

# Histologic evaluation of the atrioventricular nodal artery in healthy humans and in patients with conduction disturbances

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*The anatomy of the conduction system of the heart so relevant in the contemporary invasive cardiology is not fully understood. It has turned out that ablation procedures bring new information as to its structure and function, but in some cases can result in complete a-v block. Atrioventricular nodal artery located within the nodal-perinodal tissue can probably be damaged during the ablation procedures. Therefore, we decided to explore in detail the morphology and the topography of the atrioventricular nodal artery in healthy humans and in patients with clinical traits of a-v conduction disturbances requiring permanent pacing.*

*The microscopic study was carried out on 30 normal human hearts specimens (17F, 3M) from 17 to 86 years of age, and on 20 hearts with conduction disturbances (11F, 9M) from 39 to 85 years of age. We found that the number of the atrioventricular node arteries is different and independent of the extent that induces block causing conduction disturbances. The topography of the artery in perinodal zone was consistent in normal hearts, yet in hearts with conduction disturbances we observed about 2% of deviations in its location. It might be the reason for generation of iatrogenic complications after invasive cardiological procedures. The morphology revealed changes in 50% of the examined hearts and their vessel walls, which was declared to be connected with ageing. This correlated with certain stages of atherosclerosis as well as hypertension characteristic of elderly patients. We observed that in 33% of hearts from control group small parietal thrombi were detected and in 60% of paced group respectively. Hence, it seems that the procedures in perinodal zone should be performed in its proximal part because of a minor probability of direct and indirect (through nodal artery) damage of the atrioventricular structure of the junction.*

**key words: atrioventricular nodal artery, atrioventricular node, junctional area, microscopic evaluation, conduction disturbances, pacing, ablation**

## INTRODUCTION

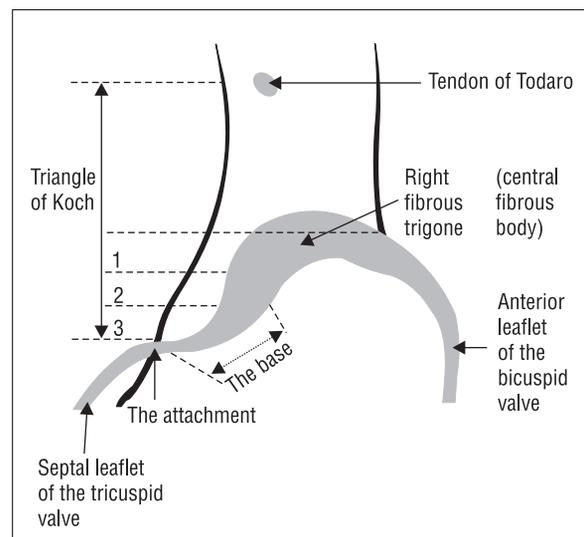
On the basis of the research history concerning the conduction system of the heart it seems that this structure so relevant in the contemporary invasive cardiology is not fully understood. It has turned out that electrophysiological study and ablation procedures bring new information as to its structure and function [7,18,22]. Invasive procedures based on the anatomical criteria are used for implantation of the pacemaker within the outflow tract of the right ventricle or the His bundle. Anatomical approach is employed in percutaneous transcatheter ablation of arrhythmogenic focus or reciprocating rhythms [5,6,9,12] in nodal-hissian area (triangle of Koch) [8] and also prenodal-perinodal zone (triangle of Siniew) [16].

The His bundle implantation mentioned above, so far experimental, is based on insertion and appropriate fixation of the lead in the proximity of atrioventricular bundle to receive the most physiological front of depolarization in proximal — intranodal atrioventricular block [5,14]. Ablation is a new method making use of radiofrequency current energy application for abolishing drug resistant arrhythmia of the re-entry (i.e. atrioventricular nodal reentry tachycardia, atrioventricular reciprocating tachycardia) [12,21,23]. Unfortunately, the results of such procedures may damage the atrioventricular part of the conduction system and generate unwanted conduction of a-v block (2–6% of cases), which is mentioned in some cardiological reports [12]. Nevertheless, ablation procedure is used at times to slow down the conduction within the a-v node as a therapeutic option in patients with drug-refractory chronic atrial fibrillation (so-called modification of the node), but not the creation of a-v block (e.g. ablation of the node) [18]. Atrioventricular nodal artery located within the nodal-perinodal tissue can be probably damaged during those procedures [11]. Therefore, we decided to explore in detail the morphology and topography of the atrioventricular nodal artery in healthy humans and in patients with clinical traits of a-v conduction disturbances with permanent pacing.

