EDITORIAL

Abdominal aortic aneurysm disease and cancer

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The incidence of concomitant abdominal aortic aneurysm (AAA) and cancer is around 6%.[1] It is an issue of controversy in terms of treatment timing, priority and clinical outcomes. In the recent European Society for Vascular Surgery (ESVS) guidelines it is recommended that patients with AAA and concomitant cancer are not recommended prophylactic aneurysm repair on a different indication (diameter threshold) from patients without cancer, including cases of chemotherapy (III C). Additionally, in patients with concomitant malignancy, a staged surgical approach, with endovascular repair of a large or symptomatic abdominal aortic aneurysm first, to allow for treatment of malignancy with minimal delay, is recommended (I C).

In a recent systematic review of the literature,[2] it was highlighted that decisions about management of AAA and cancer should be based on clinical judgment applied individually in a multidisciplinary setting ("treat first what kills first"). A two-stage treatment seems reasonable and ideally the AAA should be treated by endovascular means if anatomically suitable. The initiation of international registries would shed more light on the management and outcomes of patients with AAA and concomitant cancer.[2]

In clinical practice synchronous cancer in patients with AAA increases morbidity and mortality after AAA repair. However, the role of cancer history on AAA mortality is not clear. Recently, Ahn et al.[3] demonstrated that history of cancer in AAA patients increases long-term mortality, but does not affect short-term mortality after AAA repair.

On the other hand, a recent study[4] showed that small aortic aneurysms with concomitant malignancies are discovered at smaller initial sizes, grow at similar rates, require fewer interventions, and have fewer ruptures and acute dissections than patients without malignancy. Even in cancer patients with AAA that were treated with chemotherapy for their cancer, chemotherapy did not increase aneurysm growth compared with patients not undergoing treatment for malignancy.[5]

Evidence on the risk of malignancy in patients with AAA is scarce. Cardiovascular disease and malignancy have numerous similarities and possible interactions, as these diseases share several risk factors, epidemiological features and biological signaling pathways.[6] Wang et al.[6] showed that patients with an AAA have a substantially increased risk of developing a variety of malignancies compared with patients without AAA. Even after AAA treatment there might be an association with increased risk of cancer in AAA patients. In a population-based cohort study,[7] it was demonstrated that increased risk of abdominal cancer exists after endovascular aortic aneurysm repair (EVAR) compared with open AAA repair. The differential cancer risk needs further exploration in alternative national populations, and radiation exposure during EVAR should be measured as a quality metric in the assessment of EVAR centers.

AAA has been associated with chronic inflammation, cells apoptosis, and impairment of autophagy. Similar pathological pathways exist in the development of various malignancies.[8] Recently, there is an interest on the potential association between cancer and AAA. Studies have identified potential similar pathophysiological mechanisms for each pathology separately. For example, a study showed that BP-1-102 inhibits vascular inflammation and AAA progression through decreasing STAT3 and NF-κB activation and maintaining autophagy.[8] Compelling evidence also exists for the critical role of aberrant STAT3 activity in malignant transformation and tumor progression.[9] The complement pathway is another pathophysiological mechanism which may be involved in both pathological conditions. These are strong evidence that the complement cascade plays a role in human AAA. Based on microarray studies, the pathway is activated in AAA, particularly via the lectin and classical pathways.[10] Similarly, although the mechanisms by which complement is activated and affects tumor progression are not well understood, still there is a strong impact of complement pathway on malignancies.[11]

Another potential association between cancer and AAA is on a genetic level. In recent Society for Vascular Surgery (SVS) guidelines[12] it was reported that there are known genes are implicated in the pathogenesis of an AAA. In a recent study, results suggested that reduced CDKN2B expression and increased smooth muscle cell apoptosis may have an association with aneurysmal disease.[13] Another study showed that

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there is a similar critical role of CDKN2B inactivation in pancreatic carcinogenesis.[14]

The potential association of AAA and cancer is of great interest and future studies should focus on this research on a genetic, biochemical and clinical practice level.

REFERENCES

1 Wanhainen A, Mani K, de Borst GJ. The most important news in the new ESVS 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysm. J Cardiovasc Surg (Torino). 2019;60:485-9.

2 Peeters B, Moreels N, Vermassen F, et al. Management of abdominal aortic aneurysm and concomitant malignant disease. J Cardiovasc Surg (Torino). 2019;60:468-75.

3 Ahn S, Min JY, Kim HG, et al. Outcomes after aortic aneurysm repair in patients with history of cancer: a nationwide dataset analysis. BMC Surg. 2020 May 1;20:85.

4 Maxwell DW, Kenney L, Sarmiento JM, et al. Aortic Aneurysm Natural Progression Is Not Influenced By Concomitant Malignancy And Chemotherapy. Ann Vasc Surg. 2020 Sep 11:S0890-5096(20)30823-2.

5 Martin ZL, Mastracci TM, Greenberg RK, et al. The effect of chemotherapy for malignancy on the natural history of aortic aneurysm. J Vasc Surg. 2015;61:50-7.

6 Wang JC, Chien WC, Chung CH, et al. Increased risk of malignancy in patients with an aortic aneurysm: a nationwide population-based retrospective study. Oncotarget. 2017;9:2829-37.

7 Markar SR, Vidal-Diez A, Sounderajah V, et al. A population-based cohort study examining the risk of abdominal cancer after endovascular abdominal aortic aneurysm repair. J Vasc Surg. 2019;69:1776-85.e2

8 Wu QY, Cheng Z, Zhou YZ, et al. A novel STAT3 inhibitor attenuates angiotensin II-induced abdominal aortic aneurysm progression in mice through modulating vascular inflammation and autophagy. Cell Death Dis. 2020;11:131.

9 Yue P, Turkson J. Targeting STAT3 in cancer: how successful are we? Expert Opin Investig Drugs. 2009;18:45-56.

10 Hinterseher I, Erdman R, Donoso LA, et al. Role of complement cascade in abdominal aortic aneurysms. Arterioscler Thromb Vasc Biol. 2011;31:1653-60.

11 Kleczko EK, Kwak JW, Schenk EL, et al. Targeting the Complement Pathway as a Therapeutic Strategy in Lung Cancer. Front Immunol. 2019;10:954.

12 Chaikof EL, Dalman RL, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. J Vasc Surg. 2018;67:2-77.

13 Leeper NJ, Raiesdana A, Kojima Y, et al. Loss of CDKN2B promotes p53-dependent smooth muscle cell apoptosis and aneurysm formation. Arterioscler Thromb Vasc Biol. 2013;33:1-10.

14 Tu Q, Hao J, Zhou X, et al. CDKN2B deletion is essential for pancreatic cancer development instead of unmeaningful co-deletion due to juxtaposition to CDKN2A. Oncogene. 2018;37:128-38.