

A classification system for the bicuspid aortic valve from 304 surgical specimens

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Objective: In general, classification of a disease has proven to be advantageous for disease management. This may also be valid for the bicuspid aortic valve, because the term “bicuspid aortic valve” stands for a common congenital aortic valve malformation with heterogeneous morphologic phenotypes and function resulting in different treatment strategies. We attempted to establish a classification system based on a 5-year data collection of surgical specimens.

Methods: Between 1999 and 2003 a precise description of valve pathology was obtained from operative reports of 304 patients with a diseased bicuspid aortic valve. Several different characteristics of bicuspid aortic valves were tested to generate a pithy and easily applicable classification system.

Results: Three characteristics for a systematic classification were found appropriate: (1) number of raphe, (2) spatial position of cusps or raphe, and (3) functional status of the valve. The first characteristic was found to be the most significant and therefore termed “type.” Three major types were identified: type 0 (no raphe), type 1 (one raphe), and type 2 (two raphe), followed by two supplementary characteristics, spatial position and function. These characteristics served to classify and codify the bicuspid aortic valves into three categories. Most frequently, a bicuspid aortic valve with one raphe was identified (type 1, n = 269). This raphe was positioned between the left (L) and right (R) coronary sinuses in 216 (type 1, L/R) with a hemodynamic predominant stenosis (S) in 119 (type 1, L/R, S). Only 21 patients had a “purely” bicuspid aortic valve with no raphe (type 0).

Conclusions: A classification system for the bicuspid aortic valve with one major category (“type”) and two supplementary categories is presented. This classification, even if used in the major category (type) alone, might be advantageous to better define bicuspid aortic valve disease, facilitate scientific communication, and improve treatment.

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Bicuspid aortic valve (BAV) is the most common congenital cardiac anomaly, with an estimated incidence of 0.9% to 2% in the general population.^{1,2} The term “BAV” includes different morphologic phenotypes³⁻⁶ presenting with different hemodynamic conditions. The “purely” BAV is composed of two cusps, morphologically and functionally. However, the most frequent form of a BAV consists of three developmental anlagen of cusps and commissures instead of two. Associated with a certain proportion of BAVs is a dilatation of the ascending aorta, especially in young patients,⁷ exposing these patients to an increased risk of comorbidity owing to aneurysm formation and dissection. In recent years, BAV has gained increasing interest in research and treatment. Owing to improved knowledge of aortic valve anatomy and function, more refined reconstructive techniques are applied to the different phenotypes of BAV. A systematic classification of BAV phenotypes seems advantageous to more precisely describe BAV, to better relate valve morphologic characteristics to surgical intervention, to gain more insight into

Abbreviations and Acronyms

| | |
|-----|---------------------------------------|
| B | = balanced insufficiency and stenosis |
| BAV | = bicuspid aortic valve |
| I | = insufficiency |
| L | = left |
| No | = no insufficiency and stenosis |
| R | = right |
| S | = predominant stenosis |
| X | = nonclassifiable |

the association of BAV with other disease of the ascending aorta,⁸ and to allow more appropriate comparison of the different reports on the BAV. The presented classification system is based on our surgical experience with BAVs over a 5-year period.

Patients and Methods**Patients**

This is a single-center retrospective analysis of BAVs operated on from 1999 to 2003. In this time frame, 1206 aortic valve procedures were performed. A bicuspid or unicuspid aortic valve was found in 409 patients. Of these, 304 patients had a precise description of BAV valve pathology on operative reports, which are the basis of this study. The lack of precise information on 105 bicuspid and unicuspid valves was not valve related but due to missing awareness and intention to more precisely describe the morphologic characteristics useful for classification. The only information ascertainable from these operative reports was bicuspid or unicuspid valve, which was not enough for any kind of classification. This study was approved by the ethics committee.

Patient age at operation, gender, functional state of the patient (according to New York Heart Association classification), concomitant vascular diseases, and cardiac procedures, as well as the functional state of the aortic valve, were collected from the medical records.

Functional State of the BAV and Indications for Operation

The functional state of the BAV was determined before the operation by echocardiography and/or angiocardiology. The severity of aortic stenosis was assessed echocardiographically by the maximal pressure gradient ($= 4 \times v^2$ [m/s], where v is the peak systolic transvalvular velocity) and by the aortic valve area ($= [CSA_{LVOT} \times VTI_{LVOT}] / VTI_{AS}$, where CSA is cross-sectional area, $LVOT$ is left ventricular outflow tract, VTI is velocity time integral, and AS is aortic stenosis). Aortic stenosis was also assessed angiographically by measuring the transvalvular pressure gradient directly and by the orifice area according to Gorlin and Gorlin.