## MATERIAL AND METHODS

The investigation was carried out on a material consisting of 50 human hearts coming from people whose death was not cardiologic in nature and on the hearts of patients whose death was due to a conduction disturbance. 30 normal human hearts specimens (17F, 13M) from 17 to 86 years of age (average  $56 \pm 14$  years, normal group), and 20 hearts with different degree of atrioventricular conduction

disturbances (11F, 9M) from 39 to 85 years of age (average  $66 \pm 12$  years, paced group) were examined. These hearts were fixed in formalin-ethanol solution. The microscopic specimens were taken containing the interatrial and interventricular septum, which encompassed the entirety of the Koch's triangle. These histological parts were sectioned with the profile of the cardiac septum' long axis and stained with Masson's in Goldner's modification [10]. For precise analysis the triangle was divided (frontally) into three parts: inferior, central and superior (Fig. 1). The central and inferior parts of Koch's triangle were the most important, e.g. the level between the attachment of septal leaflet of the tricuspid valve and the attachment of the anterior leaflet of bicuspid valve as there the examined artery is placed. Additionally, this level was divided into three parts: level of attachment of the septal leaflet of the tricuspid valve with region 1–3 mm above, level of attachment of the anterior leaflet of the bicuspid valve with region 1–3 mm below and the location between these levels. The artery was examined under the magnifications of 6–400 x, and terminal small branches were described as a total narrowing of artery's diameter [11]. The atrioventricular nodal artery was analyzed in relation to the number of occurrence, and location in Koch's triangle area. Statistic analysis was conducted supported by F-Snedecor and t-Students for odd number data. In situation where the distri-



**Figure 1.** Diagram of the histologic view of the septum of the heart showing the inferior and central parts of the triangle of Koch in relation to our examination. 1 — level of the attachment of the bicuspid valve or 1–3 mm below; 2 — level between the attachments of the bicuspid and tricuspid valves; 3 — level of the attachment of the tricuspid valve or 1–3 mm above.

bution was not normal, the differential significance between two groups was tested using Mann-Whitney-Wilcoxon test. As statistically significant,  $p < 0.05$  was considered to be the level of significance.

## RESULTS

On the basis of the histological study we found that topography of the atrioventricular nodal artery was varied. It was not possible to determine the artery's origin (right or left coronary artery), because of the method that we use to prepare specimens. We define the level where the main arterial trunk was placed in the area of coronary sinus orifice in relation to the attachment of the septal leaflet of the tricuspid valve with the region of 1–3 mm above, and in relation to the level of the attachment of the anterior leaflet of the bicuspid valve with the region of 1–3 mm below, and finally in relation to location between those levels (Table 1). The majority of cases showed that in normal hearts the atrioventricular node artery, being placed in inferior part of Koch's triangle, reached the right fibrous trigone and its adventitia was connected with its fibrous tissue. The vessel branches many times both in perinodal and nodal zone in all groups of hearts. Before reaching the a-v node the atrioventricular node artery ramified once or twice. Similarly, in His-bundle zone and within the a-v node there were 2–4 ramifications in healthy hearts and in second group in the number 2–6, which in half cases created dense, vascular rete in this area (Table 2). The rami of the a-v nodal artery were also approaching the septum, the fibrous trigone and the septal leaflet of the tricuspid valve. In 70% of healthy hearts (21 hearts) the atrioventricular node artery supplied the upper part of inter-

