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Perfusion computed tomography imaging of abdominal aortic aneurysms may be of value for patient specific rupture risk estimation

Nikolaos Kontopodis [a,1], Nikolaos Galanakis [b,1], Dimitrios Tsetis [b], Christos V. Ioannou [a,*]

[a] Vascular Surgery Unit, Department of Cardiothoracic and Vascular Surgery, University of Crete Medical School, 71110 Heraklion, Crete, Greece
[b] Interventional Radiology Unit, Radiology Department, University of Crete Medical School, 71110 Heraklion, Crete, Greece

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ABSTRACT

Abdominal aortic aneurysm (AAA) continues to pose a significant cause of unexpected mortality in the developed countries with its incidence constantly rising. The indication of elective surgical repair is currently based on the maximum diameter and growth rate criteria which represent an oversimplification of the Law of Laplace stating that the stress exerted in a cylinder or sphere is proportional to its radius. These criteria fail to capture the complex pathophysiology of the aneurismal disease thus often leading to therapeutic inaccuracies (treating large AAAs with a very low actual rupture risk while observing smaller ones with a much greater risk). Aneurysmal disease is mainly a degenerative process leading to loss of structural integrity of the diseased aortic wall which cannot withhold the stresses due to systemic pressurization. Moreover aortic wall degeneration has been shown to be a localized phenomenon and rupture depends on the pointwise comparison of strength and stress rather than a global aortic wall weakening. Ex-vivo mechanical studies have related vessel wall hypoxia to loss of structural endurance and reduced wall strength. Therefore a module to capture in vivo variation of aortic wall blood supply and oxygenation would be of value for the evaluation of AAA rupture risk. Perfusion computed tomography (PCT) imaging represents a novel technique which has been already used to estimate tissue vascularity in several clinical conditions but not aneurismal disease. We hypothesize that PCT could be used as an adjunct tool during AAA diagnostics in order to evaluate aortic wall oxygenation in vivo, therefore providing a possible means to identify weak spots making the lesion amenable to rupture.

Introduction

Abdominal aortic aneurysms (AAAs) continue to represent a significant cause of mortality in the developed countries with its incidence having raised during the past 2 decades due to aging of the population and spread of tobacco use [1]. Wide availability of screening modalities (i.e. ultrasound and CT) along with the introduction of surveillance protocols have also played a significant role in the early detection of these lesions which otherwise could have escaped attention. This disorder is more common in men than in women, with estimated prevalence rates reaching between 1·3% and 8·9% in men and between 1·0% and 2·2% in women [2–5]. Most AAAs are asymptomatic and incidentally discovered through imaging for other medical conditions or inside a screening program. At the stage of diagnosis the great majority of aneurysms are small, well below the recommended size thresholds for surgical correction. In fact elective repair of AAAs is currently based on the universal maximum diameter criterion with a cut-off value of 5.5 cm [6]. Accordingly smaller AAAs are subjected to a watchful waiting strategy with serial imaging to detect enlargement while larger ones undergo intervention. The growth rate of these lesions has been used as an additional risk marker with high values (>1 cm/year) being suggestive of a high rupture risk and a subsequent need for elective repair [6]. Despite the fact that these size criteria (maximum diameter and growth rate) have been well established predictors of rupture they fail to capture the complex pathophysiology of the AAA development, evolution and rupture. Subsequently, clinical management based solely on these criteria often fails to evaluate rupture risk on an individualized basis resulting in therapeutic inaccuracies (operating on a large AAA that in fact presents a low risk of rupture while observing smaller aneurysms presenting a significantly higher risk). Indeed it is well

* Corresponding author at: Head of Vascular Surgery – Vascular Surgery Unit, Department of Cardiothoracic and Vascular Surgery, University of Crete Medical School, PO Box 1352, 71110 Heraklion, Greece.

E-mail addresses: kontopodisn@yahoo.gr (N. Kontopodis), nikos_meduoc@hotmail.com (N. Galanakis), tsetis@med.uoc.gr (D. Tsetis), ioannou@med.uoc.gr, xioannou@uoc.gr (C.V. Ioannou).

[1] Nikolaos Kontopodis and Nikolaos Galanakis have equally contributed to this paper and both qualify for first authorship.

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established that AAAs below the aforementioned thresholds present a low but actual risk of rupture while about 50% of larger AAAs will never proceed to rupture [7–9]. Despite the fact that these criteria are supposed to be based on physical principles with the law of Laplace being usually pointed out as the theoretical basis for their value (wall stress exerted in the wall of a tube increases proportionally to its radius), this probably represents an oversimplification when attempting to interpret function of the living arterial system. This is not only because this law is valid for steady flow, Newtonian fluids and simple geometric shapes like a cylinder or a sphere (none of this parameters is present in real life) but also because it does not take into account the mechanical endurance of the diseased arterial wall resisting to stress and preventing rupture, which is in turn influenced by several biological processes [10]. Reduced strength of the aortic wall is an equally significant determinant of rupture as is wall stress. The former is dependent upon tissue mechanical properties, inflammation and oxygenation as previous research has indicated [11]. More importantly all of these processes are well-localized and it is well established that regional rather than uniform properties of the aortic wall are significant in the process of rupture, since a remarkable regional variation is present throughout the aneurismal wall [12–14].

