Measuring and modeling patient-specific distributions of material properties in abdominal aortic aneurysm wall

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Received: 19 March 2012 / Accepted: 22 August 2012 / Published online: 7 September 2012
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Abstract Both the clinically established diameter criterion and novel approaches of computational finite element (FE) analyses for rupture risk stratification of abdominal aortic aneurysms (AAA) are based on assumptions of population-averaged, uniform material properties for the AAA wall. The presence of inter-patient and intra-patient variations in material properties is known, but has so far not been addressed sufficiently. In order to enable the preoperative estimation of patient-specific AAA wall properties in the future, we investigated the relationship between non-invasively assessable clinical parameters and experimentally measured AAA wall properties. We harvested \( n = 163 \) AAA wall specimens (\( n = 50 \) patients) during open surgery and recorded the exact excision sites. Specimens were tested for their thickness, elastic properties, and failure loads using uniaxial tensile tests. In addition, 43 non-invasively assessable patient-specific or specimen-specific parameters were obtained from recordings made during surgery and patient charts. Experimental results were correlated with the non-invasively assessable parameters and simple regression models were created to mathematically describe the relationships. Wall thickness was most significantly correlated with the metabolic activity at the excision site assessed by PET/CT \( (\rho = 0.499, P = 4 \times 10^{-7}) \) and to thrombocyte counts from laboratory blood analyses \( (\rho = 0.445, P = 3 \times 10^{-9}) \). Wall thickness was increased in patients suffering from diabetes mellitus, while it was significantly thinner in patients suffering from chronic kidney disease (CKD). Elastic AAA wall properties had significant correlations with the metabolic activity at the excision site (PET/CT), with existent calcifications, and with the diameter of the non-dilated aorta proximal to the AAA. Failure properties (wall strength and failure tension) had correlations with the patient’s medical history and with results from laboratory blood analyses. Interestingly, AAA wall failure tension was significantly reduced for patients with CKD and elevated blood levels of potassium and urea, respectively, both of which are associated with kidney disease. This study is a first step to a future preoperative estimation of AAA wall properties. Results can be conveyed to both the diameter criterion and FE analyses to refine rupture risk prediction. The fact that AAA wall from patients suffering from CKD featured reduced failure tension implies an increased AAA rupture risk for this patient group at comparably smaller AAA diameters.

Keywords Abdominal aortic aneurysm · Diameter criterion · Finite elements · Material properties · Wall thickness · Wall strength

