Clinical decision making in elderly with aortic stenosis
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Chapter 8

Summary and interpretation of the findings.
This thesis focuses on clinical decision making in elderly patients with aortic valve stenosis.

Aortic valve replacement (AVR) is the only possible treatment of patients with symptomatic aortic stenosis. This procedure in elderly patients was first performed in the late seventies on a limited scale (1). The past two decades it has become an established treatment and various reports has been published in the literature since. In Chapter 2 we showed the results of a systematic review of the literature on aortic valve replacement in elderly patients. Operative mortality was 5.1% in studies reporting on patients over 70 years. The operative mortality was more than twice as high in studies reporting on patients over 80 years (12.1%). A similar finding was made with the combined procedure of aortic valve replacement and coronary bypass grafting where operative mortality was 9.8% in studies on 70 years and older and 12.4% in studies on 80 years and older. The association of clinical variables with operative mortality was reported only in seven studies. Some included perioperative and postoperative variables in the analysis illustrating that the procedure and not the patient was their main interest. Heart failure, urgent procedure and postoperative infection were reported in several studies as determinants of mortality. Common early complications were atrial fibrillation (43%) and low cardiac output (27%). Other, less frequent complications were stroke (5.4%), myocardial infarction (2.1%), renal failure (5.5%), bleeding (5.1%) and tamponade (5.9%). The one and five year survival after isolated AVR was 86.5 and 66.4% and for the combined procedure 80.5 and 62.6%. Only a limited number of studies reported on the multivariate association of clinical variables and late mortality. An urgent operation, heart failure and male gender were found in more then one study to be a determinant of late mortality. Late complications as thrombo-embolism, endocarditis and major bleeding had a very low frequency (< 0.8% per year). These pooled data support are the clinician estimating operative risk with the available data.

Patients with a symptomatic aortic stenosis should be operated according to current guidelines (2). In all reports in the literature on the success of aortic valve
replacement we find the results of a procedure performed in a highly selected population. The writers do not consider the patients who did not have surgery, and they did not measure the difference in outcome between surgical and medical treatment. A randomized clinical trial would be the superior way to evaluate the efficacy of surgical treatment in elderly patient with aortic stenosis. Unfortunately this has never been performed. In Chapter 3 we report the difference in outcome between medically and surgically treated elderly patients with aortic stenosis. We used a patient cohort, over 70 years of age with a first time diagnosis of severe aortic stenosis and without major additional morbidity from three academic hospitals (AZM, AZG, AMC) in the Netherlands. Multivariate analysis showed that only patients with a high baseline risk, mainly determined by an impaired left ventricular function, had a significantly better three year survival with surgical treatment than with medical treatment. Moreover we showed that only 59% of the patients who should have had valve replacement according to the guidelines were actually offered surgery. These findings indicate that elderly patients are under treated. Physicians should be aware of that phenomenon.

In elderly patients clinical decision making is often complicated by the additional morbidity (3). The concurrent illnesses reduce the benefit of aortic valve replacement for symptomatic aortic stenosis. In these patients the life expectancy, already limited because of the advanced age, is further reduced by and the operative mortality increased by the additional morbidity. In Chapter 4 we presented the benefit of surgical treatment over conservative treatment in 16 different profiles of elderly patients with aortic stenosis. We showed that decision making is a complex process because it is influenced by 14 different clinical variables. With multivariate analysis we developed patients profiles, based on age, degree of aortic stenosis, cardiac and additional morbidity. The seven year predicted survival ranged from 6.9% to 83 % in surgically treated patients, and from 0.6% to 48% in conservatively treated patients. The benefit of surgical treatment over conservative treatment was the greatest in patients under 80 years, with a more critical aortic stenosis, cardiac morbidity, and without additional morbidity. Minimal benefit was seen in patient over 80 years, with a
less critical aortic stenosis without cardiac morbidity (as defined). These findings provide a support for clinical decision making in elderly patients with aortic stenosis.

Elderly patients with symptomatic aortic stenosis have the particular problem of concomitant diseases. The available evidence on surgical and medical treatment in these patients is limited. Current guidelines advise surgery in symptomatic patients, but as outlined before, these recommendations underestimate many aspects of clinical decision making. In Chapter 5 we showed that there are systematic differences among groups of cardiologists in their inclination to advise surgical treatment for elderly patients with symptomatic aortic stenosis, as well as in the way their advice was influenced by the clinical characteristics of these patients. In a nation-wide postal survey we investigated the advice that Dutch cardiologists would give to elderly patients with aortic stenosis. We found a wide variability in their advice for the individual case vignettes. We detected four main practice styles: 41% of the cardiologists were age-oriented decision makers, 24% were multivariate decision makers (influenced equally by age and by the severity of the stenosis and the impairment of left ventricular function), 23% were left ventricular function-oriented decision makers, and 12% were valve area-oriented decision makers. The age-oriented decision maker group and the multivariate decision maker group could each be split up into a group with a high and a low average inclination to advise surgery. A comparison of the background characteristics among these six groups of cardiologists showed small differences in age, time since accreditation, and hospital type. These findings indicate that the treatment of elderly patients with aortic valve stenosis is mainly based on habits and adapted policies rather than on clinical evidence. The variation in treatment advices also indicates that the treatment an elderly patient with aortic valve stenosis receives highly depends on the type physician he'll meet.