An aortic stenosis was defined as severe if presenting with an orifice area of 1 cm² or less or a mean pressure gradient of 50 mm Hg or more. Aortic insufficiency was assessed by color flow Doppler techniques and graded by the ratio of jet height to left ventricular outflow tract height. Grade III aortic insufficiency (47% to 64% of

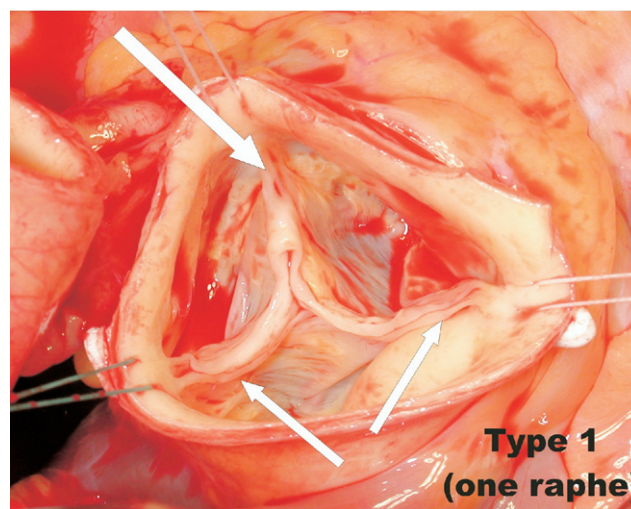


Figure 1. Intraoperative picture of a bicuspid aortic valve type 1, L/R, I (see text and Table 1 for explanation) with one completely developed noncoronary cusp, two completely developed commissures (*small arrows*), and one raphe between the underdeveloped left and right coronary cusps extending to the corresponding malformed commissure (*large arrow*) with hemodynamic signs of insufficiency due to prolapse of the conjoint cusps.

the aforementioned ratio) was considered an indication for operation in conjunction with the presence of symptoms and left ventricular size and function. Patients with severe aortic stenosis and symptoms or patients with an orifice area less than 0.7 cm² were considered candidates for operative intervention. If aortic stenosis was combined with aortic insufficiency and both of moderate degree, indicating an operation, this valve condition was called a balanced lesion.

Definition of BAVs

In this study the term “BAV” stands for congenital bicuspid aortic valve disease comprising a spectrum of deformed aortic valves presenting on gross examination with two functional cusps forming a valve mechanism with less than three zones of parallel apposition between cusps. Thus, abnormal aortic valves with two raphe resulting in a restricted orifice area that extends from the periphery to the center were included in the BAV group (type 2, valve with two raphe) and not considered to be unicuspid, unicommissural, or monocuspid as described earlier for similar valve diseases.⁹⁻¹¹ This is supported by the similarities in anatomy of BAV type 2 (valve with two raphe) to BAV type 1 (valve with one raphe).

Although the term “cusp” is a description more of a tip than an area and the term “leaflet” may be more appropriate, the term “cusp” is commonly used for the aortic valve and furthermore defines pathologic entities like the bicuspid and quadricuspid aortic valve. Therefore, we retain the term “cusp.” The term “raphe” defines the conjoint or sometimes called “fused” area of the two underdeveloped cusps turning into a malformed commissure between both cusps (Figures 1 and 2). These raphe can be developed

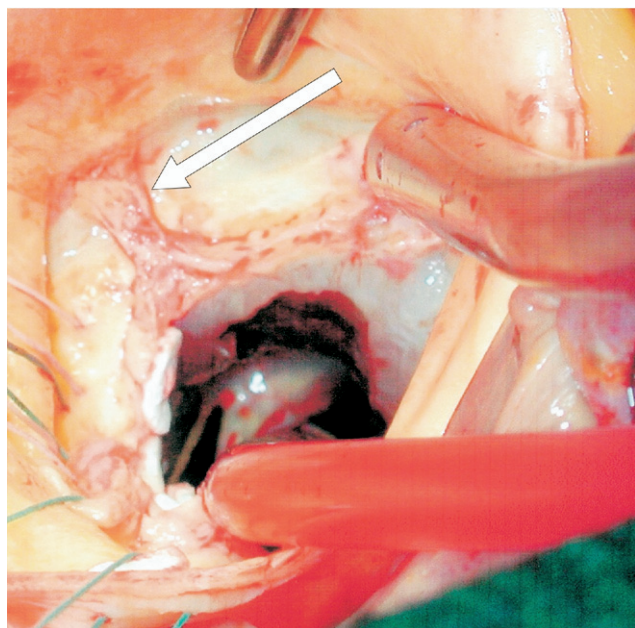


Figure 2. Situs after excision of a bicuspid aortic valve type 1, L/R, I (see text and Table 1 for explanation) showing the underdeveloped and obliterated commissure (arrow) between the left and right coronary cusps.

