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Predictors of survival in malignant aortic tumors

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Abstract

Objectives – Malignant aortic tumors (MAT) are exceedingly rare and a comprehensive review of clinical and therapeutic aspects is lacking in the literature. The aim of this study was to analyze all known cases of malignant aortic tumors, and to identify predictors of patients' survival.

Methods – All patients diagnosed with an aortic tumor treated in a single center, along with all case reports and reviews available in the literature - through a specific Pubmed search using key words such as "malignant" and "aorta" or "aortic" "tumor" or "sarcoma" or "angiosarcoma" - were analyzed. The tumor's primary location, clinical presentation, histological subtypes and treatment choice were all examined. Survival at 1-, 3-, 5-years and the possible preoperative and operative outcome predictors were evaluated using Kaplan-Meier with a log-rank test and by Cox regression for multivariate analysis.

Results – In addition to the 5 cases treated in our center, 218 other cases of MAT were reported in the literature from 1873 to 2017. The mean patient age was 60.1 ± 11.9 years and the male:female ratio was 1.59:1. The median overall survival from diagnosis was 8 (7-9) months; 1-, 3- and 5-years survival rates were 26%, 7.6% and 3.5% respectively. Chronic hypertension (p=0.03), fever (p=0.03), back pain (p=0.01), asthenia (p=0.04) and signs of peripheral embolization (p=0.007) were significant predictors of a poor result. Histological subtypes had a different impact on survival, with no statistical significance. Compared to other treatment strategies, combined - surgical+medical - therapy had the best impact on the median survival rate (surgical+medical 12 [8-24], medical 8 [5-10], surgical 7 [2-16], no treatment 2 [0.5-15] months,

p=0.001). Analyzing exclusively medical approaches, chemo- and radiotherapy had the best impact on median survival rate compared to untreated patients (chemo+radiotherapy 18 [10-26] months, radiotherapy 16 [8-20], chemotherapy 10 [7-24], and no medical treatment 6 [2-16], p=0.005); these data were not sustained by multivariate analysis.

Conclusions – Aortic tumors are a very malignant pathological condition with a short survival rate after initial diagnosis. Survival is further diminished in the presence of clinical factors, such as hypertension, fever, back pain, asthenia and signs of peripheral embolization. Combined surgical and medical treatment, particularly with chemo- and radiotherapy, has shown the highest survival rate.

Keywords – Aorta, tumor, aortic tumor, sarcoma, intimal sarcoma, angiosarcoma

Background

Aortic tumors are very rare and malignant diseases. Browdosky et al[1] reported the first case of a primary aortic tumor in 1873 and since then several case reports[2-5] and reviews[6] have been published in the literature.

Despite their rarity, malignant aortic tumors (MAT) can affect all segments of the thoraco-abdominal aorta. Their clinical presentation and imaging features can be often confounded with other aneurysmal or occlusive pathologies; therefore, the definitive diagnosis can usually be achieved only after histological examination on an intraoperative specimen or at autopsy[2,6].

The present study aims to report a case series of five primary MAT identified and treated in our institution[7,8] - 3 historical and 2 reported for the first time - and to analyze the available literature on the subject.

Methods

All patients with a diagnosis of MAT treated in our center from 1975 to 2017 were retrospectively analyzed, along with all case reports and reviews available in the literature. A specific search with the keywords “aorta tumor”, “aortic tumor”, “malignant aortic tumor”, “malignant aorta tumor”, or “aortic sarcoma” or “aortic angiosarcoma” was carried out in Pubmed. All malignant tumors arising from the iliac arteries or other vessels, not including the aorta, were disregarded. Only abstracts and articles published in English were considered.

The study was approved by the local Institutional Review Board; all patients involved in the current study signed a dedicated informed consent.

All available characteristics of the reported cases were inserted into a dedicated dataset. Age, sex and cardiovascular risk factors were reported. The tumor’s primary localization and

histological and immunohistochemical features were analyzed by a pathologist specialized in vascular diseases, who excluded all cases of a benign aortic tumor. Clinical characteristics of the MAT such as fever, back pain, asthenia, claudication, cutaneous lesions, or peripheral embolization were reported. The type of treatment, i.e. surgical or combined (medical+surgical), was analyzed. A 1-, 3-, 5-year survival follow-up was evaluated, as was the impact of preoperative characteristics and different treatment strategies on patients' survival.

Statistical Analysis

Categorical variables are expressed as frequencies and percentages, and continuous variables as mean ± standard deviation.

For all the categorical predictors survival times were analyzed with the Kaplan-Meier method and reported as a median and interquartile range (p25 – p75). Comparisons between levels of categorical data were estimated with a log-rank test; p values for further comparisons were adjusted with Bonferroni's correction.

A Cox proportional hazard regression model was performed, considering only the variables with p value less than 0.05 at univariate analysis reported in all papers, such as treatment strategy (medical, surgical, combined and none), type of medical treatment (chemo-, radiotherapy, combined and none) and type of tumor (leiomyosarcoma, angiosarcoma, hemangiosarcoma, intimal sarcoma, fibrosarcoma, fibrous histiocytoma, epithelioid angiosarcoma, spindle cell sarcoma and myxofibrosarcoma).

Considering the increasing advances of chemo -and radiotherapy in recent years, an interaction term with time was included in the model to examine potential modifications in the effect, reporting Beta coefficients and 95% confidence intervals.

For all statistical analysis, SPSS software version 21.0 and Stata SE/14.2 for Mac OS were used.

Results

Case Report

Patient 1 (1975) - A 67-year-old white man presented a 6-month history of left lower limb claudication at 50 meters and pain in the right knee, both during movement and at rest[7]. Two painful cystic formations in the right anterior tibial area were also present. On physical examination, the patient had excellent right lower extremity pulses, but no pulse was palpable on the left side.

Translumbar aortography showed aneurysmal dilatation of the infrarenal aorta and the iliac arteries, with loose thrombotic material in the lumen (Figure 1a). The left popliteal artery was occluded and the right popliteal artery was stenotic.

