ISSN: 2476-230X

Research Article

Cardiology: Open Access

Hypertension and Takayasu Disease

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Submitted: 03 Dec 2018; **Accepted**: 01 Feb 2018; **Published**: 13 Feb 2019

Abstract

Introduction: *Takayasu's disease (TD) is a primary, inflammatory, rare, segmental and multifocal arteritis of the aorta and its branches, of unknown etiopathogenesis. Hypertension is a major complication, sometimes revealing the disease, whose mechanisms are multiple, dominated by the lesion of the aorta and renal arteries.*

Patients and methods: *We report a series of 63 cases treated for Takayasu's disease resulting from a monocentric, retrospective study from April 2oo6- July 2014, with an average age of 30 years with a female predominance of 83%.*

Result: *In our series: 51 patients with hypertension, including 29 (57%) resistant hypertension (under tri see quadritherapy). In 87% of cases lesion of the supra aortic trunk, 29% with aortic lesions and renal arteries, 7.93% with isolated renal arteries and 7% with aortic coarctation cases, valvular heart disease in 7% of cases. Association with tuberculosis in 7.93% of cases and a dysthyroidism in 11.1% of cases. That 49% benefited from surgical treatment.*

Discussion: *Involvement of the aorta and renal arteries seen in half of patients with TD is the leading cause of hypertension. In general, hypertension is severe, not or poorly controlled by medical treatment and is accompanied by cardiac and renal repercussions.*

Conclusion: *Hypertension is common during TD; it is a poor prognostic factor, more serious than the cause is renovascular. Early diagnosis and appropriate therapy will help to prevent a handicap, which is sometimes major for these patients, most of whom are young. Surgical treatment of renal and aortic lesions of TD is indicated when there is severe hypertension, not or poorly controlled by heavy medical treatment, and the indications should be weighed well. The spontaneous evolution in these patients is burdened with a not insignificant mortality. Management and therapeutic decisions must be multidisciplinary.*

Keywords: Takayasu disease, hypertension, renal angioplasty, renovascular hypertension, inflammatory arteritis, non-specific aorto-arteritis.

Abbreviation

EIA: external iliac artery; **CIA:** common iliac artery; **AT:** arteritis of Takayasu; **TLA:** transluminal angioplasty; Hypertension: Hypertension; **IDR:** intradermal reaction; **NIPH:** National Institute of Public Health; **TD:** Takayasu disease; **BP:** blood pressure; **TBC:** tuberculosis; **SAT:** supra-aortic trunk; **MI:** mitral insufficiency; **AOI:** aortic insufficiency.

Introduction

Described in 1908, Takayasu's disease is an idiopathic systemic vasculitis affecting large vessels, the aorta and its main branches (supra-aortic trunks, carotid arteries and subclavian arteries, renal arteries, but also coronary and pulmonary arteries) [1]. The injury may be segmental or diffuse to the entire thoracic and abdominal aorta [2].

It is an inflammatory arteriopathy of the young subject, most often occurring between the ages of 20 and 40, predominantly female, hence its definition of the disease of women without pulse [3].

It is a medio-adventitious giant cell granulomatosis [4].

Clinical manifestations are most often related to vascular involvement, either related to arterial inflammation or related to consequences such as stenos is or thrombosis. The mechanisms of vascular obstruction are different from atherosclerosis

Hypertension is most often related to the involvement of one or more renal arteries.

A classification into account the arterial locations are the types I to V [5]:

- Type I: involvement of the aortic arch,
- Type IIa: involvement of the Ascending aorta, aortic arch and its branches,

- Type IIb: involvement of the ascending aorta, aortic arch and its branches, descending thoracic aorta,
- Type III: involvement of the Descending thoracic aorta, abdominal aorta and / or renal arteries,
- Type IV: involvement of the Abdominal aorta and / or renal arteries,
- Type V: IIb and IV.

The aim of our study is to investigate the reno-aortic involvement of takayasu disease, to evaluate the prevalence of hypertension during TD, to assess the signs of gravity, the evolution of the disease over time and prognosis as well as the results of surgical and medical treatment.

Material and methods

A retrospective nonrandomized study in a single center was conducted from April 2006 to July 2014; sixty three (63) Patients were treated for Takayasu disease. These patients were admitted to vascular surgery department at Oran University Hospital November 1st 1954; validate the criteria of the American College of Rheumatology (ACR) [8]. Table 1

Table 1: American College of Rheumatology (ACR), Criteria for Classification of Takayasu"s Arteritis

1. Age at disease onset ≤ 40 years.
2. Claudication of extremities.
3. Decreased brachial artery pulse.
4. Blood pressure difference > 10 mm Hg.
5. Bruit over subclavian arteries or aorta.
6. Arteriogram abnormality.
N.B : A diagnosis of Takayasu's arteritis requires that at least 3 of the 6 criterias are met.