partially or totally. The characteristic appearance of a raphe is a ridge with many elastic fibers.¹² The commissure of the aortic valve is the space between the two coronet-shaped, lateral, and parallel attachments of two adjacent cusps to the aortic wall

normally not adhering to each other and is different from the zone of apposition between the free edges of adjacent cusps. In BAV, however, an obliteration of the commissural area is present (Figure 2).

Central to the pathology of a BAV is the malformation of a commissure (Figure 2) and the adjacent parts of the two corresponding cusps forming a raphe. There is a continuous spectrum of the BAV from completely missing one commissure, leading to two cusps, sinuses, and commissures only (Figures 3 and 4) to a more or less underdevelopment of one or two commissures and the adjacent cusps, which occurs in the majority of cases presenting with one or two raphes (Figures 1 and 5). In these cases the developmental anlagen of three cusps, commissures, and sinuses can be identified. Taken together, there are certain different morphologic characteristics of a BAV that allow, on gross examination, separation of the BAV from other aortic valve phenotypes (Figure 3), as already addressed in part by Osler¹³ in 1886.

1. Two completely developed cusps, sinuses, and commissures, commonly called “purely” BAV.
2. Developmental anlagen of three cusps, commissures, and sinuses. However, one or two commissures are more or less malformed and obliterated, giving rise to a raphe, a fibrous ridge, which extends from the commissure to the free edge of the two underdeveloped, conjoint cusps.
 - 2a. From the left ventricle, the commissural area presents as a indentation, not a space.
 - 2b. The free edge of the conjoint cusps together is slightly larger than that of the opposite cusp.
 - 2c. The circumferential distances among the three commissures are not equal.

Description of the Classification System

The classification system is based on three characteristics: the number of raphes, the spatial position of cusps or raphes, and the

| Commonly used terms | | quadricuspid | tricuspid | bicuspid | | |
|------------------------------------|-------------------|--------------|-----------|----------|---|---|
| Scheme of morphological appearance | | | | | | |
| functional characteristics | No of cusps | 4 | 3 | 2 | 2 | 2 |
| | No of raphes | 0 | 0 | 0 | 1 | 2 |
| morphological characteristics | No of cusps | 4 | 3 | 2 | 3 anlagen, (2 under- and 1 fully developed) | 3 anlagen, (2 under- and 1 fully developed) |
| | Size of cusps | non-equal | equal | equal | non-equal | non-equal |
| | No of commissures | 4 | 3 | 2 | 1 under- and 2 fully developed | 2 under- and 1 fully developed |
| | | | | | purely bicuspid* | potentially tricuspid* |

Figure 3. Schematic presentation of the developmental phenotypes of the aortic valve and typical characteristics. *Prominent line* in schematic drawings represents a raphe, which is the nonseparated or conjoint segment of two underdeveloped cusps extending into the commissural area. *Angelini and associates.²¹