The patient underwent elective midline laparotomy, the aorta was exposed, clamped and opened, fish egg–like material was found adherent to the aortic wall[7], and the aortic lumen was almost totally obstructed by pultaceous, granular and friable material. The vessel surface was very irregular and the smooth surface had a pergamenous aspect. An aortobi-iliac bypass was performed using a Dacron conduit. The inferior mesenteric artery was re-implanted (Figures 1b and c).

Histological analysis identified malignant hemangioendothelioma with anaplastic aspects (Figure 1d). The same histology was confirmed in two cystic lesions, removed from the right anterior shin.

Nine months later, a chest x-ray revealed pulmonary nodules, likely due to a metastatic tumor; this was treated with radiotherapy, with no improvement. The patient died 12 months

after surgery due to pulmonary infection. This case report was published previously[7].

Patient 2 (1995) - A 61-year-old white man was admitted for acute left lower limb ischemia[8]. An angiography showed thrombus-like endoluminal material in the infrarenal aorta with an occlusion of the left popliteal artery and tibio-peroneal trunk.

The patient was treated with intra-arterial thrombolysis for the left leg. After few days, the patient was surgically treated through aortic thrombectomy, which was performed by median laparotomy with a transperitoneal approach, with extraction of soft whitish and granular material from the whole infrarenal abdominal aortic wall. The aortotomy was closed with direct suture. A Fogarty catheter thrombectomy of the left popliteal artery and tibio-peroneal trunk was performed, with removal of the same kind of material[8].

A histological examination showed angiosarcoma. Tumor cells were positive for the endothelial markers Factor VIII, which is an endothelial cell marker in benign and malignant diseases, considered valuable in diagnosing tumors of vascular origin[9].

Four months later, an ultrasound (US) showed a sub-fascial nodule (diameter: 12 x 8.5 mm) at the proximal third of the right medial gastrocnemius muscle, which was surgically removed and was histologically compatible with angiosarcoma[8].

Five months after surgery, a computed tomography (CT-scan) showed an endoluminal tumor relapse starting from the left posterolateral aortic wall, which was removed again, extracting the same soft whitish material found before, with identical histological characteristics. Multiple secondary lesions were found through postoperative bone scintigraphy; radiotherapy was not effective and the patient died 31 months after the first surgical procedure, for neoplasia-related pulmonary embolism. This case was published previously[8].

Patient 3 (2003) - A 53-year-old white woman presented acute thoracic pain and right hemothorax[8].

A CT-scan showed a type III thoraco-abdominal aneurysm with suspected rupture of the distal thoracic aorta and right pleural effusion, which required emergency surgery.

A ruptured thoraco-abdominal aneurysm was found through a thoraco-phreno-laparotomy. The inner surface of the blood vessel showed a number of blisters and histology revealed a poorly differentiated epitheliomorphous tumor with giant cells, compatible with malignant aortic leiomyosarcoma. An aorto-aortic bypass, using a Dacron conduit, from the descending aorta to the abdominal aorta was performed. Intraoperatively, a lung nodule was excised from the left lower pulmonary lobe. The lung nodule was a metastatic lesion.

After discharge from hospital, the patient underwent cycles of chemotherapy and died 10 months later of pulmonary infection, related to lung metastasis evolution. This case was published previously[8].

Patient 4 (2011) - A 36-year-old white male smoker was admitted with bilateral buttock claudication at less than 50 meters. Doppler US showed a bilateral aorto-iliac steno-obstruction with a 0.6 ankle-brachial index bilaterally.

A CT-scan revealed a stenosis of the infrarenal aorta (diameter: 2 x 2 cm), of the aortic bifurcation (diameter: 1 x 0.5 cm) and of the left common iliac artery. The right common iliac artery was occluded (Figures 2a and 2b). In addition, multiple reactive retroperitoneal periaortic lymph nodes of 1 cm in diameter were also present, which were probably related to the aortic lesion.

As a first treatment, the patient underwent endovascular revascularization. Intraoperative

angiography showed aortic stenosis with endoluminal thrombus-like material and occlusion of the right and left common iliac arteries with bilateral recanalization of the external iliac artery. The patient was treated with intra-arterial urokinase for 1 day and aorto-iliac angioplasty with self-expandable stents (Sinus 14x6 and 8x10mm) subsequently.

After the first treatment, the patient showed a clinical improvement with no claudication during the first postoperative months.

Two years later, the patient suffered sudden left limb claudication (< 50 meters). A CT-scan showed aortic occlusion, abdominal aortic aneurysm (diameter: 32 mm) with reactive periaortic lymph nodes and bilateral renal artery stenosis. After one day of urokinase therapy, performed using an intra-arterial catheter with omeral access, the patient underwent surgical repair with an aorto-bi-iliac Dacron bypass with polar renal artery reimplantation. During the open surgery the patient suddenly became oliguric. A selective bilateral renal artery angiography from intra-arterial catheter (with omeral access) was performed, showing a complete bilateral renal artery obstruction. With omeral access, a bilateral renal artery stenting was performed. Before suturing the surgical access, the abdominal exploration showed an important injury of the spleen, which was surgically corrected with a splenectomy. The histological intraoperative specimen revealed an intimal aortic sarcoma (Figures 2c and 2d), therefore chemotherapy with Epirubicin and Ifosfamide (2+4 cycles) and radiotherapy was initiated.

The patient was readmitted one year later for therapy-resistant hypertension and renal function worsening. A CT-scan showed bilateral renal stent occlusion without abdominal metastasis or recurrences. A bilateral renal artery angioplasty was attempted, but the distal thrombosis of these vessels made the procedure unfeasible.

Several months later, an 18F-FDG PET showed recurrences of the disease; the patient was

treated with adjunctive chemotherapy.

He died 53 months after the first endovascular treatment from a cerebral hemorrhage, probably due to cerebral metastases.