Increasingly, studies are being published that use series of case simulations (mostly in the form of written case simulations) to investigate in a systematic and
quantitative way how clinicians respond to specific characteristics of their patients when making clinical decisions. These written case simulations are easily self-administered, and data collection for large-scale studies is therefore relatively inexpensive. Full control of potentially confounding factors can be achieved by having each participant evaluate the same cases. Sophisticated factorial design and advanced statistical segmentation techniques, mostly developed in marketing research, provide an efficient way to investigate the differences among clinicians in the determinants of their decisions. We compared (Chapter 6) the treatment advices of 34 cardiologists (from three different hospitals) on written case simulations describing elderly with a severe aortic stenosis with the outcome of 147 actual elderly patients with symptomatic aortic stenosis treated in the same hospitals. We showed that in risky therapeutic decisions there is a strong agreement in the way clinicians respond to the clinical characteristics of the written case simulations and the actual patients. We also show that written case simulations can identify the patients who will be advised surgical treatment. However, the overall frequency of aortic valve replacement observed in actual patients, tended to be much lower than that of advice in favour of surgery for the written case simulations. Other differences between the actual patients and written case simulations concerned the stronger influence of the aortic valve area and sex in actual patients, as well as (but to a lesser extent) the presence of pulmonary disease. These findings emphasize that written case simulations, developed with a sophisticated conjoint analysis design, are a valuable tool to study clinical decision making.

Patients referred for coronary bypass grafting who have a mild to moderate aortic stenosis are often the subject a heated debate. Should the bypass grafting procedure be extended with an aortic valve replacement? Key point of discussion is the expected progression rate of the aortic stenosis. Data on the determinants of progression rate can further enhance the estimation of the progression. In Chapter 7 we have shown that the reported progression of aortic stenosis varies widely among and within studies. The rates vary from 0.04 to 0.16 cm²/year. We also showed that of the 25 in the literature reported clinical and echocardiographic
variables with a supposed association with progression rate only use of statins, renal failure or dialysis and initial aortic valve are reported in more than one study. Current smoking is also reported to have an association with progression rate of aortic stenosis in more than one study, but for the number of patients in the negative studies exceeds the number of patients in the positive studies. This limits the robustness of this association. All these different outcomes in studies do not result in a simplification of clinical decision making. A pooled analysis with individual patient data in the future might allow better predictions for individual patients.

Clinical problem

Among cardiologists in the Netherlands there is no consensus about the treatment advice to the 72 year old male in the introduction. Nine percent of all cardiologist indicated that they certainly would advise surgery, while 14% indicated that they certainly would not advise surgery. At other cardiologists, 77%, were uncertain about what to do. Several other cases in our survey showed similar large variations in treatment advice. Moreover, there was a large variation in the clinical variables used in the decision process.

The patient from the example was a symptomatic male with dyspnoea and a critical aortic stenosis with a valve area of 0.6 cm$^2$. His left ventricular function was severely impaired, but he had no coronary artery disease. His additional morbidity was a stroke with a slight paresis and an impaired renal function.

The average life expectancy for a 72 year old male in the Netherlands is over ten years. In Chapter 3 the life expectancy of conservative treatment in patients without severe additional morbidity is described. This life expectancy in these patients is mainly determined by the severely impaired left ventricular function. The 2 years survival rate is around 40%. This estimation is rather optimistic for this specific patient because the severe renal dysfunction will accelerate dramatically the progression of the aortic stenosis (Chapter 7).
Moreover, the additional morbidity, renal dysfunction and stroke will further decrease this estimation.

Also the surgical mortality and morbidity are high. In Chapter 2 we showed that the operative mortality for an isolated aortic valve replacement is around 4.5%. The patient had a severely impaired left ventricular function, an important determinants of operative mortality (odds ratio 3). Although in our systematic review renal failure and stroke were not identified as determinants of mortality, it might be clinically reasonable to consider them as determinants analogue to CABG surgery. Both diseases had quit a low prevalence in the different studies, on average 10% for stroke and 13% for renal failure. Moreover most studies were underpowered; only four studies with more then 200 patients reported on stroke and impaired renal function.

To estimate the late survival we obtain data from the systematic review. The average 5 year survival was around 60%, far more than the estimation after conservative treatment. Although, the determinants of impaired survival are male, heart failure/NYHA III/poor left ventricular function, and renal impairment.

From Chapter 4 we can estimate the benefit of aortic valve replacement stratified for degree of aortic valve stenosis, age, cardiac morbidity (figure 1B). The predicted 2 year survival in patients between 70 and 80 years with a critical aortic stenosis and with cardiac and non-cardiac morbidity I with conservative treatment is around 40%. After surgical therapy the predicted 2 years survival is around 80%.

We can conclude from the above data that a 72 year male has a very poor prognosis with conservative treatment. The expected survival after successful surgery is dramatically better despite the substantially increased operative mortality. These conclusions are confirmed by the prediction models which illustrate an important benefit of surgery over conservative treatment. In our opinion based, based on the available data, the 72 year old male patient should undergo aortic valve replacement to improve his prognosis.

Future perspectives
Aortic valve replacement in the elderly patient with additional morbidity is an indication with much uncertainty. In the past years aortic valve replacement itself has been the central issue in clinical research. It has been proved that aortic valve replacement can be performed in selected patients with acceptable risks of mortality and morbidity. Data about determinants of mortality and morbidity is, although sometimes scarcely, available. The selection of patients in the surgical studies and the lack of data on conservative studies hamper the extrapolation of these data necessary to determine the outcome of all paths in the clinical decision making. To improve the treatment of elderly patients with aortic stenosis future studies should focus on the follow up after the diagnosis of aortic stenosis. They should include medical and surgical treated elderly patients in order to gain knowledge on the benefits of valve replacement. Recently developed laboratory tests (4) and clinical models on new or pooled data might be helpful.
References


