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Review Article

Consensus statement on surgical pathology of the aorta from the Society for Cardiovascular Pathology and the Association For European Cardiovascular Pathology: II. Noninflammatory degenerative diseases — nomenclature and diagnostic criteria

Marc K. Halushka [a,*], Annalisa Angelini [b], Giovanni Bartoloni [c], Cristina Basso [b], Lubov Batoroeva [d], Patrick Bruneval [e], L. Maximilian Buja [f], Jagdish Butany [g], Giulia d'Amati [h], John T. Fallon [i], Patrick J. Gallagher [j], Adriana C. Gittenberger-de Groot [k], Rosa H. Gouveia [l], Ivana Kholova [m], Karen L. Kelly [n], Ornella Leone [o], Silvio H. Litovsky [p], Joseph J. Maleszewski [q], Dylan V. Miller [r], Richard N. Mitchell [s], Stephen D. Preston [t], Angela Pucci [u], Stanley J. Radio [v], E. Rene Rodriguez [w], Mary N. Sheppard [x], James R. Stone [y], S. Kim Suvarna [z], Carmela D. Tan [w], Gaetano Thiene [b], John P. Veinot [aa], Allard C. van der Wal [ab,**]

[a] Johns Hopkins University, Baltimore, MD, USA
[b] University of Padua, Padua, Italy
[c] University of Catania, Catania, Italy
[d] Russian Academy of Medical Sciences, Irkutsk, Russia
[e] Paris Descartes University, Paris, France
[f] University of Texas Health Science Center at Houston, Houston, TX, USA
[g] Toronto General Hospital, Toronto, Ontario, Canada
[h] Sapienza University of Rome, Rome, Italy
[i] New York Medical College, Valhalla, NY, USA
[j] Southampton University Hospital, Southampton, United Kingdom
[k] Leiden University, Leiden, the Netherlands
[l] Hospital Santa Cruz, Carnaxide, Portugal
[m] Department of Pathology, Fimlab Laboratories, Tampere, Finland
[n] East Carolina University, Greenville, NC, USA
[o] Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy
[p] University of Alabama at Birmingham, Birmingham, AL, USA
[q] Mayo Clinic, Rochester, MN, USA
[r] University of Utah, Salt Lake City, UT, USA
[s] Brigham and Women's Hospital, Boston, MA, USA
[t] Papworth Hospital, Cambridgeshire, United Kingdom
[u] Pisa University Hospital, Pisa, Italy
[v] University of Nebraska, Lincoln, NE, USA
[w] Cleveland Clinic, Cleveland, OH, USA
[x] St. George's Medical School, University of London, London, United Kingdom
[y] Massachusetts General Hospital, Boston, MA, USA
[z] Sheffield Teaching Hospitals, Sheffield, United Kingdom
[aa] University of Ottawa, Ottawa, Ontario, Canada
[ab] University of Amsterdam, Amsterdam, the Netherlands

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ABSTRACT

Surgical aortic specimens are usually examined in Pathology Departments as a result of treatment of aneurysms or dissections. A number of diseases, genetic syndromes (Marfan syndrome, Loeys–Dietz syndrome, etc.), and vasculopathic aging processes involved in vascular injury can cause both distinct and nonspecific histopathologic changes with degeneration of the media as a common denominator. Terminology for these changes has varied over time leading to confusion and inconsistencies. This consensus document has established a revised, unified

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* Correspondence to: M. K. Halushka, Department of Pathology, Johns Hopkins University School of Medicine, Ross Building Room 632B, Baltimore, MD, 21205, USA. Tel.: +1-410-614-8138; fax: +1-410-502-5862.
** Correspondence to: A. C. van der Wal, Department of Pathology, Academic Medical Center, University of Amsterdam, Room M2-129, Meibergdreef 9, 1105AZ Amsterdam, the Netherlands. Tel.: +31-20-5665633; fax: +31-20-5669523.

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nomenclature for the variety of noninflammatory degenerative aortic histopathologies seen in such specimens. Older terms such as cystic medial necrosis and medionecrosis are replaced by more technically accurate terms such as mucoid extracellular matrix accumulation (MEMA), elastic fiber fragmentation and/or loss, and smooth muscle cell nuclei loss. A straightforward system of grading is presented to gauge the extent of medial degeneration and synoptic reporting tables are provided. Herein we present a standardized nomenclature that is accessible to general pathologists and useful for future publications describing these entities.