Patient 5 (2016) - A 74-year-old white man was admitted into our emergency room with lumbar pain and a past medical history of endovascular treatment of an abdominal aortic aneurysm (54 mm diameter) with Medtronic Talent endoprosthesis 10 years before, a percutaneous CT-guided sac embolization from lumbar and mesenteric inferior arteries for persistent type II endoleak 4 years later, an endovascular relining of the right iliac leg for type III endoleak 3 years later. The patient was followed, with annual CT-scans, for the increasing diameter of the aneurysm sac, which was 87 mm and 92 mm 2 and 3 years after the last intervention, respectively, with a persistent endoleak of undefined origin.

The urgent CT-scan at admission showed a sac enlargement (up to 95 mm diameter) with signs of rupture, a persistent type I, II or III endoleak and multiple reactive retroperitoneal periaortic lymph nodes.

The patient urgently underwent open repair with explantation of the endograft and an aorto-bi-iliac bypass. Intraoperatively the aneurysm sac appeared inflamed and surrounded with many reactive lymph nodes, which were biopsied, especially in the juxtarenal position. The endoleak was most likely a type Ia.

The postoperative CT-scan (Figures 3a and 3b) and PET showed a hypercaptation of contrast medium in a left paraortic lesion (29x24 mm diameter) and in the reactive lymph nodes. The paraortic lesion was increased (64x55 m) at the 2-months-after CT-scan evaluation (Figures 3c and 3d).

The histological intraoperative examination revealed an epithelioid angiosarcoma of the aorta (figure 4) with a local invasion of reactive lymph nodes.

In the postoperative period, the patient suffered from pneumonia, which was unsuccessfully treated with broad-spectrum antibiotics (Piperacillin and Tazobactam) and led to acute respiratory distress. The patient died 2 months after surgery.

Metanalysis

Our research yielded 207 articles concerning MAT published on Pubmed. From 1873 to 2017, 223 cases of aortic tumors were reported, including the 5 cases of the present series. The mean patient age was 60.1 ± 11.9 years; male patients were 137/223 (61.4%) with a male:female ratio of 1.59:1.

Preoperative Characteristics

Data on preoperative characteristics are lacking in some of the reviewed case reports. In the considered population of 223 patients, 25.3% were smokers, 9.3% had type II diabetes mellitus and 48.8% had high blood pressure.

In our series of 218 case reports and 5 patients treated in our center, only 5.3% underwent aortic surgery (1.9% open repair, 3.4% endovascular repair) before the diagnostic hypothesis of a primary MAT.

Pathological Features

All 223 cases reported were primary MAT and were located in all possible segments of the thoraco-abdominal aorta, with a higher prevalence of the abdominal aorta (95/223 cases -

42.6%). The thoracic aorta was affected in 84/223 cases (37.7%) and the aortic arch segment in 17/223 cases (7.6%). The remaining 27/223 cases (12.1%) affected both thoracic and abdominal segments.

The rate of metastasis from the primary aortic tumor was 56% in the 168 cases in which it was considered.

Table I reports the incidence of the different histological types of MAT in the population examined.

Clinical Presentation

Twenty-three/223 (10.3%) patients presented a fever and 65/223 (29.1%) asthenia. The main symptoms were back pain in 71/223 cases (31.8%), intermittent claudication in 35/223 cases (15.7%) and peripheral embolization in 56/223 cases (25.1%). Thirteen of the 223 patients (5.8%) had skin lesions indicating a cutaneous metastasization of the cancer.

Treatment

One hundred seventy-nine/223 patients (80.2%) were treated for MAT; in the other 44/223 cases (19.8%) MAT was diagnosed directly at autopsy. The mean time between symptom onset and definitive diagnosis was 11.5 ± 5.3 weeks. One hundred and twenty-four of the 223 patients (55.6%) were treated by surgery, through open repair (aorto-aortic, aorto-bisiliac or aorto-bifemoral bypass) (114/223 cases, 51.1%) or endovascular repair (10/223, 4.5%). Fifty of the 223 patients (22.4%) were treated by a combination of medical and surgical therapy; and 5/223 patients (2.2%) received only medical therapy.

The medical approach consisted of chemotherapy in 34/223 cases (15.2%), radiotherapy in 8/223 cases (3.6%) and a combined chemo- and radiotherapy in 13/223 cases (5.8%).

Survival

The median overall survival from diagnosis was 8 (7-9) months; the 1-, 3- and 5-year survival rates were 26%, 7.6% and 3.5% respectively (Figure 5).

Using Kaplan-Meier with log-rank analysis, several predictors of reduced survival were found, such as chronic hypertension, fever, back pain, asthenia and signs of peripheral embolization at presentation, as shown in Table II.

The patients' survival was not influenced by the aortic segment involved in MAT, as shown in Table III.

The log-rank analysis of MAT histological subtypes on median survival led to a significant p-value (p=.035). However, a different comparison among each histological subtype did not show any statistical significance in median survival time; Table IV summarizes the median survivals of different histological subtypes. Nevertheless, some subtypes, such as Leiomyosarcoma and Hemangiosarcoma, showed longer median survival (12 [3-24] and 12 [12-24], respectively) in comparison with other rarer types, such as fibrosarcoma and myxofibrosarcoma (Table IV).

An early MAT diagnosis (before 11.5 weeks from symptom onset) was not associated with a significant survival rate improvement, if compared with patients diagnosed after 11.5 weeks (median survival: 19 [8-29] months vs 15 [6-24] months respectively, p=0.82).

Combined - surgical and medical - therapy led to a median survival time of 12 (8-24) months, significantly greater than surgical treatment alone (7 [2-16] months) and no treatment (2 [0.5-15] months), as shown in Figure 6, p=0.001.

Analyzing the exclusively medical approach, chemo- and radiotherapy showed the best impact on survival rate compared to untreated patients (chemo+radiotherapy 18 [10-26] months, radiotherapy 16 [8-20], chemotherapy 10 [7-24], and no medical treatment 6 [2-16], p=0.005). At multivariate analysis, as shown in Table V, different histological subtypes were not related to a significant improvement on survival, as well as different treatment strategies and medical approaches, analyzed with interaction term over time.

