

How long ...? Possibilities, Limits, Criteria

Max Grinberg

Instituto do Coração do Hospital das Clínicas - FMUSP, São Paulo, SP, Brazil

FN had rheumatic fever at 11, cardiac murmur at 17 and severe aortic insufficiency at 30. He received medication and was submitted to tests "to define whether surgery would be necessary". "How long...?" FN asked, but the answer was vague. "Now", his symptoms answered. Once the bioprosthesis had been implanted, the same question arose: How long...? Same question, same answer. There is no precise time when we speak of long term, only forecasts. All this because of the burden of a disease that will affect Brazilians until when...?

FN's case is a real world situation. The past, the present and the future of patients with severe valve lesions, events that can be predicted by Cardiology, but cannot be predicted by cardiologists in terms of time, that is, there is no answer to the "How long..." question. Rheumatic fever, just as a bioprosthesis, is an arrow with a pre-determined destination. We envisage where they may head to and what they may cause. We have to monitor their trajectory and check their destination.

Learning about the effects of time is part of the bedside manners of cardiologists. Cardiologists have to learn how to deal with the "How long" question. The doctor has to be knowledgeable about the effector and the time factor. In Greek mythology, Chiron, the centaur that had the gift of healing, was the son of Chronos, the personification of time.

Time to observe, time to medicate, time to operate. These are the stages of the follow up of the natural history of valvulopathies. How long... does each stage last? How long...should we wait before we deviate the arrow from its target? There are plenty of unknown factors in this route.

Any presumption on the part of cardiologists of his ability to answer the "How long" question in a precise manner has to do with interpreting the pros and cons of each case.

FN was informed that he was undergoing a natural process of progression and that each stage of the disease entailed risks and benefits as regards an intervention. FN went through toll stations, and at each stop he saw his cardiologist strive to harmonize autonomy, beneficence, and not maleficence. FN realized that the "How long" question would be answered by the effects of his complaints and tests on his doctor's concepts. FN understood that he would get an answer from his cardiologist, not from the doctor's Cardiology. The clinical conscience of a cardiologist develops in the constant struggle against the limits of propaedeutics and therapy. Cardiologists are the links that form the chain of Cardiology. This chain becomes strong and is made not only of famous practitioners, to whom statues are erected, but also of those who toil every day, and are examples that are equally worthy of recognition.

Good ideas, sound reasoning, defensible intentions, promising research results emerge all the time. Unfortunately, some advantages based on the premise of expanding boundaries clash with unpredictable biological reactions and, why not say it, with conflicts of interest¹. This is the reason why any prognosis regarding any aspect of valvulopathies should be put forward with caution, and the risk of pronouncing every word should be carefully weighed. Only those statements which accurately reflect the cardiologist's opinion about the future should be effectively issued.

At each interaction, the view of valve-related things as part of the science of probability and the art of uncertainty is renewed. Valvoplasty: certainty or high likelihood? Definitive metallic prosthesis? Does delaying the procedure mean preventing re-operation? Are ventricular diameters decisive factors? Should we act according to the signs or react to the symptoms? Do drugs slow down ventricular remodeling in a useful fashion?

The construction of knowledge and the training opportunities in Cardiology excite the creativity of cardiologists in the field of valve lesions. It is a good feeling, a very beneficial scenario as this is an area marked by the monotony of clinical manifestations, with little variety of nosological and etiopathogenic diagnosis and where new associations are rare. However, many issues remain unsolved. It is the mission of the new generations of cardiologists to enrich the heritage and it is a duty of Cardiology to prevent the old saying – from shirtsleeves to shirtsleeves in three generations – from coming true. "How long" should not really relate to knowledge but rather to attitudes.

Having a safe marker for the imminence of the onset or worsening of valvulopathy symptoms is a challenge to Cardiology as regards the "how long...?" question. Morphological values have proven ineffective² and biochemical assessments have renewed our hopes³. How long...?

