A clinical decision model for selecting the most appropriate therapy for uncomplicated chronic dissections of the descending aorta

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Objective: The optimal treatment for patients with uncomplicated chronic Stanford type B aortic dissections (chTBADs) is still matter of debate. The purpose of this study was to design a decision tool to guide the surgeon in determining the preferred treatment option.

Methods: A Markov decision-analysis model compared chTBAD patients treated with initial open surgical repair (OSR), thoracic endovascular aortic repair (TEVAR), and optimal medical therapy (OMT), followed during follow-up by OSR (OMT-OSR) or TEVAR (OMT-TEVAR), if indicated. Procedural risks, aortic growth and rupture rates, outcomes, and quality of life values were derived from the best available evidence in the literature. A chTBAD treatment strategy decision tool was developed, including the four key variables of age, sex, surgical risk, and maximum initial aortic diameter. Primary outcome was quality-adjusted life-years (QALYs).

Results: For the reference patient cohort, 55-year-old men with chTBAD with a maximum aortic diameter of 5.0 cm, medium risk for surgery, and a threshold for surgery of 6.0 cm during follow-up, OSR yielded higher QALYs, with 10.06 QALYs (95% credibility interval [CI], 9.52-10.56 QALYs) vs 9.92 QALYs (95% CI, 9.23-10.58 QALYs) after TEVAR and 9.64 QALYs (95% CI, 9.38-9.88 QALYs) and 9.40 QALYs (95% CI, 9.11-9.69 QALYs) for OMT-OSR and OMT-TEVAR. The difference between OSR and OMT-OSR was 0.42 QALYs (95% CI, 0.01-0.81 QALYs) and between TEVAR and OMT-TEVAR was 0.52 QALYs (95% CI, 0.04-0.68 QALYs). This showed that intervention is preferred over OMT. A change of the four variables resulted in a change of preferred treatment. In general, OSR was the preferred treatment in younger patients with a larger aortic diameter and in low-risk patients. TEVAR was preferred in elderly patients with large aortic diameter and if the aortic diameter threshold for repair decreased. OMT was the optimal therapy in high-risk patients, elderly patients, or in patients with small aortic diameters.

Conclusions: This decision-analysis model shows that there is no "one-size-fits-all" treatment for uncomplicated chTBADs. For the reference patient cohort, intervention is preferred over OMT. Age is the most important deciding factor, followed by initial aortic diameter. Immediate OSR is the preferred treatment option in younger patients with a large initial aortic diameter and in low-risk patients. Immediate TEVAR is preferred in elderly patients with a large initial aortic diameter and in patients with a lower threshold for OSR. OMT should be considered in high-risk patients, in patients with small initial aortic diameters, and in patients aged >80 years, unless their initial aortic diameter is >5.5 cm. However, the differences in some patient groups are clinically insignificant, allowing a major role for patient preferences and hospital-specific considerations. This clinical decision model may guide chTBAD treatment. (J Vasc Surg 2014;60:20-30.)

Aortic dissection is a potentially fatal condition with a mortality rate of up to 30%.[1] Aortic dissections are usually arbitrarily classified after 14 days of symptoms as chronic dissections. Stanford type B dissections are defined as "limited to the descending aorta, and the intimal tear is usually within 2 to 5 cm of the left subclavian artery."[2]

The optimal treatment option for patients with an uncomplicated chronic type B aortic dissection (chTBAD) is controversial. Where the original debate had two positions, optimal medical therapy (OMT) with β-blockers[3] and traditional open surgical repair (OSR),[4] a third treatment strategy, thoracic endovascular aortic repair (TEVAR), has been increasingly used during the last 2 decades. Good short-term results have been observed, with relatively low perioperative morbidity and mortality.[5-7] However, the reintervention rates after TEVAR are higher compared with traditional OSR, and aortic rupture occurs in ∼1.5% of patients after TEVAR during their remaining lifetime.[8]

Unfortunately, no single treatment strategy is clearly preferential, and level 1 evidence regarding treatment-specific outcomes is lacking. The Investigation of Stent