We received patients referred by internal medicine or cardiology department for the management of hypertension resistant to medical treatment with vascular lesions.

Para clinical exploration were done in all our patients: Chest X Ray, duplex ultrasound of supra aortic trunk, renal arteries, lower and upper limbs, computed tomography, electrocardiogram, cardiac echography and a complete laboratory tests including erythrocyte sedimentation rate (ESR) at the time of diagnosis and its fluctuations, white blood cell (WBC), rheumatoid factor (RF), C-reactive protein (CRP) and tuberculin intradermal reaction was performed in 10 patients.

The classification of Lupi Herrera (Table 2) allowed to divide our patients according to the topography of their lesions.

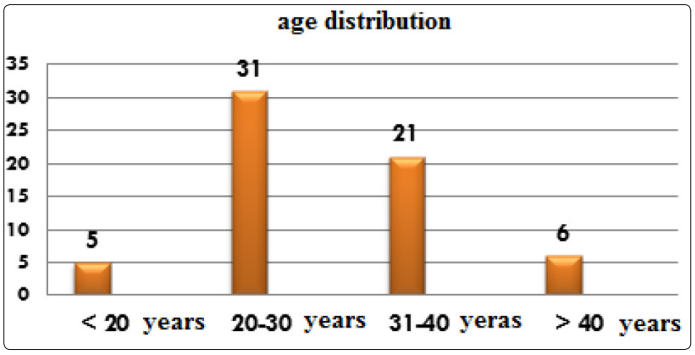
Table 2: Lupi-Herrera classification (1977)

Type	Vessel involvement
Type I	isolated involvement of the aortic arch and its branches
Type II	involvement of the abdominal aorta and its branches
Type III	Type I and II lesions
Type IV	Lesions of pulmonary arteries added to such lesions I, II or III

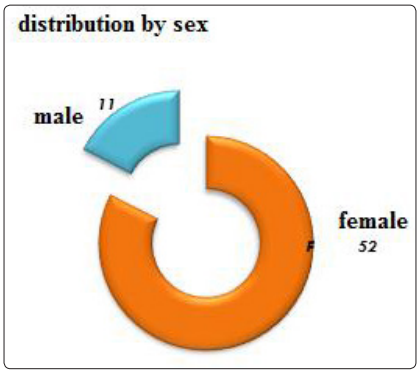
The statistical analysis was performed with IBM SPSS Statistics software 20 (IBM SPSS Inc., Chicago, IL).

Results

In our series, the mean age was 30 years with extremes from 12 to 64 years (graph No.1); with a female predominance sex ratio 5F/1H (graph No.2).



Graph 1



Graph 2

51 patients had hypertension, of which 29 (57%) were resistant (under/ tri or quadritherapy). The incidence of involvement of supra aortic trunk was found in 87% of cases (55 cases including 43 cases of bilateral lesions), the associated lesions of the aorta and the renal arteries in 29% of cases, isolated attack of the renal arteries in 7.93% of cases. , aorta coarctation in 8% of cases, involvement of the digestive arteries 02 cases, valvular heart disease in 7% of cases (04 cases of mitral insufficiency and 01 cases of aortic insufficiency). The lesional distribution of the disease is summarized in Tables 3. an association with tuberculosis in 5 cases (01cas intestinal TBC, 03 cases of pulmonary TBC and 01 cases of tuberculous adenitis), a Dysthyroidism in 7 cases, 01 cases of ankylosing spondylitis and 01 cases of systemic lupus erythematosus.

Table 3: Localization and type of lesions

Localization of lesions	Nombers of cases	Type of lesions
Carotids	19	05 bilateral stenosis 02 occlusions 05 stenosis<60% 07 unilateral stenosis
Vertebrals	22	Stenosis (bilaterale in 17 cases)
Sub Clavian	12	Stenosis/short occlusion

Axillary	02	Stenosis
Thoracic aorta	05	04 aortic Coarctation 01 aneurysm
abdominal aorta	02	01 lengthly stenosis 01 infrarenal aortic aneurysm
Renal arteries	23	08 isolated stenosis 17 associated with aortic lesions
Digestive arteries	02	Stenosis
Iliac arteries	02	01 stenosis 01Occlusion CIA (TASC A)
Valvular Heart disease	05	04 MI 01 AOI

Corticosteroid therapy was instituted in all our patients at a dose of 1 mg/kg/day, immunosuppressants in 05 patients and antihypertensives. A dual anti-platelet agent in all patients benefited from endovascular treatment.

