Increased Fluorodeoxyglucose Uptake Following Endovascular Abdominal Aortic Aneurysm Repair: A Predictor of Endoleak?

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Abstract: The main criterion for abdominal aortic aneurysm (AAA) repair is an AAA diameter ≥5.5 cm. However, some AAAs rupture when they are smaller. Size alone may therefore not be a sufficient criterion to determine rupture risk. Fluorodeoxyglucose (FDG) uptake is increased in the presence of inflammation and it was suggested that this may be a better predictor of rupture risk than AAA size. Furthermore, increased FDG uptake following endovascular AAA repair may be an indirect predictor of continuous AAA sac enlargement due to the presence of an endoleak (even if this is not detected by imaging modalities) and/or increased AAA rupture risk. The role of FDG uptake needs to be explored further in the management of AAAs.

Keywords: Abdominal aortic aneurysm, fluorodeoxyglucose, endovascular aneurysm repair, rupture risk, predictor, endoleak.

INTRODUCTION

According to current guidelines [1] the main criterion for abdominal aortic aneurysm (AAA) repair is a diameter ≥5.5 cm. However, smaller AAAs can rupture and AAAs are discovered after exceeding this diameter without rupturing [2, 3].

Fluorodeoxyglucose (FDG) uptake, measured by positron emission tomography (PET), is increased in the presence of inflammation [4]. In turn, AAAs are characterized by activation of inflammatory/immune cells causing degradation of elastin and collagen, destruction of medial elastic tissue, medial neovascularization and a decrease in vascular smooth muscle cells [5]. It follows that an association between FDG uptake by the AAA wall and the processes leading to rupture has been reported [3, 6, 7].

Although FDG correlates with inflammation of the AAA wall and rupture risk [3, 6, 7], it does not correlate with maximal AAA diameter [8]. Nevertheless, it was recently proposed that FDG may be a better predictor of AAA instability and rupture than AAA size [9]. Such an association holds implications for the management of AAAs [9]. FDG uptake may also predict endoleaks following endovascular AAA repair (EVAR) even if this is not detected by imaging modalities. This article considers this hypothesis.

INCREASED FDG UPTAKE AFTER EVAR: AN INDIRECT SIGN OF AN ENDOLEAK?

The most common complication of EVAR is an endoleak which is the persistence of perigraft blood flow inside the AAA sac [10-13]. Endoleaks are associated with adverse outcomes, including AAA sac growth, the need for conversion to open repair, high reintervention rates and rupture [10-13]. Therefore, following EVAR long-term (possibly lifelong) imaging surveillance is recommended [10-13].

Several imaging techniques for the surveillance of patients following EVAR have been described including plain radiography, ultrasound, computed tomography (CT)/CT angiography and magnetic resonance (MR) imaging/MR angiography [13, 14]. Each technique has its advantages and disadvantages [13, 14]. Despite the availability of advanced imaging modalities some endoleaks may still be missed. Poor compliance with the follow-up schedule may be a reason but in some cases, the endoleak is missed due to technical deficiencies/shortcomings [12, 15-18].

A recent report systematically reviewing the pathogenesis, etiology and timing of AAA rupture following EVAR identified a total of 270 patients with AAA rupture after EVAR [12]. The cause of AAA rupture was known for 235 patients. Endoleaks were the main cause of rupture in 160 of

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the 235 patients (type IA: 57 patients; type IB: 31 patients; type II: 23 patients; type III: 26 patients; type IV: 0 patients; endotension: 9 patients). The endoleak type was not specified in 14 cases with rupture due to endoleak [12].

The presence of an endoleak at the last follow-up before rupture was described for only 56 of the 160 patients in whom the main cause of rupture was an endoleak [12]. A description of the course of AAA sac diameter during follow-up was presented in 101 patients. Enlargement of the AAA sac during follow-up occurred in 36 of these patients, no change was seen in 39 and shrinkage was reported in 26 patients. In 35 patients no abnormalities were found during follow-up (absence of endoleak, wire fractures, migration, graft angulation, insecure fixation, signs of inflammation and sac enlargement). In another 6 patients only a small type II endoleak was found during follow-up while the AAA sac was stable or shrunken. So, in 41 patients no abnormalities were found during follow-up that required re-intervention [12].