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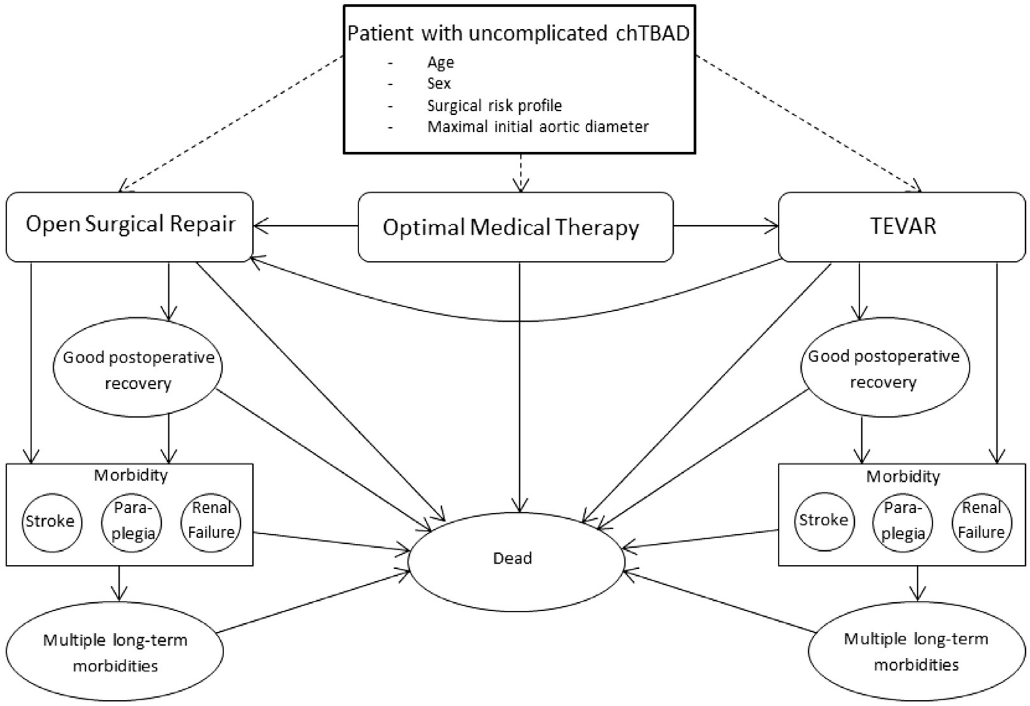

Fig 1. Simplified bubble diagram shows interaction between health states for treatment of chronic type B aortic dissection (*chTBAD*). Each health state has a possible transition to itself, which is not shown in this figure for clarity. *TEVAR,* Thoracic endovascular aortic repair.

Grafts in Aortic Dissection (INSTEAD) trial was the first randomized study to compare TEVAR, followed by OMT vs OMT only, in patients with uncomplicated chTBADs. This study showed no significant difference in rupture, survival, or reintervention after 2 years of follow-up.[9]

The primary goal of this study was to assess the effect of TEVAR, OSR, and OMT on the quality-adjusted life-years (QALYs) for specific groups of patients with uncomplicated chTBADs with a decision-analysis model, synthesizing the best available evidence from the scientific literature. The secondary objective was to provide a treatment strategy decision tool for the surgeon, based on four patient characteristics: age, sex, initial aortic diameter, and surgical risk profile.

METHODS

Model and assumptions. A Markov cohort model was developed to simulate hypothetical cohorts of patients with chTBADs suitable for OSR and TEVAR, using TreeAge Pro 2012 software (TreeAge Inc, Williamstown, Mass). A Markov model provides a convenient way of modeling the prognosis for clinical problems with ongoing risk. The model assumes that the patient is always in one of a finite number of health states. All events are modeled as transitions from one health state to another. Each state is assigned a utility, a quality of life (QOL) value, and the contribution of this QOL value to the overall outcome depends on the length of time spent in the health state.[10]

Because of differences in natural history, patients with connective tissue disorders, such as Marfan syndrome, Loeys-Dietz syndrome, and Ehlers-Danlos syndrome, among others, were not considered. Four different treatment options were evaluated in this model: (1) immediate elective OSR or (2) TEVAR, (3) OMT followed by OSR (OMT-OSR), or (4) OMT followed by TEVAR (OMT-TEVAR), if required for later complications. Indications for intervention after OMT included an aorta diameter of 6.0 cm during follow-up, emergency repair for aortic rupture, or other dissection-related complications requiring intervention. In addition, treatment strategies were examined for use of different aortic diameter thresholds for surgery during follow-up after OMT, including thresholds of 5.5 cm and 6.5 cm.[11]

For the Markov decision-analysis model, several different health states were defined for the four different treatment strategies of chTBAD. The transitions between the health states are shown in a simplified bubble-diagram in Fig 1. The model cycled in 1-year cycles, and transitions between the health states were based on probabilities derived from an extensive search in the literature (Table I). A discount rate of 3% per year was used to discount future effectiveness.[12]