Only 31 patients (49%) of whom underwent surgical treatment, 9 patients responded well to medical treatment, while the others either lost sight of them or refused the procedure. The revascularization procedures are summarized in Table 4.

Table 4: revascularization procedures

TLA-STENT artères rénales	05cas
TLA Sous clavières	07cas
TLA Carotides	01cas
Thoracic aorta Endoprothesis	02 cases for aortic coarctation
Abdominal aortic Endoprosthesis for false aneurysm	01 cases for aneurysm
TLA-Stent CIA	01 case
Resection-anastomosis for aortic coarctation	02cases
Ventral aortic bypass	02cases
Aorto- carotid bypass	02cases
Aorto-renal bypass	02cases
Carotid endarterectomy	02cases
nephrectomy	02cases

In the follow up, we deplore 01 death on the first day secondary to hemorrhagic syndrome after ventral aortic bypass for "middle aortic syndrome" in a young woman of 23 years; 02 conversions after failure of angioplasty and 04 patients have degraded their renal function. Regarding hypertension, the immediate postoperative evolution was towards the total normalization for 07 (8.77%) patients and an improvement in blood pressure in 18 patients, for whom the antihypertensive treatment has been lightened. Finally persistence of hypertension in 02 patients.

Discussion

TD is an inflammatory, rare, segmental and multifocal primary arteritis of the aorta and its main branches. It represents 5% of vasculitis. It is more common in Asia, India, South America (Mexico, Latin America). In Europe, its incidence was estimated at 2.6 cases/million/year [6]. In the Maghreb, the incidence is imprecise but a study conducted in 2009 collected 378 cases [7]. In Algeria, there have been no epidemiological studies, however several cases have been reported, revealed in particular by hypertension in the young subject (more than 279 cases of TD) [8].

Female dominance was in the majority in all studies, with a variable F/M ratio of 8/1 in Japan, 4.8/1 in France, 1.2/1 in India, 5.9/1 in Mexico [9]. In our series it was 5F/1M. The third decade of life is the period when the incidence of onset is highest, age <40 years is also a major criterion, but there may be about 20% of older patients at diagnosis. We had 06cas diagnosed> 40 years old, including 02> 60 years old.

The pathogenesis of Takayasu's disease is still unclear. Nevertheless, several hypotheses are advanced. The infectious origin has been incriminated, especially its relations with tuberculosis (tbc).

In most series there is a high prevalence of confirmed tuberculosis or positive intradermal reactions (IDR), (05 cases of tbc in our series), but this is not the only cause, because association of dysimmunitary pathology with TD, gives it the character of autoimmune disease [[10-12]. In our study we reported 01 cases of ankylosing spondylitis, 01 case of systemic lupus erythematosus and 07 cases of Dysthyroidism.

The disease evolves classically in two phases. The first, called "pre-occlusive", is characterized by general signs and a biological inflammatory syndrome. The second, known as "occlusive", results in the occurrence of ischemic clinical manifestations [9].

Hypertension is a serious public health problem, noted that worldwide approximately one billion, 978 million people with high blood pressure according to WHO "Lancet 2011," first death risk factor.

In Algeria, its prevalence is more than 35% or 7 million Algerians including 21% deaths from cardiovascular diseases in 2010 (NIPH) [13].

In Takayasu's disease, high blood pressure (hypertension) is a major complication, frequent, often revealing of the disease, dominated by the involvement of the renal arteries 30%, the thoracic or abdominal aorta above renal arteries (coarctation) and supra-aortic trunks inducing carotid bulb baroreceptor dysfunction and decreased cerebral blood flow [14, 15].

In general, hypertension is severe, not or poorly controlled by medical treatment, and is associated with cardiac and renal repercussions.

In our study, the disease was discovered during an HTA in 51 patients, of whom 27 cases had a malignant or resistant hypertension (under three /quadritherapy and poorly controlled). According to several studies, hypertension is considered one of the main factors of poor prognosis during TD [16-18].

In Algeria, the study of Mammeri et al. hypertension was severe in 54% of patients and responsible for 70% of deaths [8].