1 Introduction

Due to the high prevalence of abdominal aortic aneurysms (AAA) and subsequent high mortality in case of rupture...
(>90%) (Ockert et al. 2007), screening programs and early prophylactic AAA repair are recommended and supported by various national health care systems. However, only 25% of all AAAs rupture during the patients’ lifetime, while all other patients with stable AAAs are harmed by the non-negligible risks of prophylactic repair (Greenhalgh 2004). Consequently, surgeons have to balance the risk of rupture against the risk of elective therapy. Thereby, the established maximum diameter criterion with a threshold of 5.5 cm is well evaluated, easy to use and widely accepted in routine clinical practice for risk assessment of AAAs. For AAAs above this critical diameter, the annual rupture risk exceeds the average perioperative mortality of open AAA repair (Ockert et al. 2007). Physically, the diameter criterion is based on the Law of Laplace, which describes a linear relationship between diameter and wall stress in cylindrical geometries under the assumption of spatially constant wall thickness. Not surprisingly, rupture risk evaluation only by the diameter criterion sometimes leads to unexpected rupture in AAAs smaller than 5.5 cm, whereas larger AAAs often remain stable. A more sophisticated approach to predict the patient’s individual rupture risk has already been represented by means of finite element (FE) analyses (Fillinger et al. 2003; Gasser et al. 2010; Maier et al. 2010b; Hyhlik-Dürr et al. 2011). Firstly, the FE method enables the prediction of realistic loading even in complex three-dimensional AAA geometries, where it is agreed that rupture occurs when wall stress exceeds wall strength (Raghavan and Vorp 2000; Vande Geest et al. 2006b; Humphrey and Taylor 2008; Marini et al. 2012). Furthermore, the FE method in principle also allows for the consideration of patient-specific variations in thickness, elastic properties, or failure properties of the different AAA constituents, such as thrombus (Gasser et al. 2008; Polzer et al. 2011), calcifications (Li et al. 2008; Maier et al. 2010a), and the AAA wall itself. In this regard, knowledge on mechanical AAA wall properties has mainly been derived from uniaxial (Fung 1993; Raghavan and Vorp 2000; Marini et al. 2012), biaxial (Okamoto et al. 2002; Humphrey 2002; Vande Geest et al. 2006a), or multiaxial tensile testing (Raghavan et al. 2011b). On the one hand, physiological ranges of mechanical AAA wall properties have been well described (Raghavan et al. 1996; Raghavan and Vorp 2000). On the other hand, large individual and inter-individual variations of these mechanical properties have also been reported (Thubrikar et al. 2001; Vallabhaneni et al. 2004; Vande Geest et al. 2006b; Raghavan et al. 2011a; Marini et al. 2012). However, despite some sophisticated theoretical approaches (Watton and Hill 2009; Zeinali-Davarani et al. 2011) which apply to growth and remodeling simulations, a proper prediction of in vivo patient-specific variations is currently impossible (Breeuwer et al. 2008; Xenos et al. 2010). Most studies dealing with status-quo AAA rupture risk assessment therefore use averaged values of mechanical properties rather than accounting for patient-specific adaptations and variations. Consequently, non-invasive prediction of patient-specific variations in AAA wall properties is still one of the unsolved problems of realistic rupture risk stratification, as also stated by, for example, Breeuwer et al. (2008). Xenos et al. (2010), Doyle et al. (2011), Humphrey and Holzapfel (2012). Thus, the prediction of spatial and patient-specific changes of mechanical AAA wall properties, based on clinically available data, would be an essential contribution to a more reliable rupture risk prediction.

Consequently, the aim of this study was to develop methods for the non-invasive prediction of patient-specific mechanical AAA wall properties based on non-invasive and preoperative data. For this purpose, AAA wall specimens were harvested during open AAA surgery, after which their thickness, elastic properties, and failure properties were measured in uniaxial tensile tests. A set of non-invasively assessable patient-specific parameters was acquired for each specimen. Experimental results from uniaxial tensile tests were then correlated with these parameters. Significant parameters were identified and simple regression models were generated. The results are discussed with respect to their implications on patient-specific rupture risk stratification.

2 Methods

2.1 Study population and tissue sampling

The study included 50 AAA patients over a 30-month period, who were scheduled for conventional open surgical repair, based on the recommendations of the vascular board for different indications. Detailed patient characteristics are summarized in Table 1. Blood sampling was performed prior to surgical intervention by vein puncture. All patients underwent CT imaging as routine part of preoperative preparation. Thereby, a contrast enhanced 18F-fluorodeoxyglucose positron emission tomography/CT (FDG-PET/CT, an imaging routine to measure the metabolic activity in the patient and, e.g., the AAA wall) was performed in 28 cases. 3D reconstructions of AAA geometry and intraluminal thrombus were generated from conventional CT images utilizing the commercial segmentation software Mimics (Materialise, Leuven, Belgium). A paper print of the individual patient’s 3D AAA geometry was handed to the surgeon before each surgery. During surgery, samples from different locations of the AAA wall were excised and dissected from thrombus and peri-ortic tissue. Exact sample locations and orientations were marked in the paper print (Fig. 1). In total, samples from n = 103 different excision sites were obtained. Samples for mechanical evaluation were stored in lactated Ringer’s solution (130 mmol/l sodium chloride, 5 mmol/l potassium...