Patients in the first treatment group, immediate elective OSR, could start in five different initial health states

Table I. Reference case probabilities and ranges for transitions to health states

Variables	*Reference case*	*Range*	*References*
OSR			
Technical success, %	95	90-100	4,21-24
Perioperative mortality rate, %	9.6	5.0-15	4,21-24
Perioperative complications OSR, %[a]	23	15-25	4,21-24
Stroke, %	5.8	3.0-7.0	4,21-24
Paraplegia, %	4.8	3.0-6.0	4,21-24
Renal failure, %	0.9	0.5-3.0	4,21-24
Other complications, %	11.5	5.0-15	4,21-24
Aortic complications, %[b]	2.1	1.0-5.0	4,21-24
Mortality after aortic complications, %	4.2	3.0-6.0	4,21-24
Need for reintervention, %	4.1	3.0-15	4,21-24
Rupture after OSR, %	0.2	0.1-1.5	4,21-24
Mortality after rupture, %	50	20-80	20
Perioperative mortality emergency intervention, %	19.8	15-25	4,21-24
TEVAR			
Technical success, %	89.9	85-98	5,7-9,25-30
Immediate conversion to OSR, %	0.4	0.0-1.0	6,8-10,12,32-36
Perioperative mortality rate, %	3.2	1.0-10	5,7-9,25-30
Perioperative complications TEVAR, %[a]	19	15-25	5,7-9,25-30
Stroke, %	4.3	3.0-6.0	5,7-9,25-30
Paraplegia, %	0.8	0.5-3.0	5,7-9,25-30
Renal failure, %	2.6	1.5-4.0	5,7-9,25-30
Other minor complications, %	11.3	5.0-15	5,7-9,25-30
Aortic complications, %[b]	6.2	3.0-10	5,7-9,25-30
Mortality after aortic complications, %	5.1	3.0-7.0	5,7-9,25-30
Need for reintervention, %	14.3	10-25	5,7-9,25-30
Rupture after endovascular repair, %	1.2	0.5-4.0	5,7-9,25-30
Mortality after rupture, %	50	20-80	20
Perioperative mortality emergency intervention, %	19.8	15-25	5,7-9,25-30
OMT, %			
Mean growth male, mm/y	1.2	0.0-2.5	31-34
Mean growth female, mm/y	3.3	0.0-4.5	31-34
Average yearly rupture rate			
3.5-3.9 cm, %	0.1	0.05-0.3	32,34
4.0-4.9 cm, %	0.8	0.5-2.0	32,34
5.0-5.9 cm, %	1.9	1.0-5.0	32,34
≥6.0 cm, %	3.7	2.0-10	32,34
Average yearly dissection rate[c]			
3.5-3.9 cm, %	2.2	1.5-3.0	32,34
4.0-4.9 cm, %	2.0	1.5-3.0	32,34
5.0-5.9 cm, %	2.9	2.0-5.0	32,34
≥6.0 cm, %	3.9	2.5-10	32,34
General variables			
SMR rate for chTBAD	Life-table	...[d]	14,24
Males	×1.97		
Females	×2.83		
Excess mortality rate for chTBAD plus morbidity	Life-table	...[d]	14
Stroke,	×3.62		16
Renal failure	×3.2		17
Paraplegia	×4.9		18
Discount rate, %	3	0-5	12

chTBAD, Chronic type B aortic dissection; *OMT,* optimal medical therapy; *OSR,* open surgical repair; *SMR,* standardized mortality rate; *TEVAR,* thoracic endovascular aortic repair.
[a]Perioperative mortality defined as 30-day mortality.
[b]Aortic complications included extended or retrograde dissections, false aneurysms, and endoleaks.
[c]Dissection extension causing problems (eg, malperfusion).
[d]No range for standardized mortality rates and excess mortality of comorbidities was used.

after the initial intervention: "good postoperative recovery after OSR," "stroke after OSR," "paraplegia after OSR," "renal failure after OSR" and "dead." Stroke, paraplegia, and renal failure were chosen because these are clinically the most relevant long-term morbidities after chTBAD repair.[13] Almost all of the OSR cases were performed by direct aortic repair with posterolateral thoracotomy.

