta and iliac arteries. It includes idiopathic retroperitoneal fibrosis (the non-aneurysmatic form), inflammatory abdominal aortic aneurysm, in which there is no ureteral involvement, and perianeurysmatic retroperitoneal fibrosis, associated with fibrous tissue deposition around an abdominal aortic aneurysm, which may result in ureteric blockage. The pathophysiological mechanism is still not completely understood but there seems to be an immune-mediated inflammatory process.

Despite its idiopathic forms, chronic periaortitis and retroperitoneal fibrosis can be associated with autoimmune diseases, neoplasms, drugs, infections or radiotherapy. Little is known about the possible development of this complication after correction of abdominal aortic aneurysms (AAA) using endovascular aortic repair (EVAR) or after treatment of aortoiliac occlusive disease with percutaneous transluminal angioplasty (PTA) and stent or stent-graft implantation.

METHODS
Search methods
A systematic search of original articles was carried out by the first two authors in the MEDLINE database, about the development of inflammatory periaortitis after EVAR or aortoiliac stent/stent-graft deployment. The search was conducted on 24th September 2020, using MEDLINE database through PubMed with the following query: (“aortitis”[MeSH Terms] OR “aortitis”[All Fields]) AND (“fibrosis”[MeSH Terms] OR “fibrosis”[All Fields]) AND endovascular[All Fields] AND (“aorta”[MeSH Terms] OR “aorta”[All Fields]) AND (“stents”[MeSH Terms] OR “stents”[All Fields] OR “stent”[All Fields]).

Article inclusion
Only articles written in English were used. The first two authors evaluated all searched titles and abstracts selecting to full text-review those that report one or multiple cases of patients who developed chronic periaortitis after the implantation of aortic endoprostheses or aortoiliac stents in which a causal relationship can be inferred.

Data analysis
This systematic review was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA). Patient characteristics, condition to treat, type of treatment, devices used, time to chronic periaortitis development, and the subsequent treatment are extracted from the articles reviewed.

![Flowchart of literature search and article selection.](image-url)
RESULTS
In our MEDLINE search, we identified 99 abstracts published. After a review of the title and abstract, 94 references were excluded. All articles found were single case reports. Of the 5 studies selected based on title and abstract 1 article was excluded because it reported a case in which chronic periaortitis was present before treatment by EVAR. After an exhaustive review of the references of the selected articles, 7 more articles were included. Bearing in mind that we recently published our experience of two patients who developed retroperitoneal fibrosis after implantation of aortoiliac stents, we decided to include this paper in our review.

Chronic Periaortitis after EVAR
According to our systematic review, we identified 7 articles published about the development of chronic periaortitis after EVAR corresponding to simple clinical cases (Table 1). All cases referred to infrarenal abdominal aortic aneurysms, with atherosclerotic etiology. All the patients were men with ages ranged from 59 to 78 years. All patients were treated with EVAR using a bifurcated stent-graft and in one patient an additional bell-bottom technique was used to treat right common iliac artery aneurysm.

From the preoperative imaging study with Computed Tomography (CT) angiography, none of the cases presented any evidence of inflammatory aortic wall thickening. Routine preoperative inflammatory parameters measurement (C-reactive protein and erythrocyte sedimentation rate) was performed in all patients, whose results were in the normal range.

The type of stent-graft used was wide-ranging. In five patients endoprostheses composed of woven polyester were used and in two other patients, the endoprostheses used had an expanded polytetrafluoroethylene (ePTFE) covering. Regarding the material of the stents, in most cases, the composition was nitinol. One of the endoprosthesis is composed of stainless-steel stents (Zenith® endoprosthesis). Cases of stent-grafts with supra and infrarenal fixation were published.

The time to develop chronic periaortitis was as short as 8 days (immediate postoperative period), lasting up to 17 months after the procedure. Clinical manifestations included mainly abdominal or lumbar pain. In four of the documented cases, there was urethral involvement with hydronephrosis. Two of these required a decompression procedure (urethral stent) and in one patient the outcome was nephrectomy. In all patients, medical treatment was initiated and included the use of corticotherapy, tamoxifen or a combination of the two. The duration of treatment varies from 5 months to more than one year.

Chronic Periaortitis after stent / stent-graft implantation for treatment of occlusive arterial disease
According to our research, we only identified two cases of periaortitis that developed after the implantation of stents/stent-grafts in the aortoiliac sector. We also add two cases recently published by our group (18). All cases concern patients with intermittent claudication resulting from aortoiliac occlusive arterial disease. Two patients were men and two were women aged between 45 and 67 years. Two patients underwent kissing stenting of the aortic bifurcation and two single stenting of the left common iliac artery. Different devices were used, from nitinol stents to stent-grafts (ePTFE and woven polyester covering). The time to presentation since the procedure ranged from 2 months to 3 years. In only one of the cases, obstructive hydronephrosis was observed, requiring urethral stent placement. Medical treatment consisted of corticotherapy in three of the cases. The other patient did not initiate medical treatment, presenting a benign clinical evolution.