Mirault et al. reported a survival in Takayasu disease of 95% at 5 years and 91% at 10 years in France [19].

The main causes of death are heart failure (46%), the occurrence of stroke (10%) or renal impairment (11%) and postoperative complications (6.4%). Ruptures of arterial aneurysm were also responsible for deaths.

Scores were recently established to assess cardiovascular involvement during Takayasu's disease. The "disease extend index in Takayasu arterirtis" (DEI-TAK) developed on the basis of the Birmingham Vasculitis Activity Score (BVAS) [20].

The diagnosis of this disease is based on a set of radio-clinical arguments (Table 2), including clinical status, arterial topography (Table.3), its character (stenosis, occlusion or aneurysm) and the association with cutaneous, cardiac and visceral lesions [21].

In our study we had associations of aortic aneurysm and stenosis of subclavian arteries (fig.1), multiple localizations of arterial stenosis (fig.2), as well as aortic stenosis associated with renal artery stenosis in 8 case (fig.3)

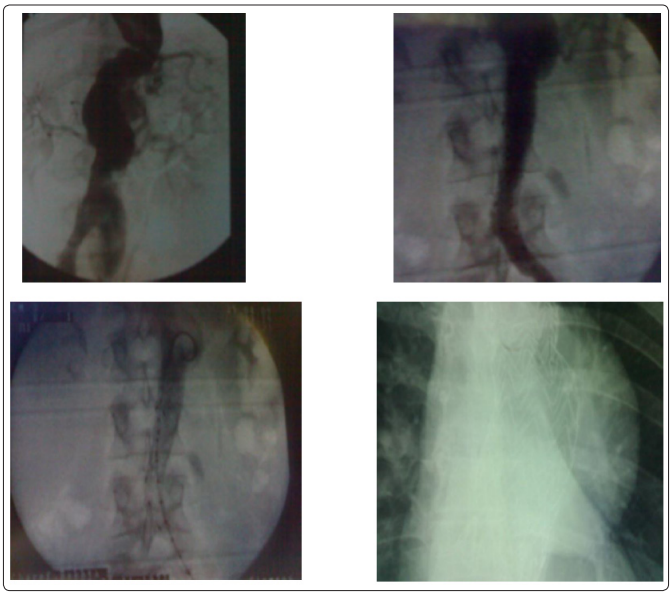


Figure 1: female, 35 years, married, Hypertension under tritherapy uncontrolled, with antecedents of tuberculous adenitis.

Lesions: Fusiform aneurysm of the descending thoracic aorta + sacciform aneurysm of the infrarenal abdominal aorta + stenosis of the left sub clavian artery.

Procedure: 1st time: Medical treatment: Corticotherapy + Anti-tuberculosis treatment

2nd time: Treatment of thoracic aneurysm with aortic endoprosthesis (Gore 40/19) dropped flush with the sub Clavian artery.

3rd time: Treatment of abdominal aortic false aneurysm

Follow up: good evolution, with improvement of blood pressure under dual therapy.

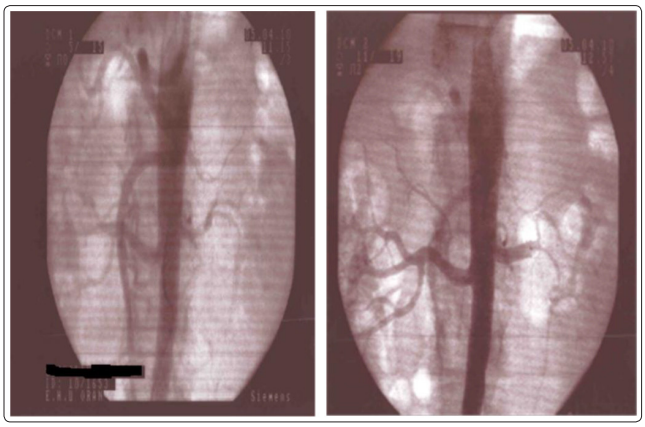


Figure 2: Female, 64 years old, with a medical history of primary infertility treated, (1 abortion).
Hypertension for 10 years under triple therapy.

Lesions: Stenosis of the right Sub Clavian artery.
-Tight stenosis of the left renal artery.
- tight stenosis of the right EIA + stenosis of the hypogastric artery.

Gesture: Medical Treatment
-TLA of Sub clavian artery + TLA of renal artery + TLA of EIA.

Evolution: Good with normalization of blood pressure.