Discussion

This study summarizes the results of the largest published series of primary MAT, with 207 articles and 223 cases, including the 5 patients treated in our center. These data confirm the rarity of the disease, for which it is still impossible to predict the real incidence on the global population.

The mean age at diagnosis (60 years) and the prevalence of males (61% of cases) are consistent with data found in other reviews published in the last 10 years [6,10,11].

The role of previous aortic procedures in the development of MAT is questionable, since only 5.3% of patients had aortic endovascular or open repair before developing the tumor in our analysis; similarly, Rusthoven et al[6] reported a 6.7% occurrence of previous aortic surgery. Thus, more data are necessary to investigate the actual role of aortic treatment in the natural history of MAT.

When suspecting a MAT, it should be taken into account that all segments of the aorta can be involved; however, the thoracic and abdominal aorta are the most common sites of tumor growth (37.7% and 42.6%, respectively), in line with what Rusthoven et al reported in 2010[10] and 2014[6]. Localization in the aortic arch or extensive thoraco-abdominal involvement is much rarer (7.6% and 12.1% each).

Metastasis is highly possible - 56% of cases in our review, despite the lack of a wide body of data. Others have found an even higher rate of metastasization, up to 85%. [2,10,12,] This is probably related to the difficult and often late diagnosis of MAT, with subsequent tumor growth and spreading.

There are several histological subtypes of aortic tumors, with a predominance of angiosarcoma and intimal sarcoma (37.2% and 30.5% respectively), both in our review and in the literature[2,6,12]. The first histological classification of MAT was made by Salm in 1972[13]; tumor types were divided into intraluminal (polypoidal), intimal and adventitial, depending on the site of origin. Wright et al[14] in 1985 classified aortic tumors in intimal - originating from the intima, either obstructive or non-obstructive and mural – when originating from the media or the adventitia. Thalheimer et al[12] in 2004 created a more complete classification of MAT. Using electron microscopical findings, tumors with an intimal origin were further divided in angiosarcoma - which shows endothelial-specific antigens in immunohistochemistry - and myofibroblastic sarcoma - which expresses mesenchymal-specific antigens. Tumors of mural origin always show mesenchymal-specific antigens on immunohistochemistry[7].

Similarly to other reports, [2,11,12] the clinical presentation of these tumors is variable and very scarcely specific, with back pain (31.8%), asthenia (29.1%) and peripheral embolization (25.1%). As a matter of fact, aortic tumors can mimic either a peripheral arterial disease -

claudication and embolization - or a symptomatic aortic aneurysm - back pain. Fever and asthenia are the only signs typical of malignant tumors, but, due to their very low specificity, are scarcely informative. For all these reasons, diagnosing MAT is not possible through a simple physical examination but requires a high rate of suspicion together with targeted exams, Computed Tomography Angiography or Magnetic Resonance Angiography, finding a heterogenous thrombus protruding in the aortic lumen[15-20]. Thereafter, the confirmatory diagnosis can only be achieved by histological examination.

Treating MAT requires the involvement of a multidisciplinary team[6]. After confirmatory diagnosis by a pathologist, the disease should be simultaneously managed by oncologists and vascular surgeons, in order to set up the most appropriate treatment, whether surgical, medical or combined.

In our metanalysis most patients (80.2%) received some kind of treatment for MAT; predominantly surgery, either as the only treatment (55.6%) or combined with medical therapy (22.4%). A small part of patients received only medical (2.2%) or no treatment at all (19.8%) as a consequence of the delay in the diagnosis. The surgical treatment was performed exclusively with open surgery until the 1990s when the endovascular era began, however, after this date as well, endovascular procedures remained confined to few cases. Medical treatment consisted most often in chemotherapy (34/223); combined chemo- and radiotherapy (13/223) and radiotherapy alone (8/223) were performed less frequently.

The inadequacy of any type of therapy is however demonstrated by the very limited median survival, 8 (7-9) months after the diagnosis, similarly to previously reported data[2,6,11,12].

Log-rank analysis showed that chronic hypertension was a predictor of lower survival in patients with MAT. This finding is new compared to the literature, as is the worse outcome in

patients with symptoms at presentation including fever, back pain, asthenia and signs of peripheral embolization. Since they are often directly correlated with the disease's progression, their role in predicting diminished survival is not surprising.

Log-rank analysis revealed a lower malignancy of some histological subtypes such as leiomyosarcoma and hemangiosarcoma (median survival 12 [3-24] and 12 [12-24] months respectively), as priorly reported by Chiche et al[2], with no statistical significance at multivariate. Our data must however be validated by further observations, since myxofibrosarcoma and spindle cell sarcoma are so rare that only 1 and 2 cases have been observed to date.

Combined (surgical and medical) therapy, at log-rank test, showed the best impact on median survival rate (12 [8-24] months), compared with surgical (7 [2-16] months) treatment and no treatment (2 [0.5-15] months). Rusthoven et al[6] underlined the same aspects, showing that the factors improving survival in patients with MAT appear to be surgical resection and chemotherapy. Analyzing the exclusively medical approach, in our metanalysis chemo- and radiotherapy had the best impact on median survival rate, compared with no medical treatment. Nonetheless, as reported by Rusthoven et al as well[6], the role of chemotherapy against soft-tissue sarcomas in the literature is controversial.

Our case-report metanalysis has some significant limitations, such as the scarce data available in the literature. Due to the presence of very old and sometimes undetailed publications, data regarding patients' preoperative characteristics are lacking. For this reason, it is not possible to analyze the real impact of preoperative characteristics on MAT occurrence. Mainly in the early reports, it is not always possible to determine if the aortic tumors described are truly primary tumors as opposed to metastatic or local invasive tumors. Furthermore, indications as to treatment can vary depending on the patient's status - i.e., patients offered

combined (surgical+medical) treatment may have had the best prognosis, while those who received medical- only or no treatment may have had more extensive diseases or other problems and not been considered good candidates for aggressive treatment.