DISCUSSION
De nova periaortitis is an extremely rare complication after EVAR or stents/stent-grafts implantation for occlusive aortoiliac arterial disease, with only a few cases described in the literature.

An inflammatory abdominal aortic aneurysm is part of chronic periaortitis spectrum and it is estimated that corresponds to about 5% of all abdominal aortic aneurysms (19). In this type of abdominal aortic aneurysm, the inflammatory process usually regresses after either endovascular or surgical treatment (20,21), although the regression seems to be more frequent after open surgery when compared to EVAR (20). What we present here is the opposite, the development of de novo periaortitis and retroperitoneal fibrosis after EVAR for non-inflammatory AAA treatment or stent/stent-graft deployment in the aortoiliac sector in patients without evidence of periaortic or systemic inflammation in the preoperative study.

Because the symptoms are nonspecific this may be an under-reported entity. In the case of post-EVAR periaortitis, one explanation is that in many cases the elevation of inflammatory markers can be attributed to post-implantation syndrome. It has been hypothesized that periaortitis after EVAR could be a more severe form of this complication.

All the cases following EVAR correspond to male patients aged between 59 and 78 years. In the case of aortoiliac stenting for occlusive arterial disease, the age range was lower (45-67 years). In this group, two of the four patients were females. This male predominance is similar to that
Table 1. Characteristics of patients who developed chronic periaortitis after endovascular treatment of abdominal aortic aneurysm with endoprosthesis.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Endovascular treatment</th>
<th>Device</th>
<th>Time to CP development</th>
<th>Clinical manifestations</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simons PCG et al (2002)</td>
<td>59-year-old man; infrarenal AAA</td>
<td>EVAR bifurcated graft</td>
<td>Talent LPS Medtronic™</td>
<td>17 months</td>
<td>Left-sided abdominal pain; unilateral hydronephroisys</td>
</tr>
<tr>
<td>Jetty P et al (2004)</td>
<td>76-year-old man; 5.4-cm infrarenal AAA</td>
<td>EVAR bifurcated graft</td>
<td>AneuRx device Medtronic™</td>
<td>5 months</td>
<td>Anuria Bilateral hydronephroisys</td>
</tr>
<tr>
<td>Brouw et al (2007)</td>
<td>60-year-old man; infrarenal AAA</td>
<td>EVAR bifurcated graft</td>
<td>–</td>
<td>3 years</td>
<td>Severe abdominal pain radiating to the back, malaise and fever</td>
</tr>
<tr>
<td>Brouw et al (2007)</td>
<td>72-year-old man; infrarenal AAA</td>
<td>EVAR bifurcated graft</td>
<td>–</td>
<td>3 months</td>
<td>Back pain and fatigue</td>
</tr>
<tr>
<td>Vijaynagar B et al (2011)</td>
<td>63-year-old man; 5.5-cm infrarenal AAA</td>
<td>EVAR bifurcated graft</td>
<td>Zenith device Cook™</td>
<td>9 months</td>
<td>Left flank pain; unilateral hydronephroisys</td>
</tr>
<tr>
<td>Taguchi T et al (2014)</td>
<td>78-year-old man; infrarenal AAA</td>
<td>EVAR bifurcated graft</td>
<td>–</td>
<td>15 months</td>
<td>Severe abdominal pain and fever</td>
</tr>
<tr>
<td>Alomran F (2014)</td>
<td>63-year-old man; 51-mm AAA</td>
<td>EVAR bifurcated graft</td>
<td>Endurant Medtronic™</td>
<td>8 months</td>
<td>Acute onset renal failure Bilateral Hydronephroisys</td>
</tr>
<tr>
<td>Frech et al (2015)</td>
<td>70-year-old man; 6.5-cm infrarenal AAA</td>
<td>EVAR bifurcated graft</td>
<td>Endurant II Medtronic™</td>
<td>3 months</td>
<td>Back pain</td>
</tr>
<tr>
<td>Mansour et al (2015)</td>
<td>67-year-old man; 5.3-cm infrarenal AAA and right CIAA</td>
<td>EVAR bifurcated graft; bell-bottom technique</td>
<td>Excluder, Gore™</td>
<td>8 days</td>
<td>Lumbar pain and lower limb swelling</td>
</tr>
<tr>
<td>Trinder et al (2019)</td>
<td>64-year-old man; 6.8-cm infrarenal AAA</td>
<td>EVAR bifurcated graft</td>
<td>Excluder, Gore™</td>
<td>2 months</td>
<td>Abdominal pain and night sweats</td>
</tr>
</tbody>
</table>

AAA – abdominal aortic aneurysm; CIAA – common iliac artery aneurysm.