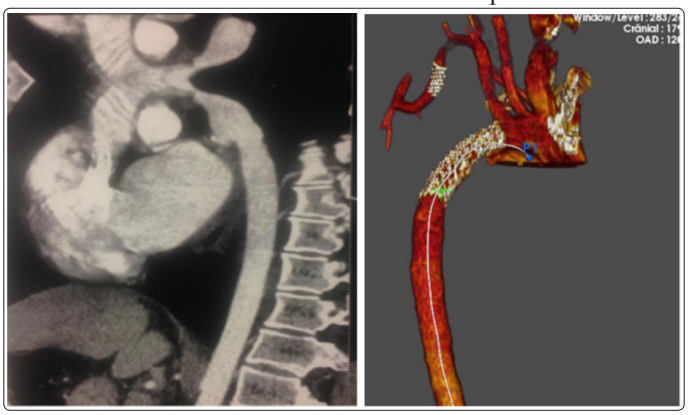


Figure 3: female, 23 years old,
Hypertension under tritherapy + claudication of the right upper limb.

Lesion: aortic coarctation + tight stenosis of the sub clavian post vertebral artery.

Procedure: Thoracic endoprosthesis + TLA -Stent of sub clavian artery

Evolution: good, improvement of the blood pressure under monotherapy with a good right radial pulse.

New imaging tools such as computed tomography or magnetic resonance angiography, positron fludeoxy glucose computed tomography emission tomography and recently high contrast ultrasound is frequently used diagnostic and to evaluate vascular inflammation [22]. Biology has no specific test for MT and its only interest is to show an inflammatory syndrome. In our study 39 patients had a biological inflammatory syndrome [23].

The treatment of Takayasu's disease is medical, according to data in the literature, corticosteroid therapy is the first-line treatment and if failure, the addition of methotrexate may stabilize the disease [24].

All our patients received corticosteroid therapy at a dose of 1 mg / kg / day, immunosuppressants, and more antihypertensive, as well as anti-tuberculosis treatment in 05 patients.

Biological agents such as anti-tumor, necrosis factor, tocilizumab and rituximab can be used effectively in refractory cases [25]. Surgical treatment of hypertension during Takayasu arteritis is indicated in case of failure of medical treatment.

Revascularization may be made by endovascular or open surgery. The latest 2009 EULAR recommendations on the treatment of vasculitis of large vessels reflect the low level of evidence (level 3) series of open surgery in the reported cases, hence the low grade (C) recommendations [26].

However, revascularization during the active phase may increase the risk of procedural complications [27], including restenosis, dissection, and anastomotic pseudoaneurysms; for this a medical treatment first is warranted before any surgical procedure or angioplasty (ATL). This was the case in all our patients.

(The criteria for activity and remission of the disease are shown in Table 5) [2].

Table 5: Disease Activity Criteria (NIH)

Recent appearance or aggravation of at least 2 of the following criteria:
Signs of ischemia or vascular inflammation: limb claudication, decrease or abolition of a pulse, breath or vascular pain, asymmetric blood pressure
Typical angiographic abnormalities
Systemic symptoms such as fever, arthromyalgia
Increase in sedimentation rate
The criteria for remission are:
Complete resolution or stabilization of all clinical signs
Stable nature of vascular lesions

Endovascular treatment of occlusive or aneurysmal lesions during MT is a minimally invasive, feasible, safe and effective procedure, and may be indicated as first-line. According to the literature excellent results have been reported ranging from 81% to 100% and low morbidity and mortality. [28]

Nevertheless, the success and results of balloon angioplasty alone are variable depending on the degree of stenosis and the length of the lesion, since the rate of restenosis could reach up to 80% [29] due to thickening of the wall and the parietal fibrosis, hence the implantation of a stent. Some studies have reported improved results in stenting [30, 31].

In our series, we have performed 04 TLA-stent of supra-aortic trunks, 03 TLA-STENT of subclavian, Endoprosthesis for aneurysm of the thoracic aorta and the abdominal aorta (Fig1.) 05 TLA -renal arteries (Fig.2), 02 ATL-Stent of iliac arteries, 01 Endoprosthesis for coarctation of the aorta (Fig.3) and TLA of the abdominal aorta and right renal artery for aortic hypoplasia, surgically taken after failure of the angioplasty (fig.4).