At the core of these considerations are the everyday

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Point of View

questions faced by cardiologists, who are urged to harmonize the tools Cardiology makes available to them with those he has to select in view of a certain circumstance, as he is aware of the absence of ideal assumptions.

There is plenty of asymmetry as to procedures, and in view of this, cardiologists got used to depositing knowledge into the data bank of Cardiology, and withdraw such knowledge in the form of organized packages, on behalf of the specialty's good quality. There is something somewhat like solidarity in procedures which are recommended or discouraged, in those that are advisable and those that would be ineffective. Different medical facilities adopt specifications for the care of patients with valve diseases which are more or less common, but variations in these procedures are needed, even if only to ensure adaptation to cultural differences. In large centers, different attitudes towards the same clinical situation are just a few miles apart, whereas in a medical congress they're only centimeters apart. However, here there is no place for "How long...?", as the plurality of views among cardiologists is the high-yield fuel that makes Cardiology advance.

Specialization has been considered a affront to the essential unity of Medicine, a misjudgment of the principles of medical practice. Some have worried about the "How long...?" and have contributed to overcome this concept. In the transition from the 20s to the 30s, "experts in heart" were no longer mere consultants but rather became the clinicians in charge of cardiac patients⁴. This was consolidated in 1940, when the American Board of Internal Medicine recognized cardiovascular diseases as one of the four authorized subspecialties, together with allergy, gastroenterology and pneumology. The American Heart Association, the only society of the then recently declared specialty became responsible for the evaluations aimed at the granting of the title of specialist.

At present, Cardiology, a sixty-year old legal entity, and the cardiologists themselves, the individuals, whether old or not, make decisions together, share responsibilities and communicate with each other through certain processes such as the trial guidelines education¹. This is a mature scientific way of taking "bedside imagination" to the laboratory and recover it within the triad of limits made up of technique, ethics and legality.

There are many seeds to be sown in the ample and fertile ground of valvulopathy. Let us not forget that rheumatic disease is of interest to Brazilians – "How long...?" – and that the rising average age of our population increases the percentage of valvulopathy of degenerative etiology, reflecting a global trend.

The specialty is now mature. The related knowledge has been consolidated, and resonates with legitimacy and currency. The recommendations of Cardiology are available to cardiologists, and they become agents. Their adherence to these recommendations oversimplifies their decisions, and although at the risk of reductionism, it makes their tasks lighter in terms of the literature they have to consult, and prevent them from distancing themselves from the position of the majority. It is part of the value of Cardiology as the cement that keeps cardiologists together. At the same time, cardiologists are flexible, they adapt the recommendations to their practice, to what they see and to the way they perceive clinical situations.

The FN case allows us to make some considerations in our relentless pursuit of the method that best meets the objectives of physicians and patients.

The Past

If the past of rheumatic disease dates back to when the "How long...?" question was asked for the first time, in the case of FN, history takes us back to Thomas Duckett Jones (1899-1954), with his pioneer view on how to organize guidelines for cardiologists to use at the patient's bed side.

Jones' criteria were developed in the 1940s in response to a request of the Subcommittee on Cardiovascular Diseases of the National Research Council, in an effort to cooperate with the American Armed Forces, then concerned about rheumatic fever outbreaks in the barracks during World War II. At that time, the criteria for the diagnosis of rheumatic fever outbreaks were not precise, and each observer applied a criterion subject to enormous divergence. Greater specificity was required.

The criteria were developed by Jones based essentially on his own experience. He was the head of an infirmary for rheumatic fever patients at the House of Good Samaritan ⁴, under the coordination of Paul Dudley White (1886-1973) from the Massachusetts General Hospital, Boston. In the period from 1921 to 1931, his casuistics reached the total of 1,000 consecutive patients (2 new cases per week), with a mean age of 8 years, 70% female⁵. Strangely enough, the diagnostic appraisal of rheumatic fever by Jones and the development of his criteria (1921-1944) were concurrent with the discovery by chance of penicillin by Alexander Fleming (1881-1955) and the commercial availability of penicillin for preventive purposes (1928-1945).