**Table 1.** Location of the a-v nodal artery in human heart before the a-v node

Levels Central and inferior part of the Koch's triangle	Normal heart Number of hearts (%)	Heart with conduction disturbances Number of hearts (%)
Level of the septal leaflet of the tricuspid valve or 1–3 mm above	16 (53.3%)	6 (20%)
Level of the anterior leaflet of the bicuspid valve or 1–3 mm below	10 (33.3%)	4 (15%)
Level between these levels	4 (13.3%)	12 (60%)
	30 (100%)	20 (100%)

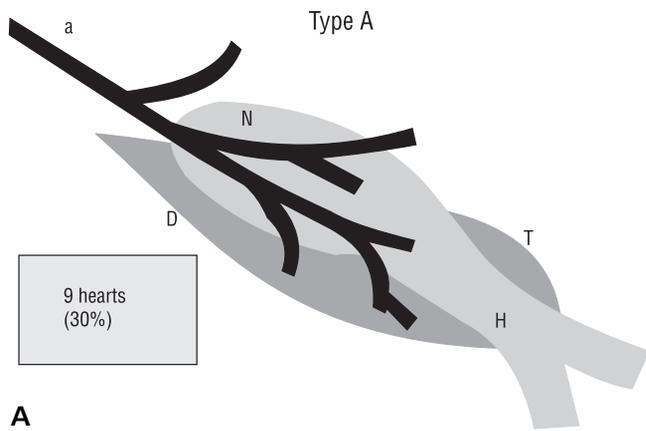
**Table 2.** Ramifications of the a-v nodal artery in perinodal and nodal tissue in human heart

Location of the ramifications	Normal heart Number of hearts (%)	Heart with conduction disturbances Number of hearts (%)
Before the a-v node 1–2 ramifications	25 (83,3%)	15 (75%)
In compact zone of the a-v node 2–4 ramifications	24 (80%)	20 (100%)
In fascicular zone 1–2 ramifications	15 (50%)	7 (35%)

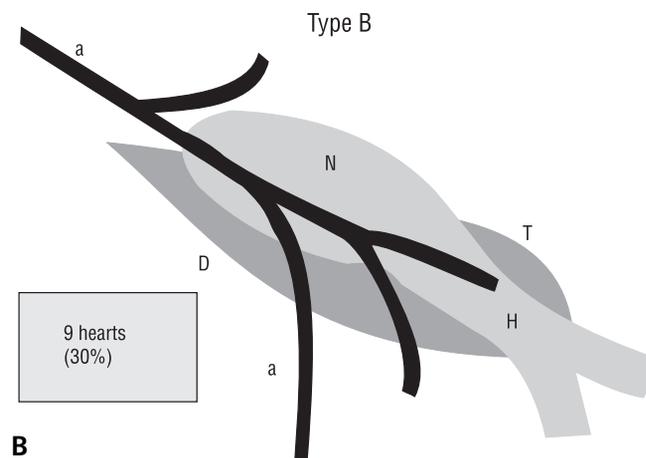
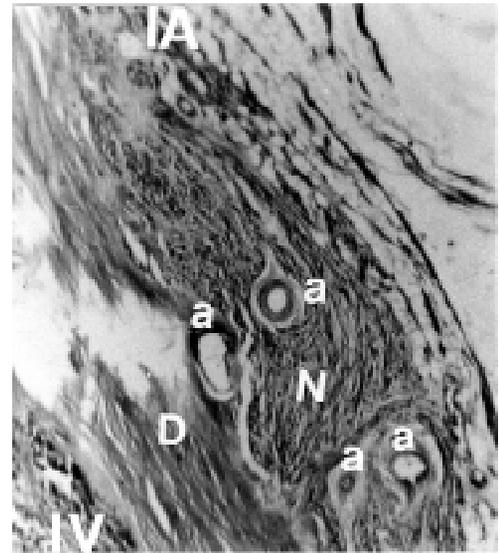
ventricular septum, and in 60% (18 hearts) supplied the lower part of the interatrial septum. Respectively, in the second group it was 70% and 45% (not significantly) (Table 3). In majority of normal hearts (23 hearts) the a-v nodal artery supplied the His bundle as well as the node and the same situation occurred in 18 hearts from second group (not significant). Additionally, in all cases we observed small rami, usually the final ones going towards the septum: interatrial (9 normal hearts — 30%, 6 paced hearts — 30%) and interventricular (12 normal hearts — 40%; 11 paced — 55%) or to the both septa (9 normal hearts — 30%; 3 paced hearts — 15%). It constituted a basis to distinguish three main types of vascular supply of nodal artery in healthy hearts: the junction and interatrial septum (Fig. 2A), both septa interatrial and interventricular (Fig. 2B) and the junction and interventricular septum (Fig. 2C). A similar division was done to the hearts with conduction disturbances: the junction and interatrial septum (Fig. 3A), the junction and interventricular septum (Fig. 3C), and both septa (Fig. 3B).