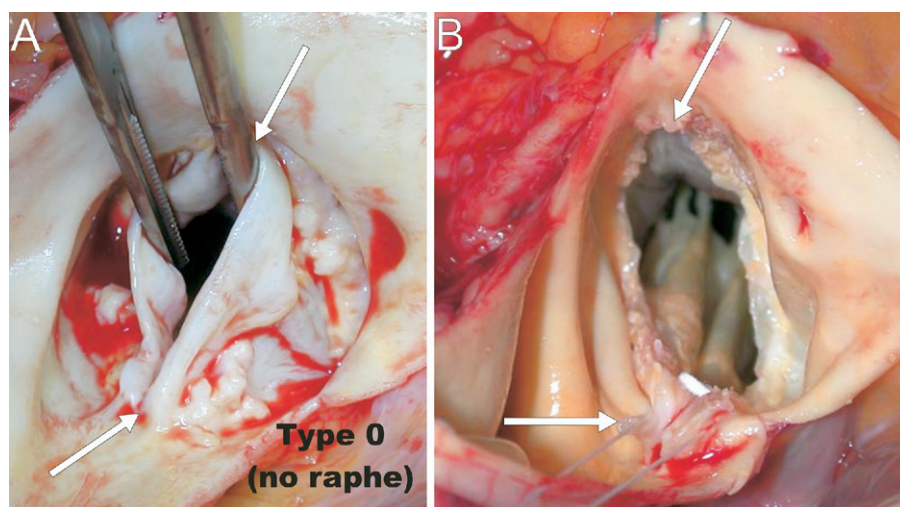


Figure 4. Intraoperative picture of a “purely” bicuspid aortic valve type 0, lat, S (see text and Table 1 for explanation) with two equal-sized cusps, no raphe, lateral arrangement of the free edge of the cusps, and presenting predominantly with stenosis before (A) and after excision (B). Note that there are only two commissures (arrows).

functional status of the valve. BAVs were classified into three categories in accordance with the characteristics (Figure 3 and Table 1). The main category is of major importance, can stand on its own, and is therefore termed “type.” The subcategories are supplementary. The main category represents the number of raphes, codifying the BAVs into three types: type 0, valve with no raphe; type 1, valves with one raphe; and type 2, valves with two raphes.

The first subcategory relates to the spatial arrangements of the free edge of cusps in type 0 (valve with no raphe) and the raphes in types 1 and 2 (valve with one and valve with two raphes) as detailed in Table 1. For type 0 (valve with no raphe), the orienta-

tion of the free edge of the cusps was found to be either antero-posterior or lateral. For types 1 and 2 (valve with one raphe and valve with two raphes), the orientation of the raphes in relation to the sinuses defines this subcategory; for example, BAV type 1, L/R, means BAV type 1 (valve with one raphe) with the raphe positioned between the left (L) and right (R) coronary sinuses.

The second subcategory is determined by the functional status of the valve: predominant insufficiency (I), predominant stenosis (S), balanced insufficiency and stenosis (B), or no insufficiency and stenosis (No).

A missing or nonclassifiable subcategory is presented by an “X.”

Thus, the classification system of a BAV may be presented in three blocks—type, spatial position, and valvular function—using the aforementioned codifications.

Statistical Analysis

Categorical data are given as total numbers and relative frequencies. Continuous data are given as mean ± standard deviation. Characteristics for patients of different groups were compared by the Fisher exact test for categorical variables and the *U* test and Kruskal–Wallis test for continuous variables. Statistical analyses were performed with statistical software SAS (SAS 8.2; SAS Inc, Cary, NC).

Results

Patient Characteristics and Operations

Mean age of 237 (77.9%) male and 67 (22.1%) female patients was 53 ± 15.4 years (range 14.6–82.5 years) (Figure 6). Patients with BAV type 2 (valve with two raphes) were significantly younger at operation (*P* = .007, 40 years for type 2 versus 53 years for type 1 [valve with one raphe] and 51 years for type 0 [valve with no raphe]). The proportion of male to female subjects was 3.5 to 1.

Preoperatively, most patients were in a clinical condition corresponding to New York Heart Association class II (mean value 2.1 ± 0.84). Body surface area was 1.96 ±

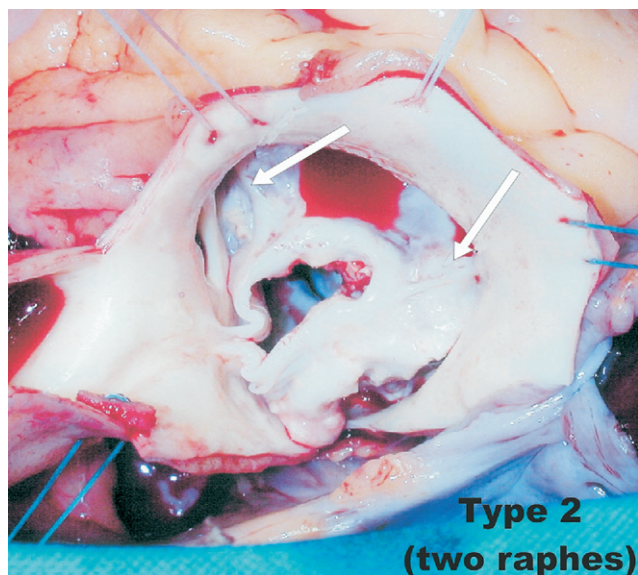
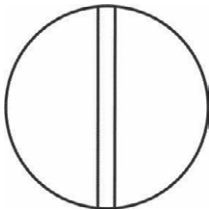

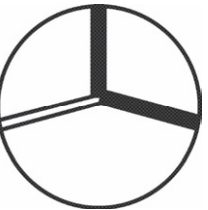








Figure 5. Intraoperative picture of a bicuspid aortic valve type 2, L/R-R/N, S (see text and Table 1 for explanation) with two raphes (arrows) but developmental anlagen of three cusps with a high degree of stenosis.