It is worth noting that this contribution was made by a single cardiologist unlike today when guidelines are authored by many specialists. It is remarkable that Jones, when he gathered nonspecific points, felt the need to classify what he thought to be more or less valuable⁶. Therefore, Jones recommended diagnostic combinations, which was a strong intuition as to the use of different levels of evidence.

From a pedagogic point of view, we should think about the concept that creativity does not entail commitment to absolute truth. The fact is that the original criteria were imperfect, and they would not be useful today. They were, however, the first step to allow the existence of reviewed and modified criteria, years later, as a result of the sharing of information and opinions. The current criteria are those of the 1992 update, carried out under the auspices of the American Heart Association. Four versions later, the only mandatory question for each new update, "How long...?" remained unchanged. In other words, the criteria initiative, of great historic value, became widely accepted as it eliminated abdominal pain and epistaxis as minor criteria, established the difference between arthritis and arthralgia and upgraded erythema marginatum. This is a consequence of the reproducibility which is essential to any commitment to quality.

The updated criteria proposed by Jones are related to greater specificity than sensitivity. False diagnostics (-) usually match false infectious endocarditis (+), despite

Point of View

the modification of the original criteria of Duke University with the greater emphasis placed on blood culture and transesophageal echocardiography. It is exciting to realize that the "How long...?" of the criteria of Von Reyn et al. lasted for thirteen years, and that the current change of the criteria of Duke University appeared in less than half the time⁷⁻⁹. The improvements usually take less time than the creation of novelties.

The Present

The follow-up of the natural history of valvulopathies enables cardiologists to experience ambiguities and to decide on one direction. There goes the arrow, but the bow stays put. After all, according to Article 2 of the Brazilian Code of Medical Ethics, we need the bow to hit the target of human health.

At a certain point, in the case of FN, the cardiologist had to identify the moment when further procedures were required, procedures of a preventive nature as regards the rheumatic disease and infectious endocarditis; this was done by adding the input of Cardiology on the consequences of volume overload associated with chronic aortic insufficiency.

This therapeutic decision usually takes place when the patient is in Functional Class II, a common name that qualifies different anatomical and clinical combinations.

Cardiologists who follow up on patients with valvulopathies learn that this functional class is clinically fragmented. They see an initial point that we could call post-I stage of functional class II, usually with no need for therapy, and which progresses to a final point, pre-III stage of functional class II, which requires specific diagnostics and therapy. The imminence of class III is a real transition, so clear-cut regarding the psychological and social preparation for surgery as it is unclear regarding its recognition. The recent VMCP Score proposed to Cardiology¹⁰ aims at facilitating the monitoring, on the part of cardiologists, of the clinical and anatomical evolution of patients with cardiomyopathies.

It is in the pre-III stage of functional class II of patients with cardiomyopathies that the meaning of a therapeutic action may vary. An intervention that may be correct from a technical point of view may be deemed incorrect from an ethical point of view because of divergences regarding the timing of the intervention. A technically incorrect decision, however, will always seem unethical.

Since Cardiology is ambivalent in terms of agreements and disagreements, cardiologists have to keep to the natural history of "how long...?" This expression synthesizes the doubts regarding the harmony between beneficence and nonmaleficence. It can be too early, it can be timely and it can be too late, but those who look at them may have their eyes on the eyepiece or in the objective of a binocular and it is known that the clinical eye does not need this instrument.

There is a school of thought that does not accept interventions unrelated to the aim of restoring the patient's quality of life, impaired by the disease, and therefore will not accept the triggering of a postoperative history of valvulopathy during functional class II ("early indication"). The possibilities and limits of the intervention then restrict the imagination on the possible meaning of a repaired major valve lesion. This idea is teleologically advantageous, were it not for the criticisms based on situations experienced at the patient's bedside. For this line of thought, when the risk of morbimortality during the surgery and in the postoperative period is weighed against the potential benefit for the patient's quality of life favors the view that it is better to not replace the valve, however severely impaired, of asymptomatic patients with normal ventricular function. In other words, there would be enough advantage on the natural order of things to warrant a conservative attitude. We endorse this line of thought which seems to better allow the balance of beneficence/non-maleficence and better contribute to the equitable allocation of resources.