**Table 3.** Area supplied by the a-v nodal artery in human heart

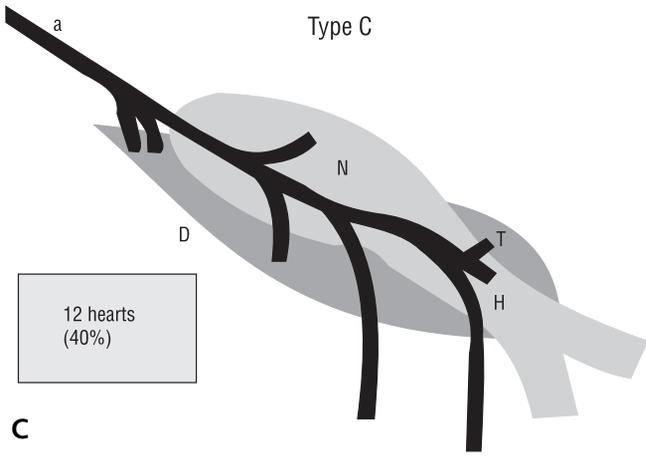
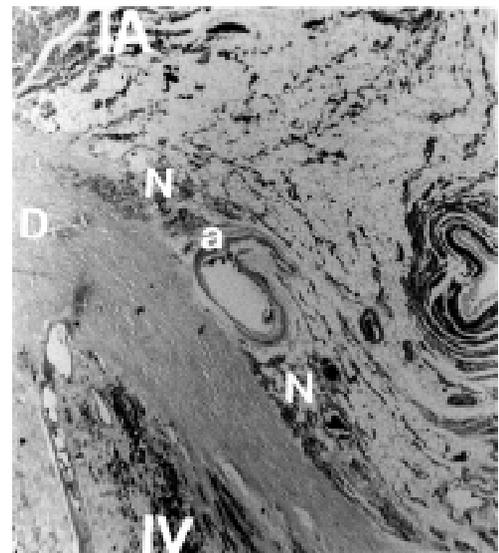
Anatomical area	Normal heart Number of hearts (%)	Heart with conduction disturbances Number of hearts (%)
Only upper part of the interventricular septum and a-v node	12 (40%)	11 (55%)
Only lower part of the interatrial septum and a-v node	9 (30%)	6 (30%)
Both interatrial and interventricular septum and a-v node	9 (30%)	3 (15%)