TABLE 1. Schematic presentation (as viewed from the surgeon's position with the left coronary sinus on the left side) of the classification system of BAVs with one main and two subcategories, including the number of specimens (percent in parenthesis)

| main category: number of raphes | 0 raphe - Type 0 | | 1 raphe - Type 1 | | | 2 raphes - Type 2 | | |
|---|---|---|---|--|---|---|-------|-------|
| |  |  |  | | | | | |
| | 21 (7) | | 269 (88) | | 14 (5) | | | |
| 1. subcategory: spatial position of cusps in Type 0 and raphes in Types 1 and 2 |  lat 13 (4) |  ap 7 (2) |  L - R 216 (71) |  R - N 45 (15) |  N - L 8 (3) |  L - R / R - N 14 (5) | | |
| 2. subcategory: | | | | | | | | |
| V A L V U L A R F U N C T I O N | I S B (I + S) No | I | 6 (2) | 1 (0.3) | 79 (26) | 22 (7) | 3 (1) | 6 (2) |
| | | S | 7 (2) | 5 (2) | 119 (39) | 15 (5) | 3 (1) | 6 (2) |
| | | B (I + S) | | 1 (0.3) | 15 (5) | 7 (2) | 2 (1) | 2 (1) |
| | | No | | | 3 (1) | 1 (0.3) | | |

Prominent lines in schematic drawings represent a raphe. The codification for the main category is Type (Type 0 for valve with no raphe; Type 1 for valve with one raphe; Type 2 for valve with two raphes); for the first subcategory: ap, lat, L-R, R-N, N-L, and L-R/R-N; and for the second category: I, S, B, and No. Thus, the classification system may be presented as a codification in three blocks: Type, spatial position, and valvular function (eg, BAV Type 1, L-R, S, meaning a bicuspid aortic valve with one raphe between the left and right coronary sinus, and with valvular stenosis, which was the most frequent specimen). One specimen of a BAV Type 0 (valve with no raphe) could not be categorized in the first subcategory, resulting in the codification BAV Type 0, X, S. *ap*, anterior-posterior; *lat*, lateral; *L*, left coronary sinus; *R*, right coronary sinus; *N*, non-coronary sinus; *I*, insufficiency; *S*, stenosis; *B*, balanced valvular lesion; *No*, normal function; *BAV*, bicuspid aortic valve; *X*, not ascertainable.

0.22 m². Concomitant diseases were coronary artery disease in 86 (28.3%), hypertension in 167 (54.9%), hyperlipidemia in 111 (36.5%), diabetes in 31 (10.2%), Marfan syndrome in 2 (0.7%), and history of cancer in 17 (5.6%).

The underlying aortic valve disease was an insufficiency in 117 (38.5%), stenosis in 156 (51.3%), balanced combined

valve disease in 27 (8.9%), and active endocarditis in 15 (4.9%) patients; 4 of these were without valve dysfunction but had large vegetations.

Aortic aneurysms (diameter > 5 cm) were present in 90 (29.6%) patients, with involvement of the aortic root in 18 (5.9%), ascending aorta in 88 (28.9%), aortic arch in 2 (0.7%), and descending aorta in 1 (0.3%). A significantly higher proportion of aneurysms of the ascending aorta was present in BAV type 2 (valve with two raphes; $P = .022$; Figure 7).

Most patients had a Ross procedure ($n = 111$, 36.5%), 96 (31.6%) a bioprosthesis, and 72 (23.7%) a mechanical prosthesis (as a conduit/Bentall procedure in 17, 5.6%). Reconstruction of the valve was performed in 17 (5.6%), reimplantation technique according to David and Feindel¹⁴ in 5 (1.6%), and remodeling technique according to Yacoub and associates¹⁵ in 3 (1.0%).