In order to conclude that a severely impaired valve is better than prosthesis, we have to go back in time, and review the history of valve replacements, or resort to the artifice of actuarial curves. It is very likely that the sense of parsimony should prevail. It is exactly within this context of restraining valve replacement that proposals emerge such as Ross's surgery¹¹, which combines the elimination of the impaired valve with the reduction of risks associated with the prosthesis that replaces it. This exemplifies our frustration with good ideas, which has been going on for 35 years. This surgery has not become a routine procedure, and has not become outdated either. The obstacles of practice have prevailed.

There is a school of though that focuses on more objective aspects of valvulopathies, such as diameters and degree of morphological lesions, and therefore, by making use of cutoff lines determined by statistical appraisals on prognosis, does not rule out interventions during functional class II. The percentage increase in the use of a conservative technique of valves, especially in patients with mitral lesion¹² attests to the enthusiasm linked with this trend of anticipating the postoperative history.

Current guidelines provide an overview on the adoption by Cardiology of the two lines of thought of cardiologists about the "how long...?", that is, what the prevailing understanding would be, relative to the pro-beneficence/non-maleficence principle as to the limits between clinical and surgical treatment, despite the fact that, when this is applied, the patient's subjectivity has to be factored in.

FN had the "how long...?" question answered when he realized the physical limitations imposed to his routine activities, when he passed to functional class III. The answer "Now!" matched the orientation established in the current AHA/ACC Guidelines for class I, published six years ago¹³. We should highlight that although many studies have been made available in the literature since then, the recent Guidelines on Valvulopathy Surgery issued by the Brazilian Society of Cardiology needed very little updating¹⁴.

Thanks to the consultations that allowed the immediate recognition of the change in the clinical profile of his valvulopathy, FN didn't have to experience yet another "how long...? This recognition has to do with the expression of the highest level of anxiety as to operative risk and postoperative prognosis since it reached an advanced stage in the natural history of valvulopathy. How long...Not contraindicating a traditional surgery or not opting for heart transplant is a challenge in terms of beneficence/non-maleficence.

Point of View

Future

Dogmas in Cardiology? A historical overview does not warrant them. Remember the words of Carey Coombs, in 1924: "...all of the acquired mitral valve diseases and unexplained cardiomegalies in children are rheumatic, as there is no other alternative theory available as to their etiology...". Fifty-five years went by before C. Ward wrote: "...It is not possible to prove the rheumatic nature of a large number of isolated valvulopathies. There is evidence that more than one etiological agent is responsible for the so-called classic rheumatic valve disease..."¹⁵.

There are "trendy" procedures, there are regional preferences, and there are dissociations between Mathematics and Biology which reflect disagreement between statistical behavior and bedside practice. Veracity is not an absolute duty, and cardiologists are not bound to make perfect and consistent recommendations by any law of Cardiology.

New pieces of information and conclusions of studies add nuances, challenge "truths" and rehabilitate outdated opinions. Chance drives improvements, and mistakes relating to false positives and false negatives are rectified. Fully believing while doubting something is no contradiction. On the contrary, it is the Boy Scout's "be prepared" attitude reflected on medical practice as there is an antithesis for every thesis. Who would dare disagree that Medicine is a set of provisional truths oscillating between always and never?

The strategy adopted by FN's cardiologist yielded good results. He enjoyed good quality of life with an expressive degree of reverse ventricular remodeling. The developments of his case reflected the principles of beneficence/non-maleficence/ autonomy¹⁶. In other words, the good result obtained validated the strategy.

