

## Can Aneurysm be Treated Chemotherapeutically?

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### Abstract

Aneurysm is a pathological dilation of blood vessels beyond elastic return characterized by bulging of the affected part. The predispose factors are age, gender, species of animals and underlying cardiovascular pathology. Aneurysmic vessel of diameter > 5 cm portend a high risk of rupture. However, average diameter of the affected vessels is 4.6 cm. Affected vessels have increase of 0.9 mm and 0.7 mm in diameter of man and woman over 1 year respectively. Fungi such as *Graphium* species, *Spirocercus lupi*, *Salmonella*, *Pasteurella* and *Staphylococcus* species can also cause fatal aneurysm which can be treated using antifungal and antibiotic. Beta blocker (atenolol), ACE inhibitor (captopril), losartan and statins can also be used for management of non-infectious aneurysm. Surgical intervention is the gold standard and when supported by chemotherapy improve the quality of life for years.

**Keywords:** Aneurysm; Chemotherapy; Statin; Endovascular Repair

### Introduction

Aneurysm is defined as permanent dilatation [1] which may affect thoracic and abdominal artery causing mortality in individuals affected with Marfan's and similar disease [2]. *Pasteurella multocida* can cause aortitis that can cause mycotic aneurysm after cat bite that can be treated by antibiotic [3]. Aortitis can be divided into non-infectious associated with vasculitis and systemic lupus erythematosus [4] and infectious aortitis associated with *Salmonella* and *Staphylococcus* and *Pasteurella* species with prevalence in cat (75%) and dog (50%) bites [5] respectively. Aortic size was the principal factor related to aortic event in thoracic or thoracic abdominal aortic aneurysm. Aortic diameter of 5 cm – 6 cm portend high aortic rupture after 1 year [6].

### Pathophysiology of Aneurysm

Elastin quality delays collagen fiber recruitment and causing extensibility, and collagen quality delays fiber damage causing strength [7] at greater and lesser curvatures with circumferential or longitudinal direction [8]. Endoleaks are the most common complication that occurs in association with endovascular repair [9]. Spirocercosis caused aortic thromboembolism in dog which was treated using doramectin (0.5 mg/kg subcutaneously) every 2 weeks for 12 weeks against *Spirocercus lupi*. Aspirin (6 mg/kg daily for 2 weeks) and low molecular weight heparin (50 iu/kg subcutaneously twice daily for 72h) were used to stop thrombogenesis [10]. Chymase inhibition may become a useful strategy for preventing abdominal aortic aneurysms [11]. Lohexol was injected intravenously in the aortic arch via the carotid artery for radiographic angiogram [12].

Aorta plays a vital role of controlling systemic vascular resistance and heart rate. An increase in aortic pressure results in decreased heart rate and systemic vascular resistance [13]. But aortic diameters do not usually exceed 4 cm and taper gradually, usually affected by several factors including age, gender, body size (height, weight), BSA and blood pressure. But the rate of aortic expansion is 0.9 mm in men and 0.7 mm in woman for each decade of life [14]. Aortic diseases are often associated with comorbidities such as coronary artery disease (CAD), chronic kidney disease, diabetes mellitus, dyslipidemia, hypertension among others.

### Chemotherapy of Aneurysm

The inability to institute effective pharmacotherapy of the disease is due to lack of comprehensive knowledge about mechanisms of aortic dilation [15]. The use of prostaglandin synthase inhibitors (indomethacin, ibuprofen) to reduce dilated part of thoracic or abdominal aorta has been reported [16]. But ultrathion polyester fabric nitiriol stent showed healing characteristic of thoracic aorta in canine model [17]. The transition between the more elastic intrathoracic aorta and the more collagenous extra-thoracic was 5 cm (Margaret, *et al.* 2017) and upregulation of elastase activity in aorta may be due to increased cytokine expression [18] signifying that elastase inhibitor can be used in treatment and prevention of aneurysm.

Pharmacotherapy of abdominal aortic aneurysms is limited, although statins have been shown to be effective [19]. Pharmacological agents such as free radicals, barbiturates, corticosteroids, cocaine-derived anaesthetics, opiate antagonists and papaverine are used for spinal cord protection during thoracoabdominal aneurysm repair [20]. *Capnocytophaga canimorsus* causes mycotic abdominal aortic aneurysm that can be treated using penicillin [21]. Imipenem, doxycycline, rifamycin, ofloxacin, ciprofloxacin, erythromycin and clindamycin can also be used [22]. The role of the rennin-angiotensin system in aortic aneurysms has been established and proven by angiotensin (ATi) receptors which prevented ascending aortic aneurysm in a mouse model of Marfan's disease. Clinical study is ongoing to test efficacy of ATI receptor antagonist in humans [23]. The exciting field of drug delivery devices might provide novel strategies for the treatment of aneurysm via endogenous and physiologically – occurring release of paracrine for targeting aneurysic aorta [24].

*Graphium* species caused fatal aneurysm in dog [25] suggesting antifungal agent can be administered for treatment of mycotic aneurysm caused by susceptible fungi. Cessation of smoking and moderate exercise prevent progression. In patients with Marfan syndrome, beta-blockers (e.g. atenolol), angiotensin converting enzyme inhibitor (e.g. Captopril) and angiotensin receptor blocker (losartan) reduce progression of aortic dilation or the occurrence of complications [26] and caused improved survival after repair of aortic abdominal aneurysm reducing the risk of cardiovascular death [27]. There is linear relationship between the cross sectional aortic diameter and the square root of BSA ( $BSA^{0.5}$ ) [28]. But BSA that considers height and weight or  $BSA^{0.529}$  may correlate much better [29]. Signifying that therapeutics for aneurysm that may be developed in future may require application of BSA.

### Assessment of Chemotherapeutic Success of Aneurysm

Because surgical intervention has reduced mortality due to aneurysm by 1 - 3%, it exposes bicuspid aortic valve to risk of damage [30]. But prophylactic surgery can reduce morbidity and mortality [31]. But Z-score can be used to demonstrate beneficial treatment effect [32]. A change in Z-score value overtime is suggestive of a change in the size of cardiovascular structure taking account of normal growth of the affected patient [33,34].

### Conclusion

Aneurysm of  $\geq 5$  cm in diameter portend high risk of aortic rupture. Therefore, surgical intervention combined with chemotherapy such as betablocker (atenolol) ACE Inhibitors (captopril) antigitensin receptor blocker (losartan) and analgesic can improve the quality of life for few years. Antifungal and antibiotic can be applied for aneurysms caused by fungal and bacterial infectious respectively.

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