1. Introduction and practical approach

Surgical specimens from the ascending and/or thoracic aorta are generally removed for aortic aneurysm or dissection, the consequences of a wide range of diseases, syndromes, or aging processes. Across this spectrum of disease, there is an overlapping collection of histopathologic changes to the aorta. Central to the histopathologic appearance of diseased aortas are degenerative changes of the media, specifically impacting the lamellar unit. The lamellar units are the primary constructs of the media composed of a single layer of smooth muscle cells, collagen, and proteoglycans sandwiched between elastic fibers [1]. Medial degeneration is the primary pathologic substrate in heritable connective tissue diseases of the aorta, and it occurs as a secondary phenomenon in many other pathological aortic conditions as detailed below. Over the years, the meaning of histopathologic terms used to describe medial degeneration has become confused and often misused. This consensus document is designed to cover three overarching themes. The first is to provide a unified nomenclature to the histopathologic findings of the noninflammatory degenerative ascending aorta. The second is to provide a new grading scheme to better and more consistently classify aortic lesions. The third is to briefly catalog the primary medial degenerative diseases of the aorta along with current knowledge regarding mutated genes and known associated histologic findings.

The approach to grossing an aortic surgical specimen was presented in an earlier consensus document [2]. The need to sample six or more full-thickness aortic segments is recommended because of marked local differences in the extent of degenerative medial changes. These differences relate to specific sites (proximal more than distal in the aorta and in the outer curvature more than inner curvature but marked differences may also occur randomly). In the case of noninflammatory diseases, the majority of the aortic samples are from the ascending aorta; however, aortic arch, descending aorta, and even thoracoabdominal or abdominal resection specimens are seen. In addition to taking six pieces of aorta in two cassettes for review, here we strongly recommend obtaining both a hematoxylin and eosin (H&E) stain and an elastic stain (Movat's pentachrome, Verhoeff–van Gieson [VVG], combined Masson's elastic [CME], etc.) for each case. A collagen stain (Masson's trichrome, etc.) is routinely ordered at many institutions but is not required unless findings of other stains suggest a need. A smooth muscle actin (SMA) immunohistochemical stain is also used at some institutions to more easily describe smooth muscle cell changes. If inflammation is noted in the specimen, we recommend following the approach outlined in the prior consensus document on inflammatory aortic pathology [3].

2. Histology of the normal ascending aorta

The aorta is an elastic artery of which the main structural components are elastin and collagen fibers, smooth muscle cells, and a proteoglycan-rich ground substance (Fig. 1). The thickness of the intima increases gradually with age; in newborns, the intimal layer is very thin, and endothelial lining is closely apposed to the first elastic lamella of the media (Suppl. Fig. 1). Due to a process of low-grade injury and repair over many years, the intimal layer gradually expands and is composed of extracellular matrix proteins (mainly collagen and mucopolysaccharides, as well as sparse mesenchymal cells, best visualized with an antibody for the alpha-1 isoform of actin (vascular smooth muscle cell actin, SMA-1 antibody). The media constitutes the largest component of the artery. The media is composed of concentrically arranged lamellar units of fenestrated elastic laminae that enclose smooth muscle cells, collagen fibers, and large amounts of proteoglycans (Alcian blue stains strongly positive in normal aorta) [1]. The lamellar units are approximately 11 μm in thickness. The number and thickness of lamellae varies by age and topographic site in the aorta; at birth, there are about 35 lamellar units, increasing to 50–60 in adult life. In contrast to muscular arteries, the aorta contains no prominent internal elastic lamina, nor does it have a distinctive external elastic lamina. Thus, these innermost and outermost elastic lamellae do not differ substantially from other laminar units of the media. The adventitia is composed of loosely arranged connective tissues, vasa vasorum, including lymphatic vessels and low numbers of perivascular leukocytes. In the aorta, these vasa vasorum normally extend into the outer third of the media and produce nonpathologic disruptions of the lamellar units. It must be noted that the "normal" aorta at older ages displays increasing degenerative changes of all structural components, as described later (age-related changes), related to longstanding (many decades) "wear and tear" (Suppl. Fig. 2).

3. Consensus terms and definitions of degenerative aortic histopathology

The earliest terminology of degenerative aortic histopathology was the classic description of medionecrosis by Erdheim in 1930 [4]. Since then, different groups have used a variety of terms to describe the histopathologic changes they have observed in the ascending aortas affected by diseases and aging [5–7]. Unfortunately, no specific terms have gained full acceptance and often a common term — such as "cystic medial degeneration/necrosis" — indicates disparate histopathologies in different studies. As a result, it is often not possible to distinguish subtle histopathologic variation among diseases [8].

The following terms and definitions are the result of an arduous consensus process to create a single unified and consistent set of terms to describe noninflammatory degenerative aortic pathologies. The members of this consensus committee were solicited from the membership of the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology. Consensus, but not necessarily unanimous agreement, was obtained for the terms and their use. Where there were sharper disagreements in the development of this document, they have been noted as such in the text. The opinions put forth here do not necessarily represent the opinions of all members of the Society for Cardiovascular Pathology or the Association for European Cardiovascular Pathology. These terms and definitions are recommended for use in general surgical