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Risk-corrected impact of mechanical versus bioprosthetic valves on long-term mortality after aortic valve replacement

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Objective: Choice of a mechanical or biologic valve in aortic valve replacement remains controversial and rotates around different complications with different time-related incidence rates. Because serious complications will always "spill over" into mortality, our aim was to perform a meta-analysis on overall mortality after aortic valve replacement from series with a maximum follow-up of at least 10 years to determine the age- and risk factor-corrected impact of currently available mechanical versus stented bioprosthetic valves.

Methods: Following a formal study protocol, we performed a dedicated literature search of publications during 1989 to 2004 and included articles on adult aortic valve replacement with a mechanical or stented bioprosthetic valve if age, mortality statistics, and prevalences of well-known risk factors could be extracted. We used standard and robust regression analyses of the case series data with valve type as a fixed variable.

Results: We could include 32 articles with 15 mechanical and 23 biologic valve series totaling 17,439 patients and 101,819 patient-years. The mechanical and biologic valve series differed in regard to mean age (58 vs 69 years), mean follow-up (6.4 vs 5.3 years), coronary artery bypass grafting (16% vs 34%), endocarditis (7% vs 2%), and overall death rate (3.99 vs 6.33 %/patient-year). Mean age of the valve series was directly related to death rate with no interaction with valve type. Death rate corrected for age, New York Heart Association classes III and IV, aortic regurgitation, and coronary artery bypass grafting left valve type with no effect. Included articles that abided by current guidelines and compared a mechanical and biologic valve found no differences in rates of thromboembolism.

Conclusion: There was no difference in risk factor-corrected overall death rate between mechanical or bioprosthetic aortic valves irrespective of age. Choice of prosthetic valve should therefore not be rigorously based on age alone. Risk of bioprosthetic valve degeneration in young and middle-aged patients and in the elderly and old with a long life expectancy would be an important factor because risk of stroke may primarily be related to patient factors.

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Appendices E1 and E2, Table E1, and References E1 to E32 are available online.

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Choice of a prosthetic heart valve in aortic valve replacement (AVR) remains controversial. Current guidelines recommend a mechanical valve in patients aged less than 65 years, but this is based on class II evidence (conflicting evidence or opinion).[1] The only class I evidence is for choosing a mechanical valve in patients with an expected long life span,[1] which may be gaining increasing significance for 2 reasons. First, life expectancy is increasing in the general population in the industrialized world, for instance, to 17 years for a 65-year-old white man in the United States in 2002.[2] Second, life expectancy calculations in the general population include mortality from chronic debilitating or fatal diseases (eg, dementia and cancer), which are prevalent in the elderly and which contraindicate valve replacement. Even patients aged more than 70 years may achieve normal or longer than average life expectancy after AVR.[3-5] Long life spans may make

Abbreviations and Acronyms

AC	= anticoagulation
AVR	= aortic valve replacement
CL	= confidence limit
INR	= international normalized ratio
NYHA	= New York Heart Association
SD	= standard deviation
SVD	= structural valve degeneration

structural valve degeneration (SVD) of a bioprosthetic valve almost inevitable in the elderly.[5,6]

Recent years have nonetheless witnessed a shift in prosthetic heart valve preference from mechanical to biologic valves, which is not just explained by the increasing age of patients. Bioprosthetic valves are increasingly being implanted in younger patients[7] spurred by the belief that third-generation stented xenografts have superior durability compared with previous models.[E1] The risk of SVD accelerates with time (ie, requires long follow-up to become apparent) and is inversely related to age.[6] High SVD rates of earlier models implanted in younger patients through the 1970s and 1980s resulted in a high proportion of redo AVR causing the preference to swing back toward mechanical valves. Our knowledge base on SVD of third-generation xenografts is consequently based predominantly on valve series with too few young patients who underwent operation too late in the series to have an impact at the present time. Extrapolation from seemingly low rates of SVD in current relatively short "old age series" to younger patients may thus be in error.

Thromboembolism and anticoagulant-related bleeding remain the dominant complications of mechanical valves. The incidence rates of these complications seem to be fairly constant after AVR, but reported rates vary considerably especially for bioprosthetic valves including rates of zero or below the age-specific stroke rates of the background population.[6,8] Meta-analysis of published data taking both death and the main prosthesis-related complications into account to assess the benefits of mechanical versus biologic valves[9-11] may thus be misleading. Previous meta-analyses have, furthermore, included series with obsolete mechanical valves[9,10] and bioprosthetic valve series with follow-up of less than 10 years with related low SVD rates.[10,11] Finally, meta-analyses have been coupled with microsimulation, which is difficult to comprehend and for which the chosen modeling parameters may introduce bias.[9,11]

A death is an extremely well-defined event, and it would make common sense to postulate that a prosthetic valve complication entity that does not impact mortality of the patients is merely trivial, and none of them are. We therefore had as our primary aim to perform a meta-analysis on pertinent publications from 1989 to 2004 to determine the age-corrected impact of currently available mechanical (bileaflet and single disc) versus stented bioprosthetic (porcine and bovine pericardial) valves on crude mortality after AVR and to correct for the impact of other well-known risk factors using standard and robust regression analysis techniques. To minimize bias related to mortality of various complications with peculiar time effects, which may differ between mechanical and biologic valves, we chose to include only publications with a maximum follow-up of at least 10 years.

Materials and Methods

We followed a predetermined formal study protocol as suggested by methodologic guidelines for observational studies.[12] Our primary effect variable was overall death rate. We performed a dedicated literature search of MEDLINE using 2 search engines: PubMed of the US National Library of Medicine and the European EMBASE. We used a broad Boolean search string: "(aorta OR aortic) AND valve AND replacement AND (survival OR mortality OR death rate OR hazard rate)," thus avoiding exclusion terms that could cause articles of interest to be overlooked. We chose articles in English published between 1989 and 2004 because 10-year results with most currently available prosthetic heart valves did not appear earlier. PubMed and EMBASE yielded 2007 and 1954 hits, respectively, and these publications were scrutinized according to the criteria given below.

Inclusion and Exclusion Criteria and Essential Data Extraction

Articles were included if essential data (defined below) could be extracted from a pure mechanical or stented bioprosthetic AVR series with a longest follow-up of at least 10 years, with at least 75 patients and a maximum of 5% aged less than 15 years, and with currently available prosthetic valves. We accepted up to 10% obsolete valve types in mixed mechanical or biologic valve series and excluded articles in which the operative period started before 1975 to avoid time bias. We included only articles that claimed conformance to either the original[13] or current[14] guidelines for reporting (or that detailed comparable definitions and method of follow-up), had at most 5% of patients lost to follow-up,[13,14] and originated in the industrialized world (Appendix E1). To avoid confounding between case series by factors not related to AVR per se, we excluded series with prevalences of redo operations, concomitant surgery *other than coronary artery bypass grafting (CABG)*, and operation for active endocarditis of more than 20%. It was essential that we could extract the following data: (1) Death statistics: total number of deaths (early and late) of any cause and total follow-up (accumulated number of patient-years). (2) Demographic and operative data: mean age of the patients with standard deviation or range; prevalence of women, concomitant CABG, concomitant other procedures, redo operation, and operation for active endocarditis. (3) A measure of disease severity: We chose New York Heart Association (NYHA) functional classes because they are usually reported. Other "disease severity" variables including left ventricular function and comorbidities could only be extracted from a fraction of the included articles (Appendix E1).