Patients in the "good postoperative" state could remain well without complications or could develop aortic or dissection-related complications such as rupture, expanding dissection, recurrent pain, or false aneurysms. These patients could die of these complications, or stay alive. If they survived these acute complications, an emergency reintervention was required. Patients could subsequently recover well, die of the reintervention, or develop long-term morbidity. The same options were possible for the patients in the "stroke," "paraplegia," and "renal failure" health states. However, we assumed that if a patient in one of these health-states sustained another complication that led to long-term morbidity, they transitioned to another health state: "multiple long-term morbidities." Once in this health state, the health of the patient was decreased to a minimum, and we assumed that a third long-term morbidity or complication would be equivalent to death.

For the patients in the TEVAR treatment group, the model structure was comparable with the OSR treatment group, although there were some differences; for example, patients could develop an endoleak or retrograde dissection. In addition, different probabilities for transitions between the different health states (eg, risks of complications, aortic rupture rates) were used for the TEVAR treatment group compared with the OSR treatment group. Patients in the TEVAR and OSR group received computed tomography follow-up every year.

Patients who started in the two conservative treatment groups received OMT, with computed tomography follow-up every 6 months. Once the patient developed dissection-related complications (rupture, extended dissection, endoleak) or when the aortic diameter reached the threshold for surgery according to the size criteria, they required an emergency or elective intervention, respectively. Risk for dissection-related complications depended on the size of the aorta (Table I). Higher procedural risks were used for emergency repair compared with elective repair, as reported in the literature. A patient who underwent OSR or TEVAR moved to the health states of the OSR and TEVAR treatment group, as described above.

Mortality rates for men and women were obtained from the Centers for Disease Control and Prevention Mortality File.[14] To adjust mortality for the chTBAD, the patients were subjected to excess mortality for presence of chTBAD, independent of the treatment group. The excess mortality was modeled higher in women than for men because female sex is an important risk factor for long-term mortality in patients with vascular disease.[15] Patients with long-term morbidities (stroke, renal failure, and paraplegia) were subjected to a higher excess mortality due to their reduced life expectancy.[16-18]

To perform an analysis for low-risk, medium-risk, and high-risk patients, mortality rates and perioperative mortality risk were adjusted by using a relative risk (RR). Risk profiles included low risk (RR, 0.5), medium risk (RR, 1), and high risk (RR, 2). For example, a low-risk patient (RR, 0.5) had 50% less risk of death after both OSR and TEVAR in elective and emergency settings compared with the average risks for each of these situations. Furthermore, the complication rate was similarly adjusted with the RR. The RR was tested over a wide range (0.5-5).

OSR, TEVAR, and OMT. An extensive search was performed using the MEDLINE database with a language filter for English articles. The only articles that were considered eligible were those that described perioperative morbidity and mortality for elective and emergency interventions, acute and long-term complications, technical success, rupture, dissection and reintervention rates, growth rates, rupture and dissection rates, and importance of initial size of the aortic diameter of the descending aorta performed with OSR or TEVAR. Furthermore, studies were considered eligible if they (1) contained original data and (2) were comparative studies, large single-treatment studies (>10 patients), or described conservative management of chTBADs.

All articles were subjected to critical appraisal as recommended by the Oxford Centre for Evidence Based Medicine.[19] The references of these articles were screened for any missing relevant articles. Outcomes retrieved from the 20 remaining articles were examined, evaluated for consistency, and integrated into a weighted mean. Furthermore, differences in natural course of the disease regarding aortic growth and mortality rates for men and women were determined to make the model specific for unique patient situations. The reference case characteristics were equal to the characteristics of patient data retrieved from literature. All the rates, risks, and probabilities were converted into annual probabilities and are reported in Table I.[4-8,20-34]

QOL and interventions. To calculate the expected QALYs, the number of cycles spent in each health state was multiplied by the QOL value for the specific health states. A slightly higher QOL was used for patients who underwent repair than for patients treated with OMT based on documented evidence in the literature.[35,36] The QOL values for patients with long-term morbidities (stroke, paraplegia, and renal failure) were reduced according to evidence from the literature regarding those specific morbidities.[37-39] For the interventions, disutilities or "tolls" were included. These disutilities were applied every time an intervention was required and were based on the average recovery time for these interventions (Table II). A wide range for all the QOL values was used to explore the effect of the assumptions.

Data analysis. The reference case was a hypothetical cohort of 55-year-old men with an uncomplicated chTBAD with an initial aortic diameter of 5.0 cm and medium risk for perioperative death. For patients undergoing OMT, a threshold for intervention during follow-up was a maximum aortic diameter >6.0 cm (Table III).