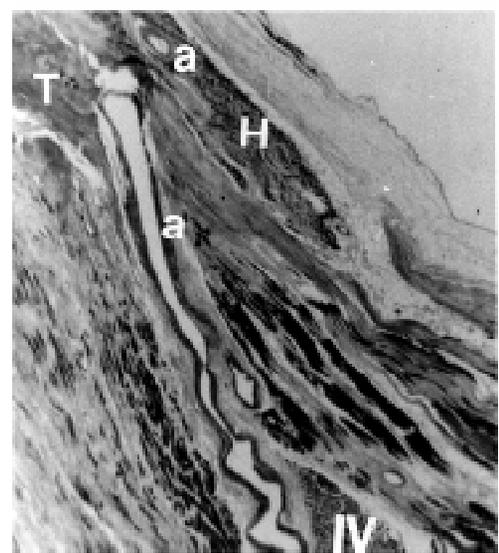
A



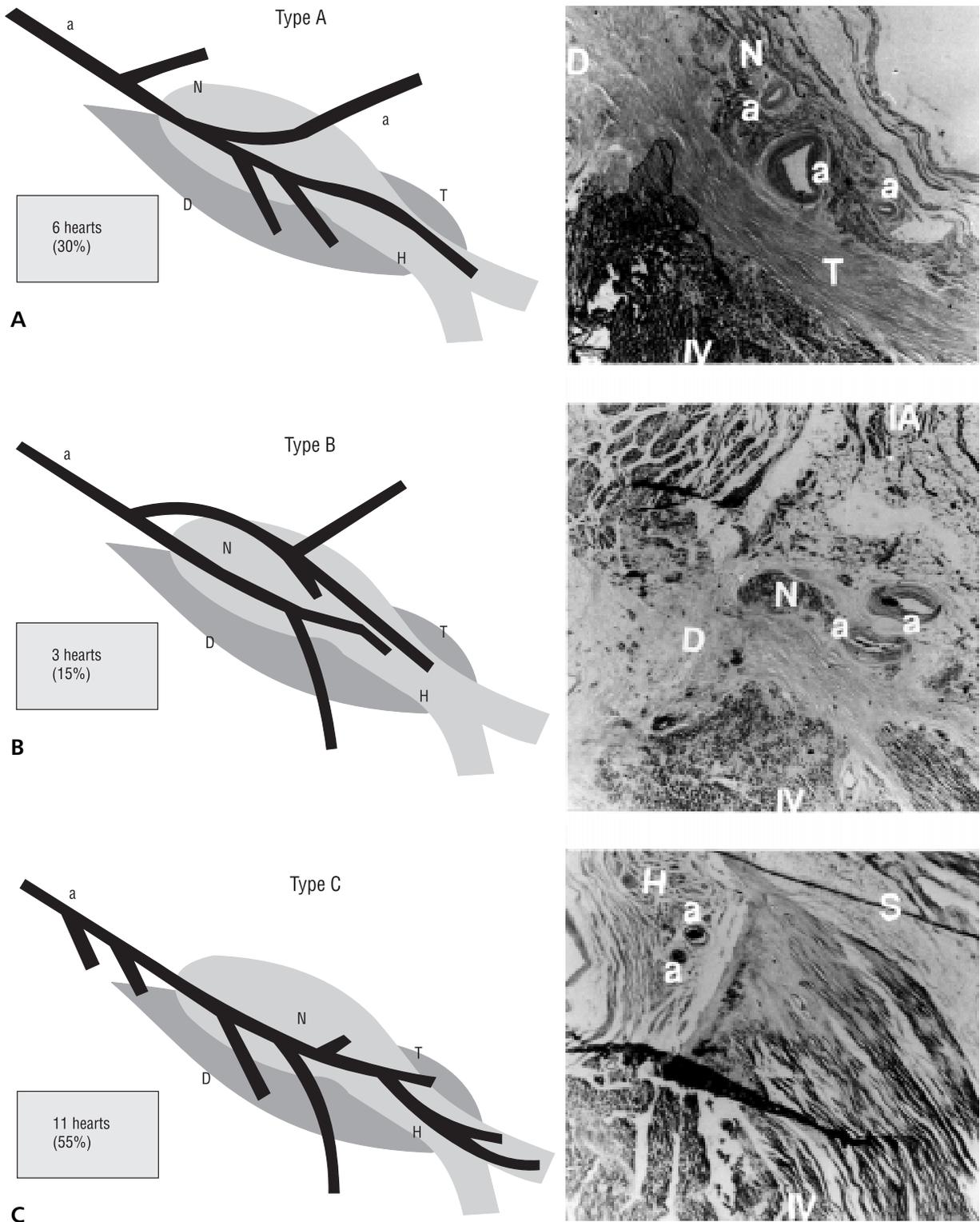
B



C



**Figure 2.** The types of ramifications of the atrioventricular nodal artery in the heart of a healthy man. a — atrioventricular nodal artery, N — atrioventricular node, H — atrioventricular bundle/His bundle, T — right fibrous triangle, IA — interatrial septum, IV — interventricular septum, D — base of tricuspid valve.