Another study evaluated the incidence and impact of previously unrecognized type II endoleaks using a modified intraoperative angiographic protocol (namely the use of digital subtraction fluoroscopy continuously for 60 sec after injections of 20 ml iodinated contrast both in the pararenal aorta and within the endovascular graft) [16]. A total of 391 patients undergoing EVAR were evaluated (standard completion angiograms: 264 patients; modified angiographic protocol: 127 patients). Type II endoleaks were detected intraoperatively in more patients in whom the modified compared with the standard angiographic protocol was used (53 of 127 vs 12 of 264, or 41% vs 6%, respectively; $p<0.001$) [16]. A third study aimed to analyze the clinical implications of endoleaks documented by CT angiography which were missed by color duplex ultrasound in 232 patients undergoing EVAR during a 5-year period [17]. All patients were followed by both CT angiography and color duplex ultrasound at 1 month following the procedure and every 6 months thereafter. A total of 39 endoleaks were detected using CT angiography compared with only 28 using ultrasonography. Overall, color duplex ultrasonography failed to identify an endoleak in >25% of the cases (11 of 39 endoleaks [28%]; 2 late type I, 6 early type II, 2 late type II and 1 early type IV) [17]. Finally, in a single-center report of 445 AAA patients treated endovascularly, late AAA rupture occurred in 3 cases [18]. In all cases, the reason for rupture was type I endoleak that was not diagnosed during post-EVAR surveillance scans [18].

COMMENT

Despite a wide variety of imaging modalities, some endoleaks are missed [12, 15-18]. Ultrasonography is a cost-effective and reproducible method that identifies an endoleak in the majority of the cases; nevertheless, it may miss as many as 28% of endoleaks [17]. Due to its cost-effectiveness, ultrasonography should remain the primary diagnostic tool for detecting endoleaks following EVAR. When a follow-up ultrasound examination is negative, however, FDG uptake could represent an investigation which could alert the physician about the presence of an endoleak following EVAR. However, since most ultrasound examinations will be negative, the cost of an additional investigation by FDG uptake is prohibitive unless there is a high index of clinical suspicion of an endoleak. Moreover, the FDG uptake will not accurately reveal the location of the endoleak and AAA infection could lead to increased FDG uptake (due to local inflammation) and result in misinterpretation [19]. As FDG represents an inflammatory state [3-7], it would be interesting to explore the role of drugs possessing anti-inflammatory action. Through inhibition/decrease of AAA expansion rates, statins may play a role in the management of AAAs [20]. Oxidative stress may play a role in the pathogenesis of AAAs; thus statins may exert their growth inhibitory effect by interfering with this pathway [21]. Irrespective of an effect on AAA growth, all AAA patients undergoing surgery [22] or a percutaneous intervention [23] should receive statin therapy to improve perioperative morbidity and mortality rates. Future studies should investigate the effect of statin therapy on post-EVAR patients exhibiting increased FDG uptake.

Apart from research applications, FDG uptake may prove useful in predicting the risk of rupture in AAA with a diameter below the threshold for intervention as assessed by ultrasound. This is of interest since there is a current debate as to whether there are grounds for intervening with EVAR in AAAs below the threshold diameter. Based on the lower perioperative mortality rates associated with EVAR compared with open surgical procedures [24], it was proposed that the current size threshold for elective AAA repair may need to be lowered in the endovascular era [25, 26]. Two ongoing multicentre randomized controlled trials, Comparison of surveillance versus Aortic Endografting for Small Aneurysm Repair (CAESAR) [25] in Europe and Positive Impact of endoVascular Options for Treating Aneurysms earLy [PIVOTAL] [26] in the United States are currently comparing EVAR vs surveillance for AAAs <5 cm in size. This argument would be supported even further if a reliable predictor (i.e. FDG uptake) of expansion and possible eventual rupture risk was available. This option requires further consideration.

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