There was no difference in coronary artery disease between types of BAVs (33% for type 0 [valve with no raphe], 29% for type 1 [valve with one raphe], and 14% for type 2 [valve with two raphes]).

Concomitant procedures were performed as follows: coronary artery bypass grafting in 43 (14.1%), maze procedure

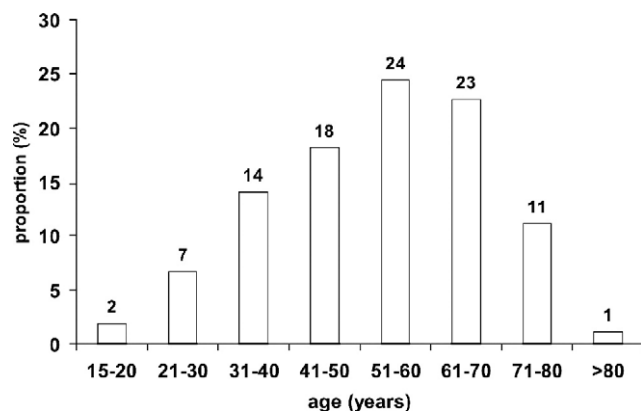


Figure 6. Age distribution of the 304 patients with a bicuspid aortic valve.

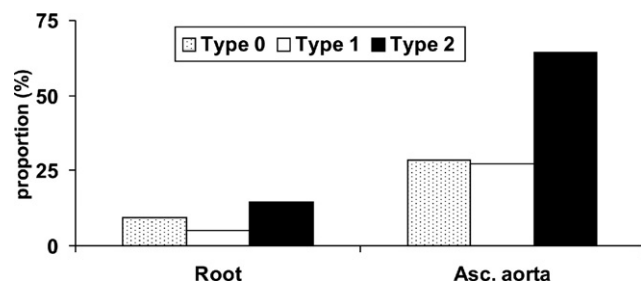


Figure 7. Proportion of an aneurysm of the aortic root or ascending aorta in relation to the type of bicuspid aortic valve. A bicuspid aortic valve type 2 (valve with two raphe) was associated with a significantly ($P = .022$) higher proportion of aneurysms.

in 4 (1.3%), left ventricular myectomy in 7 (2.3%), mitral valve reconstruction in 16 (5.3%), closure of a patent foramen ovale in 3 (1.0%), and closure of a ventricular septum defect in 1 (0.3%).

Classification of Surgical Specimens

The results are summarized in detail in Table 1. There were 21 (7%) patients with BAV Type 0 (valve with no raphe). One of these specimens with predominant valvular stenosis could not be categorized into the first subcategory owing to lack of specification of the orientation of cusps in the operative report, resulting in the codification type 0, X, S. Most patients ($n = 269$, 88%) had BAV type 1 (valve with one raphe). Within this group the predominant finding was type 1, L/R, S ($n = 119$, 39%), which means a BAV with one raphe between the left and right coronary sinuses and with valvular stenosis. There were 14 patients with BAV type 2 (valve with two raphe).

Discussion

The BAV, appearing on gross examination as an aortic valve with two cusps, has clinical relevance¹⁶⁻¹⁸ and has gained increasing interest in the medical community from a pathogenetic and especially surgical point of view.^{19,20} The BAV represents a certain segment of the developmental spectrum of aortic valve phenotypic continuity. Developmentally, the BAV is not simply the fusion or nonseparation of two cusps but a more complex process involving the cusps, sinuses, commissures, position of the coronary orifices, and possibly the texture of the wall of the ascending aorta. BAVs are not equal among each other in morphologic, positional, and functional aspects, which is of significance for treatment. We found the number of raphe to be the most practical and readily recognizable distinctive characteristic of BAVs, representing the main category of this classification, called “type.” Typically, no raphe is present in the so-called “purely” BAV with two completely devel-

oped cusps and commissures (type 0), which is, however, the case in the minority of patients (7% in this series); this is comparable with the results of Angelini and colleagues.²¹ In this configuration, valve implantation in general, and especially the Ross procedure, is more challenging, and a circular, not scalloped, proximal suture line seems preferable. In addition, the vis-à-vis orientation of the coronary ostia requires special consideration when arranging the three new commissures of the autograft. In roots with this kind of unfavorable anatomy, it is sometimes advisable not to perform a Ross procedure.