The decision to change the course of the history of mitral valvulopathy from the natural course to the postoperative course followed current arguments. For FN, the arrow of Cardiology was shot and hit the target based on the best

References

- 1. Fye WB. The power of clinical trials and guidelines, and the challenge of conflicts of interest. J Am Coll Cardiol. 2003; 41: 1237-42.
- Bonow RO, Lakatos E, Maron BJ, et al. Serial long-term assessment of the natural history of asymptomatic patients with chronic aortic regurgitation and normal left ventricular systolic function. Circulation. 1991; 84: 1625-35.
- Spina GS. Níveis de citocinas proinflamatórias e seus antagonistas em pacientes com insuficiência aórtica crônica importante/. São Paulo, 2004. Tese (Doutorado) – Faculdade de Medicina, Universidade de São Paulo.
- Grinberg M. Epônimos em Cardiologia. Homenagem e exemplo. São Paulo: Livraria Roca; 1999.
- Bland EF, Jones TD. Rheumatic fever and rheumatic heart disease. A twenty year report on 1000 patients followed since childhood. Circulation. 1951; 4: 836-43.
- 6. Jones TD. The diagnosis of rheumatic fever. JAMA. 1944; 126: 481-4.
- 7. Von Reyn CP, Levy BS, Arbeit KD, et al. Infective endocarditis: an analysis based on strict case definitions. Ann Intern Med. 1981; 91: 505-18.
- Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. Am J Med. 1994; 96: 200-9.
- 9. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria

rationale available at that moment. It doesn't matter if Cardiology shall change the tightening of the bow due to any new concepts on the replacement of an insufficient aortic valve.

FN is now a prisoner of the behavior of a prosthesis, and is therefore subject to a change of opinion as regards the future of the prosthesis. The matters discussed at the time of his surgery and that may have influenced the decision and its acceptance may eventually be changed, with no prior notice to FN. Our considerations in this article reinforce the fact that as regards valve replacement, the real clinical facts about functional class III should count more than potential benefits envisaged during functional class II. Experiencing the medium and long term risks of having a bioprosthesis should have a meaning, should be warranted by the urgency of benefits.

FN's postoperative history is a continuum of his natural history. The change was essentially of a hemodynamic nature, that is, instead of an impaired valve, he now has a provisional bioprosthesis. This is why there are so many variables which are still unclear, and that preclude an accurate answer for the "how long...?" question.

As cardiologists have duties which are inherent to Cardiology and those that arise from the respect owed to the patient's individuality, guesswork using the "crystal ball of experience" is hazardous, delusions are inadmissible and arguments of evidence-based medicine might not apply. The postoperative period of a valve implant is slippery ground, and either the doctor or the patient may slip. In order for them to walk together, the cardiologist - the technician – should bear the humanization of Cardiology in mind. Then the answer to the "How long...?" question will hinge on a more important criterion, the class I level of evidence!

for the diagnosis of infective endocarditis. Clin Infect Dis. 2000; 30: 633-8.

- Grinberg M, Spina GS. Índice Valvar & Escore Valvar: Uma nova forma de comunicação do continuum da história natural da valvopatia. Arq Bras Cardiol. 2005; 84(2): 101.
- 11. Ross DN. Replacement of aortic and mitral valves with a pulmonary autograft. Lancet. 1967; 2: 956-8.
- Pomerantzeff PM, Brandão CM, Rossi EG, et al. Mitral valve repair. Quadrangular resection of the posterior leaflet in patients with myxomatous degeneration. Arq Bras Cardiol. 1999; 73: 273-80.
- 13. Bonow RO, Carabello B, de Leon Jr AC, et al. Guidelines for the management of patients with valvular heart disease: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients with Valvular Heart Disease). Circulation. 1998; 98: 1949-84.
- Pomerantzeff PM, Barbosa GV, Sousa Filho BS, et al. Diretrizes de cirurgia nas valvopatias. Arq Bras Cardiol. 2004; 82(Suppl 5): 22-33.
- 15. Ward C. A reappraisal of the clinical features in acute and chronic rheumatic heart disease: etiological implications. Am Heart J. 1979; 98: 298-305.
- Grinberg M, Cohen C. Falando com o coração: auscultando a bioética. Rev Soc Cardiol Estado de São Paulo. 2002; 6: 805-20.