The small number of patients reported to now - 223 - leads to a statistically weak analysis, and consequently a significant selection bias.

Conclusion

Aortic tumors are very rare, with less than 250 cases reported in the literature at present.

Their high malignancy is confirmed by the short median survival time after the initial diagnosis, which might be associated with the presence of specific clinical factors, such as hypertension, fever, back pain, asthenia and signs of peripheral embolization.

Some histological subtypes, such as leiomyosarcoma and hemangiosarcoma, might possibly be related to a longer survival rate.

Despite the lack of sustained data, combined surgical and medical therapy, particularly with chemo- and radiotherapy, has shown the highest survival rate.

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Figure 1

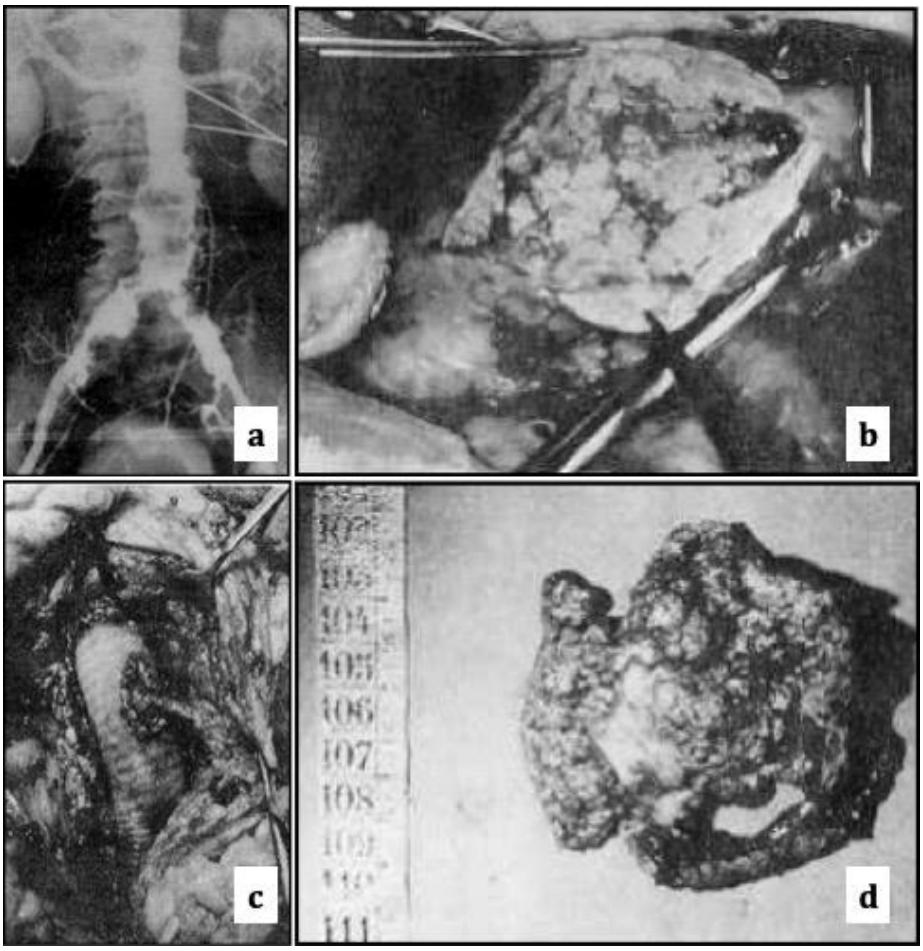


Figure 2

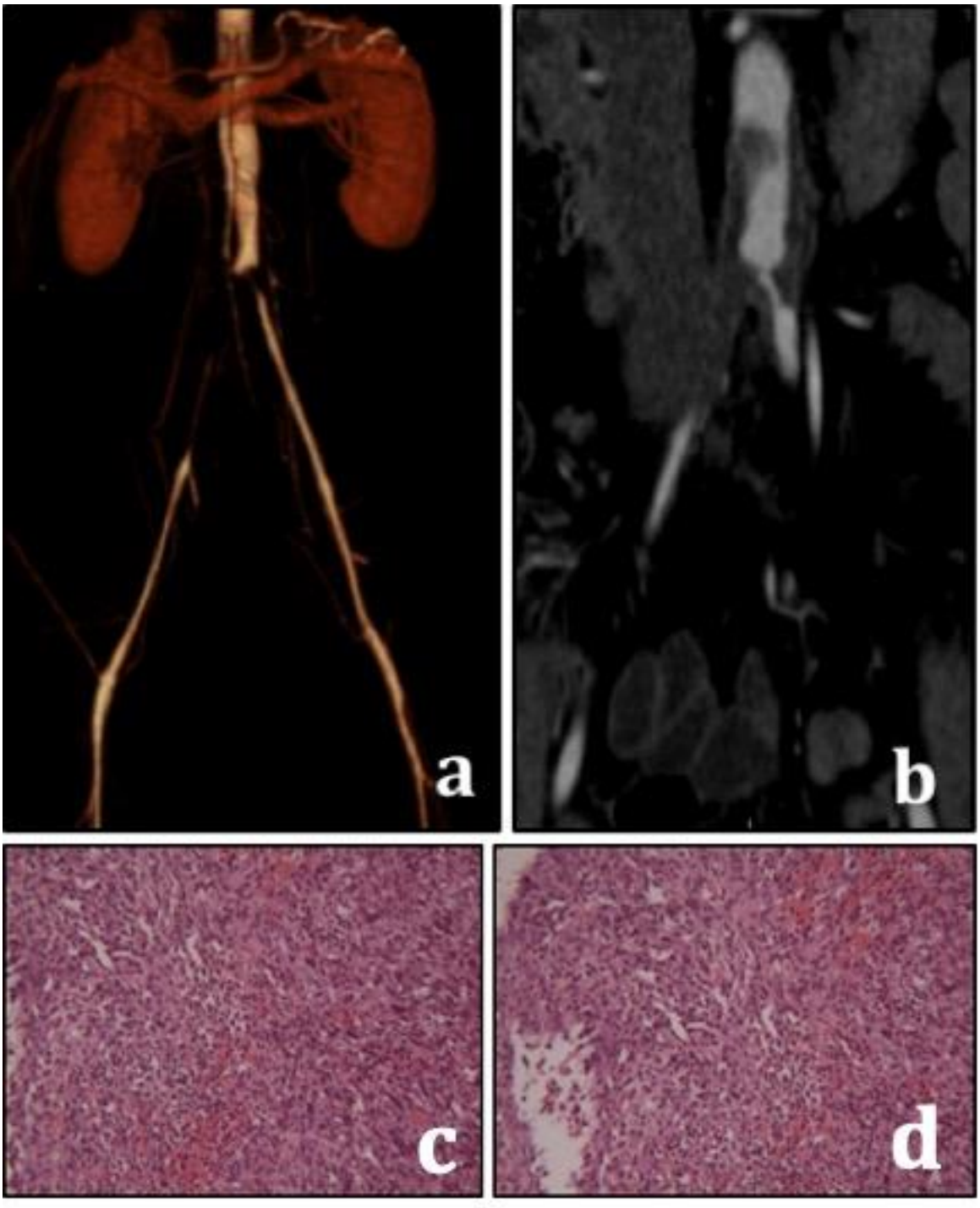


Figure 3

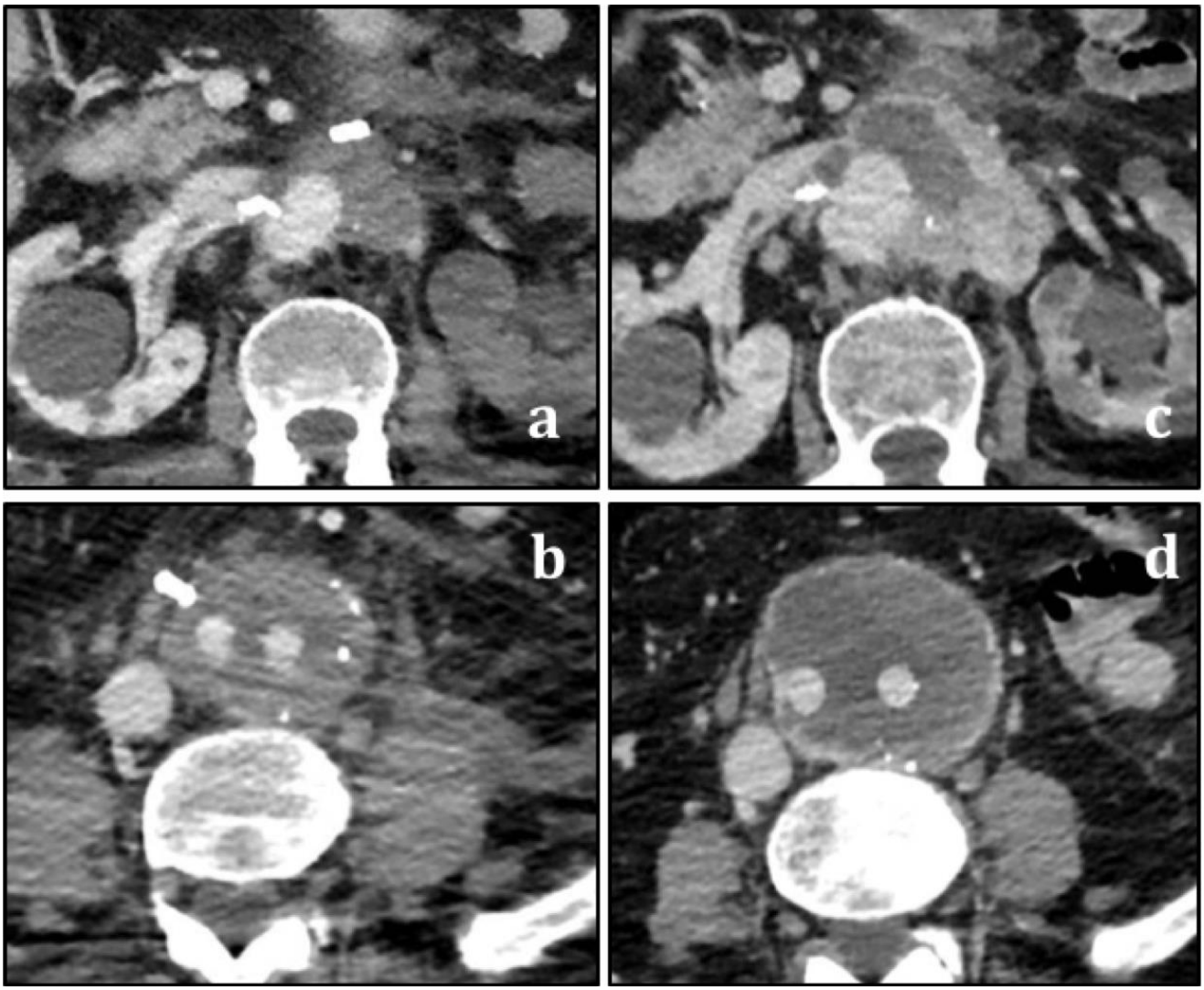


Figure 4

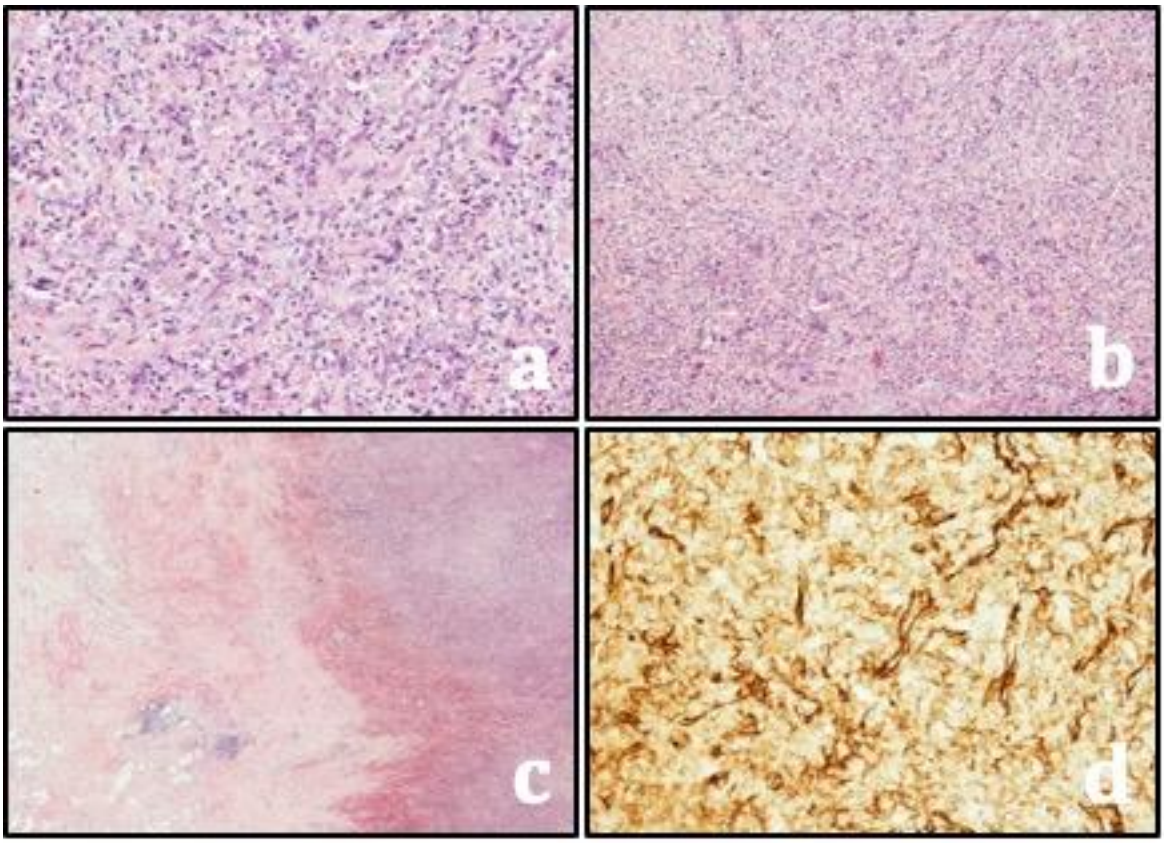
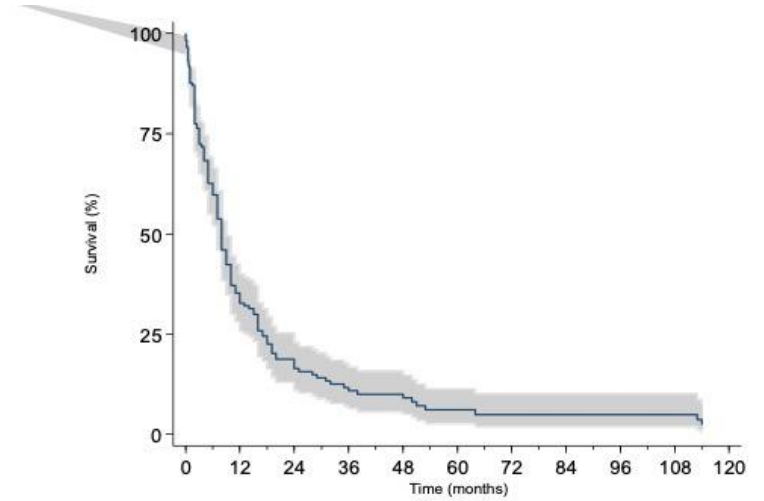
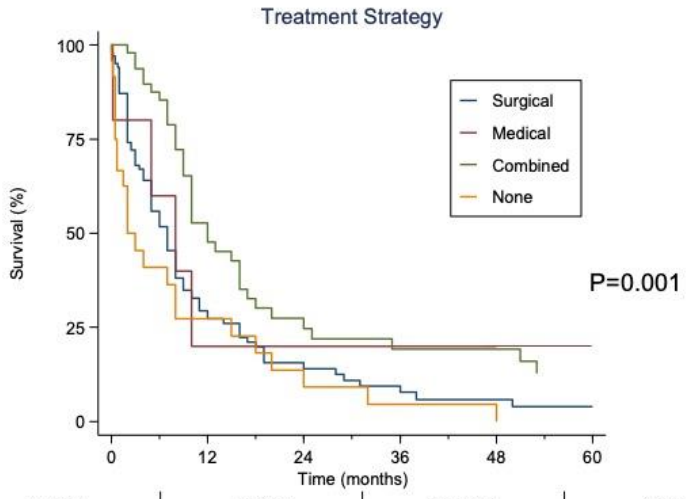


Figure 5



Months	0	12	24	36	48	60	72	84	96	108	120
N at risk	223	58	25	17	12	8	4	4	4	4	2
Survival Function	100	26	11.2	7.6	5.3	3.5	1.7	1.7	1.7	1.7	0.8
Standard Error	-	3.6	3	2.6	2.4	2.2	2	2	2	2	1.5

Figure 6



	Surgical						Medical						Combined						None					
Months	0	12	24	36	48	60	0	12	24	36	48	60	0	12	24	36	48	60	0	12	24	36	48	60
N at risk	126	27	10	6	4	2	8	2	2	2	1	1	59	21	10	7	7	5	30	8	3	2	0	0
Survival Function	100	21	8	4.7	3.1	1.5	100	25	25	25	12	12	100	35	17	12	12	8	100	27	10	7	0	0
St Error	-	4.5	3.8	2.9	2.5	1.1	-	17	17	17	8	8	-	7.6	6.8	6.3	6.3	5.6	-	9.3	6.1	4.4	-	-