**Figure 3.** The types of ramifications of the atrioventricular nodal artery in the heart with conduction disturbances. a — atrioventricular nodal artery, N — atrioventricular node, H — atrioventricular bundle/His bundle, T — right fibrous triangle, IA — interatrial septum, IV — interventricular septum, D — base of anterior leaflet of the mitral valve.

Taking the topography of the atrioventricular nodal artery into consideration, an insignificant relationship in the position of the artery was observed between examined groups of normal versus paced hearts. Correspondingly, we described the results for both groups together. According to the above-mentioned division of the triangle of Koch, a very varied position of the atrioventricular artery was distinguished. At the level of the triangle's apex, artery was positioned in the central part in 94% (removed from endocardium 3–6 mm) of specimens and in 6% (2–5 mm) in the inferior part only. At the level of the triangle's base it was positioned in the central part in 72% (1–4 mm subendocardially) of specimens and in 28% (1–3 mm) in the inferior part. Within the triangle's center this artery was located in 88% (1–3 mm) in the central part and in 22% (2–3 mm) in the inferior part of triangle. We did not notice its localization within the superior part of Koch's triangle. We also paid attention to pathological changes in the wall of atrioventricular nodal artery, which can be responsible for direct or indirect narrowing of the arterial lumen. We observed the changes of the vessel walls in 50% of examined hearts and this showed connection with certain stages of atherosclerosis (migration of myofibrotic cells from media to the tunica intima and hypertrophy of this layer in this place) as well as hypertension characteristic of an elderly age (the positioning of the fibers in the tunica media were in the shape of goose feathers). In some cases we found little thrombi in lumen of vessel (33% of hearts from control group and 60% from paced group respectively) ( $p < 0.05$ ). We also observed connection of adventitia with right fibrous triangle and the presence of vasa vasorum in media and intima (Table 4).

**Table 4.** Pathological changes in the wall of atrioventricular nodal artery in human hearts

Pathological changes	Normal heart Number of hearts (%)	Heart with conduction disturbances Number of hearts (%)
Thickening of intima	16 (53.3%)	15 (75%)
Presence of little thrombi in the arterial lumen	10 (33.3%)	12 (60%)
Presence of vasa vasorum in media and intima	3 (10%)	4 (20%)
Migration of cells from media to intima	21 (70%)	18 (90%)
Connection of adventitia with right fibrous body	24 (80%)	20 (100%)

## DISCUSSION

Anatomical research entailed a scrutiny of the atrioventricular nodal artery with regards to morphology and topography, however, without any reference to clinical inquiry. Krupa [13], on the basis of the macroscopic examinations of material of 120 human hearts, found that the nodal artery supplied "heart's crux" that is the place where the coronary sulcus, the interatrial septum and interventricular septum run across. The results are affected by using the corrosive technique which is of limited clinical value, because it is difficult to compare the artery with atrial elements. These results are similar to our previously performed coronarographic examinations [22] — 90% from right coronary artery, 10% from left coronary artery, but they are different from the histological findings of ours. In the examinations we could investigate scrupulously the terminal ramifications of an artery finding that the artery was not supplying both of the septa (interatrial, interventricular), which stands in contradiction to Krupa's results.

Anderson and Murphy [1] found that in 90% the artery ends with atrioventricular node, in 10% with prenodal zone, and furthermore in 64% the artery is supplying the atrioventricular bundle. They carried out the histological examinations on the material of 50 infantile hearts (below 1 year of age) with regard to the blocks of conduction. We observed that the artery's terminal ramifications in atrioventricular bundle area of the paced group could be noticed in 35% of cases only. The exploration of location of the atrioventricular nodal artery was also carried out by Dean et al. [4] and others during microscopic examinations of the node in the aspect of clinical anatomy. Its course is similar to our findings from the base of Koch's triangle to its apex. Spirina and Soskin [17] analyzed the course of artery on material of 80 human hearts coming from adults, paying special attention to the topographical relations to the structure of the right atrium, joining it with angiographic examinations. The authors claimed that the course of artery is different in every heart. The artery was located 15–25 mm from inferior margin of fossa ovalis and 5–18 mm in anterior part from the coronary sinus orifice. Unfortunately, there was no data concerning the part of Koch's triangle where it was located, so we cannot compare it with our findings. Mitsuoka et al. [15] found, that the range of vascularisation of the artery depends on type of the heart's coronary vascularisation. They analyzed the same type of vessels, first with blind catheterization of living dogs and next of postmortem examinations. They differentiated three types of vascularisations (two