In BAV type 1 (valve with one raphe), there are two smaller malformed cusps bearing the conjoint part or raphe and one larger cusp, most frequently the noncoronary. The commissure between both underdeveloped cusps is also malformed. This is, however, of no major surgical concern because the surgical annulus for implantation of prostheses and also for the Ross procedure is largely maintained (Figure 2) or even flattened to a more ringlike configuration in relation to the extent of malformation of this commissural area. The surgical annulus is composed of the proximal part of the semilunar attachments of the cusps to the wall, extending from the nadir of the sinuses to the point where this line approaches that of the adjacent cusp.²² The larger noncoronary annulus and sinus can easily be matched by a plication suture at the nadir and/or the sinus during closure of the aortotomy. Even in BAV type 2 with two raphe, three sinuses are identifiable, facilitating the pulmonary autograft procedure or conventional valve replacement.

In patients with an insufficient BAV type 1 (valve with one raphe), usually the two conjoint leaflets with the raphe are prolapsing, giving the appearance that there is some cusp tissue missing at the area of the raphe. This can be replaced by prosthetic material or pericardial tissue, but preferably the raphe is plicated or resected and thus the cusps are raised up to the coaptation area of the nonprolapsing cusp. This procedure, however, produces inevitably some degree of stenosis, which seems not to be of clinical significance even at exercise.²³ Nevertheless, the deficiency of cusp tissue may require other surgical techniques, such as annuloplasty or cusp extension, to increase coaptation area or elevation of commissures.

In BAVs type 0 (valve with no raphe), plication of the prolapsing cusp also restores coaptation area. Long-term results of reconstruction of insufficient BAV type 1 (valve with one raphe) and type 0 (valve with no raphe) are likely different partly as a result of different morphologic characteristics.

The first subcategory is related to the position of the raphe. This is of minor direct surgical impact but may have some pathophysiologic relevance. In this respect, it is of interest that BAVs type 2 (valve with two raphe), L/R-R/N were associated with the highest incidence of aneurysms of