In the case of periaortitis after EVAR, it appears that this complication can occur with different types of endoprosthesis. In five cases the graft material consists of woven polyester: Talent®, AneuRx®, Endurant® and Endurant II® from Medtronic™ (Medtronic AVE, Santa Rosa, CA, USA) and the
Periaortite "de novo" após EVAR ou stenting do setor aorto-ilíaco: uma revisão

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Table 2. Characteristics of patients who developed chronic periaortitis after endovascular treatment of intermittent claudication due to aortoiliac occlusive disease

<table>
<thead>
<tr>
<th>Patient / condition</th>
<th>Endovascular treatment</th>
<th>Device</th>
<th>Time to CP development</th>
<th>Clinical manifestations</th>
<th>CP treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sapoval et al (1995)⁸</strong></td>
<td>45-year-old woman; intermittent claudication of the left lower extremity; PTA of the left CIA followed by stent-graft implantation (dissection)</td>
<td>Dacron-covered nitinol stent (Cragg EndoPro)</td>
<td>2 months</td>
<td>Occasional finding on CT</td>
<td>No treatment Had resolved</td>
</tr>
<tr>
<td><strong>Sakr G et al (1998)⁹</strong></td>
<td>46-year-old woman; Bilateral intermittent claudication; PTA and kissing stent to common iliac arteries</td>
<td>?</td>
<td>3 months</td>
<td>Nausea, vomiting, right flank pain Bilateral Hydronephrosys</td>
<td>Oral steroids (uretral stents)</td>
</tr>
<tr>
<td><strong>Mendes et al (2017)⁴</strong></td>
<td>58-year-old man; intermittent claudication of the left lower extremity; PTA of the left common iliac artery followed by stent implantation</td>
<td>Nitinol stent</td>
<td>3 years</td>
<td>Disabling low back pain</td>
<td>Methylprednisolone (8 months);</td>
</tr>
<tr>
<td><strong>Mendes et al (2017)⁴</strong></td>
<td>67-year-old man; Bilateral intermittent claudication; PTA and kissing stent to common iliac arteries</td>
<td>ePTFE – nitinol covered stent</td>
<td>4 meses</td>
<td>Disabling low back pain</td>
<td>Prednisolone (1 year);</td>
</tr>
</tbody>
</table>

PTA – percutaneous transluminal angioplasty; CIA – common iliac artery.

Zenith® endoprosthesis (William Cook, Brisbane Australia). In 2 cases, the endoprosthesis used was an ePTFE graft: Gore excluder® (W. L. Gore and Associates, Flagstaff, Ariz). Most of these stent-grafts are made up of nitinol stents, however, it was also found that this complication developed with an endoprosthesis made of stainless-steel stents - Zenith® device (William Cook, Brisbane Australia). In the same way, in the treatment of occlusive disease, the development of periaortitis was also observed with different devices.

In the case of the development of periaortitis after EVAR, it is interesting to note that the two cases with the earliest clinical presentation (8 days and 2 months) were patients treated with Gore excluder® endoprostheses. The exact mechanism of these patients’ secondary periaortitis, to our knowledge, remains unknown. Some studies have shown that chronic periaortitis could be the result of an abnormal reaction to antigens contained in atherosclerotic plaques in the abdominal aorta. It could thus be hypothesized that stent/stent-graft deployment by interfering with the integrity of the arterial wall, could expose these antigens and trigger the inflammatory response⁵⁴.

In most cases this complication developed between several months to years after the implantation of the endoprosthesis, and in only one of the cases it manifested in the immediate postoperative period with lumbar pain and lower limb swelling⁵⁴. Most patients had low back or abdominal pain associated with constitutional symptoms (low fever, anorexia and fatigue).

Concerning the treatment of idiopathic cases of retroperitoneal fibrosis, the first goal is to reverse ureteral obstruction, when present, and protect kidney function. Medical therapy should be started as soon as possible to reverse the inflammatory phase, leading to the resolution of symptoms and the normalization of acute phase reagents⁶⁵. Patients were treated with steroids and tamoxifen. The rationale for the use of tamoxifen was the fact that its effectiveness has been demonstrated in cases of idiopathic retroperitoneal fibrosis⁶⁵. However, a recent randomized clinical trial showed that prednisolone is more effective than tamoxifen in preventing recurrences of idiopathic retroperitoneal fibrosis⁶⁶, possibly because the use of corticosteroids could also be important since, unlike in the case of infection, there is no uptake in inflammatory periaortitis⁶⁷.

Four patients presented with acute kidney injury resulting from hydronephrosis due to urethral obstruction requiring urinary...
Therapeutic regimens with corticotherapy and tamoxifen, titis, urethral involvement is the most frequent complication after stent-graft implantation. This complication can occur with different types of endoprosthesis and stents. The demography appears to be similar to that described for idiopathic retroperitoneal fibrosis, the delay from the procedure to the onset of inflammation is highly variable. Early treatment appears to be essential to avoid long-term renal impairment. Therapeutic regimens with corticotherapy and tamoxifen, similar to those used in idiopathic retroperitoneal fibrosis, appear to be effective. It is important to exclude infection before starting treatment.

**REFERENCES**