main: A and B, with two accessory types in B), which indirectly can be related to our microscopic examinations. They also found that there was a possibility of occurrence of a double and triple nodal artery, which is similar to our results of histological examinations (case 1). It was interesting that these scientists made intravascular administration of various drugs, causing various types of arrhythmia (for example atrial fibrillation) and disorders of conduction (I–III<sup>o</sup> atrioventricular blocks) trying to determine any morphological influence of artery on arrhythmogenicity of the myocardium. The results of our research of normal hearts proved a similar topography of the atrioventricular nodal artery yet with small deviations of the main trunk in its course. We think that the difference can be a result of a small number of hearts with rhythm disorders examined in relation to clinically healthy hearts. Other papers of Clark [3] and van der Hauwaert et al. [20], with respect to the morphological and coronarographic examinations, confirmed our findings but their data encompassed different density of capillary vessels of the nodal artery in the area of the junction (from the node to the bundle). It is not similar to our findings, but van der Hauwert and others examined material consisting of 10 hearts only. Cabrera et al. [2] examined the nodal artery in coronarographic picture in relation to a control group. They did not notice any differences in topography of the atrioventricular node artery between healthy and sick people with atrioventricular nodal reentry tachycardia.

The morphology of the area with the a-v artery placed is very important from clinical point of view because energy application could directly damage and coagulate the artery during ablation procedure. Our results confirm this hypothesis, especially on the basis of the triangle, where the artery 1–4 mm deep beneath the endocardium was located. Tanaka et al. [19] confirmed that during direct nodal ablation producing atrioventricular blocks a-v in dogs nodal artery showed only slight intimal edematous fibrosis and slight medial edema with up to 25% stenosis. With regard to our results, in hearts with a-v block parietal thrombi occurred in 60% of cases and 33% in control group respectively. On the other hand, we were able to confirm that a fair distance between the artery and junction area could protect the heart against potential damage due to applied energy. Therefore, it seems that the only explanation of such a complication is a direct damage of the atrioventricular junction. However, the modification of the nodal area (e.g. slowing of conduction for control of ventricular response) performed by Stabile et al.

[18] showed unwanted ablation of the node (e.g. creation of the total a-v block) in some patients even when performed far from the conduction system. As we assume on the grounds of the outcome of our research, this could be obtained by coagulation of the node artery within this region. Walczak et al. analyzed 54 coronarographic examinations of patients with tachyarrhythmias and the topographical relation between the artery and the coronary sinus orifice during the same contrast injection [22]. They concluded that in 8% of patients with arrhythmias a-v nodal artery is close to the sinus ostium, which is the risk factor of iatrogenic block during ablation in the posteroseptal region (e.g. ablation of the nodal slow pathway, incisional atrial tachycardia or typical atrial flutter). Our morphological research confirms also the possibility of such complication.

The inquiry proves that the atrioventricular node artery is a stable structure in all hearts, undergoing involutory changes with age. It seems that morphological changes (thickening of intima, migration of cells) observed in our findings could narrow the lumen of the artery, which can change conduction conditions between atria and ventricles. In these hearts we observed a smaller number of ramifications of the a-v nodal artery before its reaching the node. The topography of the artery in the prenodal zone was rather consistent but the deviations in its location can be responsible for potential generation of a-v blocks as complications after invasive cardiological procedures. In conclusion, from the clinical point of view invasive electrophysiological and surgical procedures in the perinodal zone should be performed in its proximal part because of minor probability of direct and indirect (through the nodal artery) damage of an atrioventricular structure of the junction. Although this is far from the a-v compact node and a risk of creation of the proximal atrioventricular block is unlikely, the possibility of damaging a-v conduction, requiring permanent pacing, should not be underestimated.

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