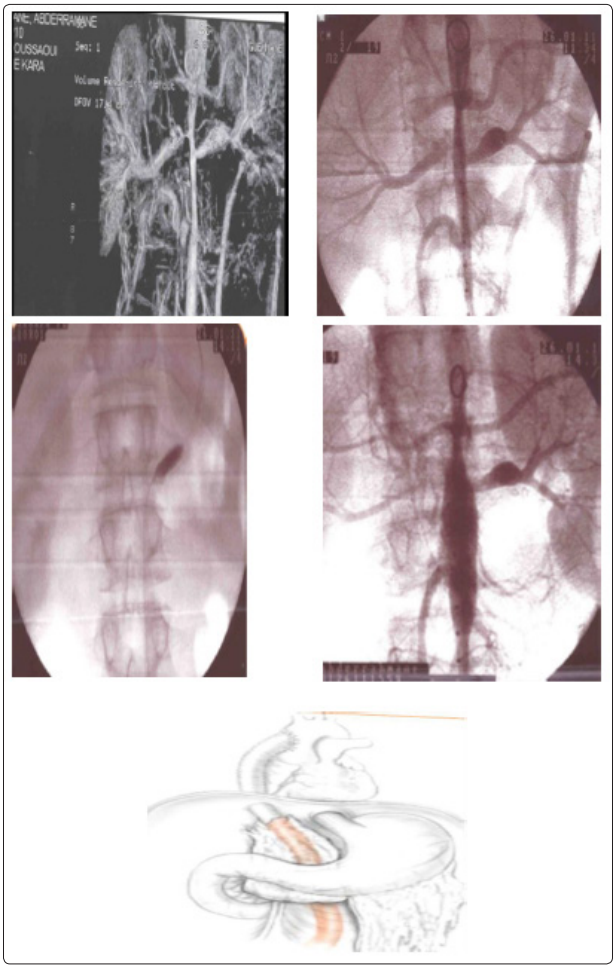


Figure 4: young male, 16 years old,
Hypertension uncontrolled under triple therapy.

Lesion: length tubular stenosis of the abdominal aorta and tight stenosis of the right renal artery.

Procedure: Medical Treatment.

1st time: abdominal endoprosthesis +angioplasty of the right renal artery

Evolution: failure of the endovascular treatment.

2nd time: conversion with aorto bi-iliac bypass from the ascending aorta

Evolution: good with stabilization of the blood pressure.

The surgical treatment of our patients was in all cases motivated by the severity of hypertension that was resistant to medical treatment and the failure of angioplasty, either by difficulty of catheterization, dissection or restenosis.

We performed 02 bypass by ventral aorta, 02 aorto-renal bypass, 02 aorto-carotid bypass, 02 carotid endarterectomy, 02 resection-anastomosis for aortic coarctation and 02 nephrectomies.

Chaudhry suggests renal revascularization in all cases of renal artery stenosis ≥ 70% with or without renovascular hypertension and according to Kim et al. surgery is an effective method in patients with lesions of supra aortic trunk. This would avoid major complications such as stroke [32, 33].

Other therapeutic modalities are under study for the treatment of Takayasu arteritis, such as TNF inhibitors and active angioplasty by eluting drug balloons, but they have not yet proven effective. [34, 15]

The evolution and prognosis of the disease are related to complications. Park et al examined the influence of severe complications on survival rates [16]. The presence of more serious complications increases the mortality rate in five years (69.9%) and 10 years (36.7%).

Ishikawa and Maetini found that survival varies not only depending on the time of diagnosis, but also to the presence of major complications that included valvular heart disease, stroke, heart failure, retinopathy and renovascular hypertension [17].

In addition, ischemia and bleeding are also common causes of death in the TD [35]. The right time for surgery requires further investigation.

Overall, surgical results have been improved over time, aided by advances in surgical and endovascular techniques, as well as optimization of pre, peri and postoperative care. Early postoperative death has become rare in many centers.

Some cases are illustrated (Figures.1-2-3-4).

Conclusion

Hypertension is common in the TD. It is a factor of poor prognosis all the more serious that the cause is renovascular.

Early diagnosis and appropriate treatment will help to avoid certain handicaps in the future, sometimes major for these patients, mostly young.

Surgical treatment of renal aortic lesions is indicated when there is severe hypertension not controlled by heavy medical treatment.

The spontaneous evolution in these patients in fact burdened with a significant mortality, the same for operated patients whose disease can progress either locally or remotely, which may require multiple and successive interventions, for this reason the surgical indications must be carefully weighed.

The multidisciplinary medical-radiological-surgical approach for the diagnosis and management of patients with Takayasu arteritis is essential to obtain satisfactory results.

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