Conventional anatomical imaging with ultrasound, CT and MRI may accurately define the aneurysms dimensions but offers no additional information on several biological processes occurring simultaneously. In the same time, functional imaging with PET CT or MRI using nanoparticles may unreveal several of these biological processes, namely provide a map of inflammatory markers uptake throughout the aortic wall. These techniques despite being anticipated with much enthusiasm not only are expensive and present very limited availability, but more importantly have presented conflicting data regarding their value [15–20].

On the same time the significant technological progress on abdominal imaging with the use of modern spiral CT scanners and the use of specifically developed software for image post-processing have allowed for new possibilities with the development of CT perfusion imaging (PCT). Such technology has gained applicability in diagnostics of central nervous system pathology like acute stroke, head trauma and tumors but also cardiac imaging, liver disease and oncology [21–26]. To the best of our knowledge there has been no report on PCT imaging of AAAs in the published literature.

The hypothesis

PCT may be able to capture in vivo real time regional variation in blood flow and volume reaching the aneurysm sac providing oxygenation and nutrients to the aortic wall. Therefore it may serve as a useful adjunct in the identification of the most degenerated and weak spots presenting reduced endurance and render the aneurysm susceptible to mechanical failure and ultimately rupture. This technique being readily available in a clinical setting may be a valuable tool in evaluating risk of rupture in a patient-specific basis and guide individualized treatment of AAA patients beyond the one-size fits all maximum diameter criterion.

Technical details regarding image acquisition/post-processing

In our center we have already performed PCT in AAAs in several occasions in order to evaluate feasibility and diagnostic value of this modality. CT angiography was performed with a 128-slices dual-source CT Revolution GSI (GE Healthcare, Chicago, Il, USA). Following initial Multi Dimensional CT angiography of abdominal aorta from the diaphragm to the symphysis pubis, the patient also underwent abdominal aortic aneurysm perfusion examination. The volume acquisition (14 mm) was selected to obtain the aortic aneurysm and normal-size aorta superior and inferior to the aneurysm. Images were obtained after injection of 70 ml of iodinated non-ionic contrast medium (Ultravist 370, iodine at 370 mg/ml Bayer Schering Pharma AG, Leverkusen, Germany) followed by 40 mL of saline solution at a flow rate of 4 mL/s. A cine mode technique (continuous tube rotation without patient movement), encompassing the acquisition volume previously selected, was carried out with the following parameters: 0.625 mm × 64 mm collimation, 0.4-s gantry rotation time, pitch of 1.375, reconstruction slice thickness 1.25 mm, number of passes 28, time per pass 1,7 s, tube voltage 100 kV, fixed tube current 150 mA, total acquisition time 47.6 s. Scan delay was individualized for each patient, using GE's proprietary bolus-tracking software (SmartPrep) to capture 120 HU on the right ventricle in order to assess the first circulation of contrast medium in the aorta. We advised the patient to breathe very shallowly and slowly during the examination to minimize organ movement. Moreover, placing a restraint strap tightly around the patient helped to minimize breathing motion along with slow shallow breathing. PCT images were transferred to a dedicated workstation (AW server 3.2, GE Medical Systems) and analyzed using commercial CT software (CT Perfusion 4D, GE Medical Systems, Waukesha, WI, USA). CT perfusion parameter maps of various hemodynamic parameters such us blood volume [BV], blood flow [BF], mean transit time [MTT], time to peak (TTP), permeability surface [PS] and mean slope of increase (MSI) were created.

Evaluation of the hypothesis and discussion

Our hypothesis has been developed and based on three key points.

. Tissue oxygenation is critical for maintenance of aortic wall structural integrity and strength, which resists rupture.
. Mechanical properties and strength of aneurismal wall presents a remarkable variability through the surface of the AAA and therefore rupture mainly depends in the existence of weak points rather than a global weakening of the vessel.
. PCT can capture regional distribution of blood flow and therefore tissue oxygenation.

Regarding the first point, it is now well understood that AAA disease is principally of degenerative nature [1,10]. This means that except in specific cases (mycotic aneurysms, connective tissue disorders, aortic dissection) the great majority of patients presents a progressive loss of aortic wall structural endurance leading to reduced strength, vessel enlargement and finally rupture [27]. Previous research through ex-vivo mechanical testing has indicated that localized hypoxia may occur in regions of thicker intraluminal thrombus (ILT) in AAAs which may in turn lead to increased, localized neovascularization and inflammation and relate to regional wall weakening [11,28]. These authors initially performed measurements within the AAA during operation by use of a PO_2 electrode dictating the existence of significant differences between cases depending on the presence and amount of ILT but also a significant variation in each case and a gradient from lumen to wall. In turn, vascular tissue responded to hypoxic conditions through a series of events leading to inflammation and neovascularization as subsequent ex-vivo pathologic analysis proved. Finally, strength was found to be significantly reduced in segments under a thick ILT layer which were also those presenting the most pronounced hypoxia [11]. Moreover, recent research employing animal models, suggests that chronic hypoxia due to hypoperfusion of the adven-