Table I

Histological type	*N*	*%*
Angiosarcoma	83	37.2
Intimal Sarcoma	68	30.5
Leiomyosarcoma	24	10.8
Fibrosarcoma	16	7.2
Fibrous Histiocytoma	14	6.3
Epithelioid Angiosarcoma	11	4.9
Hemangiosarcoma	4	1.8
Spindle Cell Sarcoma	2	0.9
Myxofibrosarcoma	1	0.4
Total	223	100

Table II

	Median (p25-p75) survival rate (months)* Yes vs No	*P*
Risk Factors		
Male Sex	8 (4-18) vs 7 (2-16)	0.22
Hypertension	5 (2-10) vs 8 (3-19)	0.03
Smoking	7 (2-13) vs 7 (2-15)	0.6
Diabetes	6 (3-9) vs 8 (2-16)	0.09
Previous Aortic Surgery	6 (2-8) vs 8 (3-18)	0.13
Clinical Presentation		
Metastasis	8 (3-18) vs 8 (2-16)	0.96
Fever	2 (1-11) vs 8 (3-18)	0.035
Back Pain	5 (2-12) vs 9 (5-19)	0.013
Asthenia	5 (2-10) vs 8 (3-18)	0.042
Peripheral Embolization	6 (2-9) vs 10 (3-19)	0.007
Lower Limb Claudication	9 (4-29) vs 8 (2-16)	0.20
Skin Lesions	8 (4-25) vs 8 (3-17)	0.74

*Interquartile range

Table III

Aortic Segment	*Median (p25-p75)* survival rate (months)*	*P*
Arch	7 (1.5-16)	0.8
Thoracic	8 (4-16)	
Abdominal	8 (3-19)	
Thoraco-abdominal	9 (5-19)	

*Interquartile range

Table IV

Histological type	*Median (p25-p75)* survival rate (months)*
Leiomyosarcoma	12 (3-24)
Angiosarcoma	8 (5-18)
Hemangiosarcoma	12 (12-24)
Intimal Sarcoma	7 (2-16)
Fibrosarcoma	4 (4-48)
Fibrous Histiocytoma	8 (2-10)
Epithelioid Angiosarcoma	8 (3-17)
Spindle Cell Sarcoma	7 (2-15)
Myxofibrosarcoma (1 patient)	0.5

*Interquartile range

Table V

	Beta Coefficient (95% C.I.)	P
Histological subtype (Reference category Angiosarcoma)		
Leiomyosarcoma	-.24 (-.813 - .316)	0.389
Hemangiosarcoma	-.03 (-1.47 - 1.39)	0.958
Intimal Sarcoma	.26 (-.151 - .673)	0.215
Fibrosarcoma	.08 (-1.13 - 1.30)	0.892
Fibrous Histiocytoma	.54 (-.158 - 1.24)	0.129
Epithelioid Angiosarcoma	.41 (-.284 - 1.11)	0.245
Spindle Cell Sarcoma	.30 (-1.69 - 2.31)	0.762
Myxofibrosarcoma	2.3 (.246 - 4.46)	0.069
Treatment strategy (reference category surgical)		
Medical	-.47 (-2.70 – 1.75)	.675
Medical + Surgical	-.80 (-2.83 -1.22)	.436
None	.33 (-.182 - .853)	.204
Medical treatment (Reference category none)		
Chemotherapy	58 (-44.3 – 160)	.266
Radiotherapy	104 (-170 – 378)	.458
Chemo- and Radiotherapy	-36 (-207 – 134)	.676
Interaction Term		
Chemo*Year	-.02 (-.079 - .022)	.267
Radio*Year	-.05 (-.189 - .085)	.458
Chemo- and Radiotherapy*Year	.01 (-.066 - .103)	.676

Figure Table Legend

Figures

Figure 1: (a) Small infrarenal abdominal aortic aneurysm and dilated iliac arteries bilaterally, with loose thrombotic material in the lumen; (b) Tumor in the abdominal aorta; (c) Reconstruction with aortoiliac bypass and reimplantation of the inferior mesenteric artery; (d) Excised aortic tumor specimen. (From Paragona O, Bertoni F, Tarantini P, D'Addato M. Hemangioendothelioma of the abdominal aorta. Vasc Surg 1982; 16:117–129, with permission).

Figure 2: (a) 3D reconstruction CTA shows a stenosis of the left common iliac and a complete occlusion of the right common iliac artery; (b) Multiplanar reconstruction (MPR) shows thrombotic material in the lumen of the infrarenal aorta and common iliac arteries; (c) and (d) Haematoxylin-Eosin stain 20x magnification shows the histological appearance of intimal sarcoma of the aorta (Case 4).

Figure 3: (a) and (b) Post-operative CT-Scan of patient number 5; (c) and (d) Two-months CT-Scan shows increasing of pararenal tumor and sac enlargement.

Figure 4: Histological appearance of epithelioid angiosarcoma of the aorta (Case 5); (a) and (b) Densely-packed atypical epithelioid cells (Haematoxylin-Eosin stain, 20x and 10x magnification) with hemorrhage and wide areas (c) of ischemic necrosis (Haematoxylin-Eosin stain, 2x magnification); (d) At immunohistochemistry, neoplastic cells are diffusely positive for CD31 (20x magnification).

Figure 5: Survival of 223 patients with malignant aortic tumors.

Figure 6: Impact of different treatment strategies on the survival curve.

Tables

Table I: Histological analysis of 223 malignant aortic tumors.

Table II: Association of risk factors and clinical presentation on survival.

Table III: Association of the affected aortic segments on survival.

Table IV: Median survival rate for each aortic tumor histological subtype.

Table V: Multivariate analysis of predictors of survival.