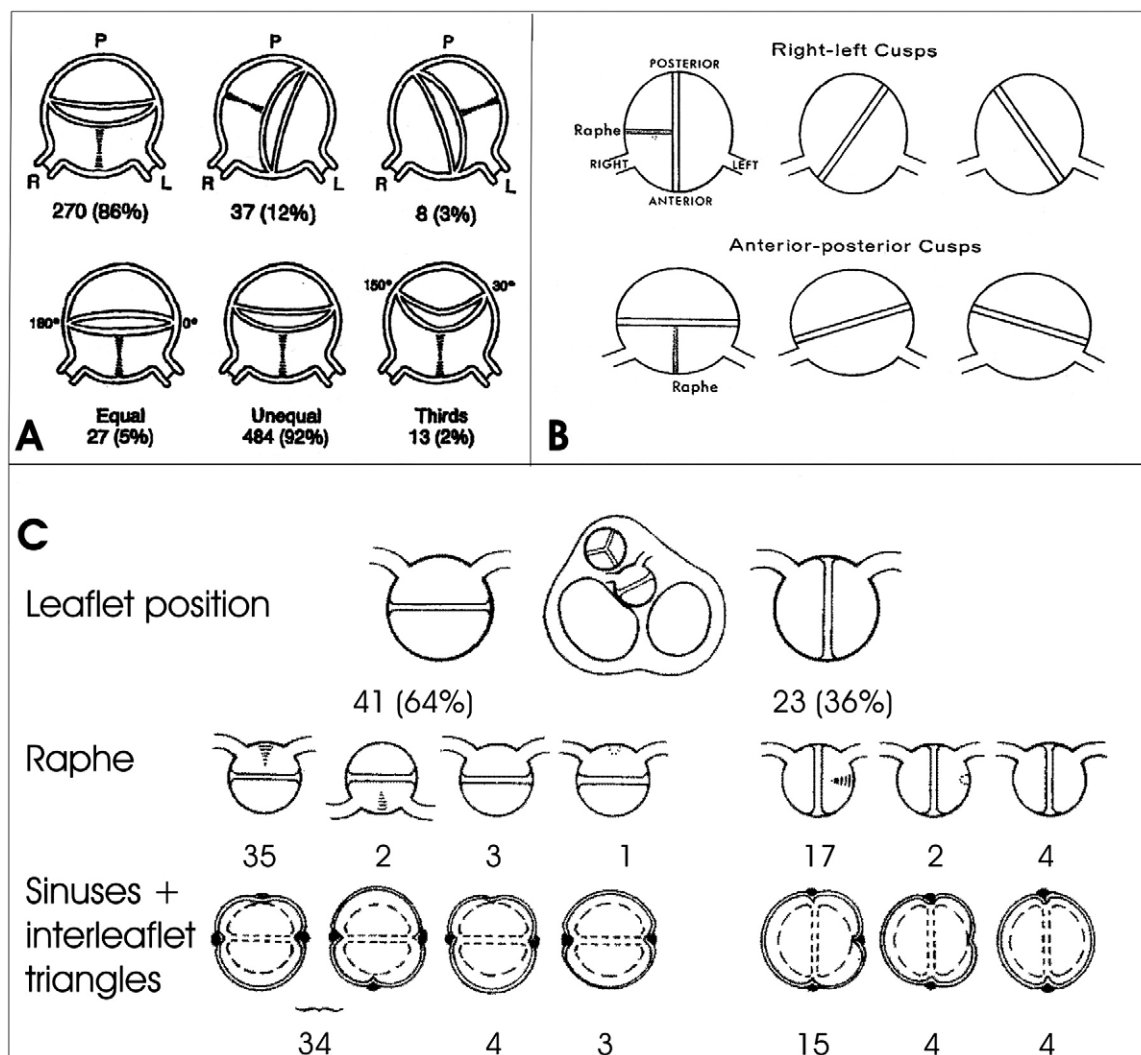


Figure 8. Schemes of bicuspid aortic valve classifications of different authors: **A**, Sabet and associates⁴; **B**, Roberts and associates¹²; **C**, Angelini and associates.²¹ The position of the raphe and cusps, the relative sizes of cusps, as well as the number of sinuses and interleaflet triangles as described from the left ventricular outflow were main but not uniform determinants for classifying bicuspid aortic valves.

the ascending aorta (Figure 7). The flow through this reduced opening area is directed to the convexity of the ascending aorta, where typically the aneurysms are located. Whether this increased local wall stress acts as a trigger for aneurysm formation is questionable. Probably these typical dilatations of the ascending aorta are related more to BAV intrinsic aortic disease than to hemodynamics.

The second subcategory provides information on the functional status of the valve, which is not only of diagnostic interest but also may have some prognostic information on ventricular performance, timing of operation, and operative technique.

With this classification system, it was possible to group all BAV phenotypes at least by the main category.

For other studies on BAV morphology it was also possible to apply this classification system to the main category.^{3,4,6,21} Other authors^{4,5,9,21} principally found similar results concerning the distribution of purely BAVs and those with one raphe, as well as the position of the raphes. They also used the position of both the cusps and the raphes, the number of sinuses, the interleaflet triangles from below, and the cusp sizes for BAV description (Figure 8). These classifications, however, are not uniform, not widely used, and are not condensed in a concise, easily applicable, graduated classification and codification including morphology (number of raphes), spatial position of cusps or raphes, and valvular function,

nor were abnormal aortic valves with two raphe included in the BAV group. From a surgical point of view especially, the number and position of raphe is easily assessable and applicable for classifying and codifying BAVs in the vast majority of patients.

Nevertheless, this classification system has some limitations. Valve calcification may render the classification difficult, especially if a congenital tricuspid valve becomes calcified, leading to acquired fusion of the cusps. However, after excision of the calcified leaflets, the developmental status of the commissures can be identified in most cases. An obliterated commissure is typical for BAV (Figure 2). This also holds true for a BAV with two raphe (type 2) and corresponding underdeveloped commissures. Furthermore, the assessment of the distance among the three commissures, which is more or less equal in tricuspid valves, but not equal in most BAVs, may help for classification.¹² In addition, the coronary artery anatomy with a higher incidence of left main dominance⁷ might help the identification of a BAV in these cases. On the other hand, if there is some kind of a raphe in a “purely” BAV with two cusps, which is the proposed type 0 (valve with no raphe), there is no category in the described system for classifying this valve. However, these cases are extremely uncommon and may be described separately.

It is imaginable that additional subcategories could even more precisely specify the valve, for example, size of cusps,⁴ the concomitant existence of an ascending aortic aneurysm, extension and size of raphe, microscopic details, genetic markers, heritability signs,²⁴ and annulus dilatation, just to mention some. However, these additional items would make the classification system more complex and probably less practical.

We believe that the proposed classification, with the main category termed “type” alone or preferably together with the two subcategories, would yield advantages to more precisely and comparably describing the BAV as a further step for improved management of this entity.

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