Consistent with decision-modeling practice, the treatment with the highest QALYs was considered the preferred treatment option for patients with chTBADs. A difference between two treatment strategies of <0.1 QALY, comparable with <1.5 months in perfect health, was considered to be clinically meaningless. After the reference case analysis, deterministic one-way, two-way, and three-way sensitivity

Table II. Quality of life (*QOL*) values and disutilities for interventions

Health state or intervention	*QOL value*	*Range tested*	*Reference*
Good postoperative recovery	0.95	0.90-1.00	[36]
Conservative treated chTBAD	0.93	0.90-1.00	[36]
Renal failure	0.49	0.40-0.55	[37]
Stroke	0.47	0.40-0.55	[38]
Paraplegia	0.45	0.40-0.55	[39]
Multiple morbidities[a]	0.20	0.10-0.30	Assumption
Dead	0.00		
OSR	−0.12	−0.15 to −0.09	Assumption
TEVAR	−0.05	−0.08 to −0.02	Assumption
Acute complication	−0.04	−0.06 to −0.02	Assumption

chTBAD, Chronic type B aortic dissection; *OSR,* open surgical repair; *TEVAR,* thoracic endovascular aortic repair.
[a]Combination of two of the following comorbidities: stroke, renal failure or paraplegia.

Table III. Input variables for reference-case patient

Parameter	*Reference case*	*Range*
Sex	Male	Male/female
Age, years	55	50-100
Surgical risk category	Medium	Low-high
Initial aortic diameter, cm	5.0	3.5-6.5
Threshold for intervention, cm	≥6.0	5.5-6.5

analyses were performed to assess the influence of different patient and procedural characteristics.

A probabilistic sensitivity analysis was performed using 10,000 random samples to assess the uncertainty around the variable values using distributions of the values rather than deterministic values. Probabilistic sensitivity analysis can test the robustness of the results of a model in the presence of uncertainty and can also test the preferred treatment based on the frequency of the selection show the preferred treatment. Credibility intervals (CIs) in Bayesian approaches are analogous to confidence intervals in frequentist statistics. Finally, a clinical decision tool for treatment of chTBADs was created as a chart based on four patient characteristics: age, sex, maximum initial aortic diameter, and low risk, medium risk, and high risk for surgery.

RESULTS

Reference-case. The reference case was simulated in 10,000 patients. OSR was the preferred treatment in 87% of the samples for a 55-year-old man with an uncomplicated chTBAD and medium risk for perioperative mortality. The results of the analysis showed that this would result in 10.06 QALYs (95% CI, 9.52-10.56 QALYs) after OSR, followed by 9.92 QALYS (95% CI, 9.23-10.58 QALYs) after TEVAR, which is similar to a difference of 2 months in full health (95% CI, −0.21 to −0.47). OMT appeared to be less desirable for these patients, with 9.64 QALYS

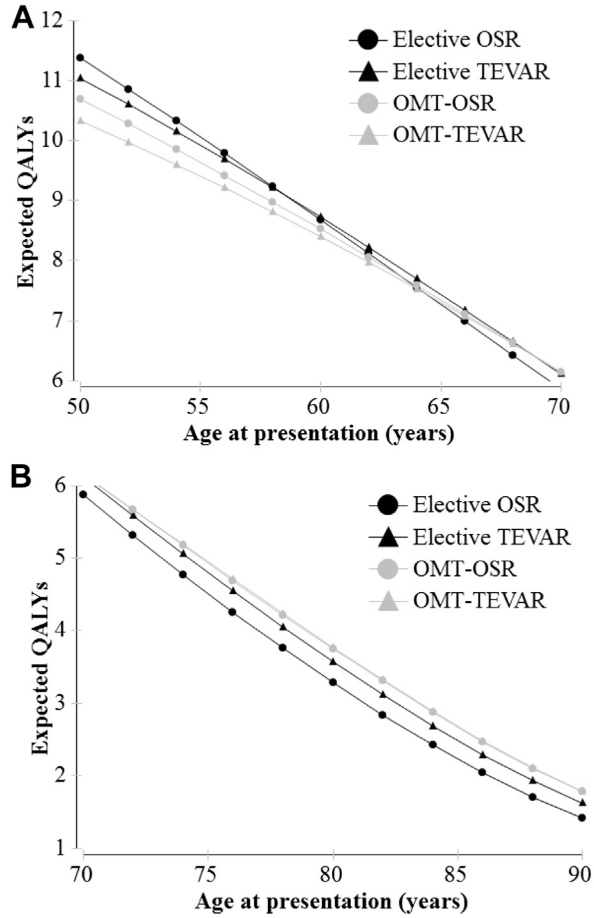

Fig 2. Total expected quality-adjusted life-years (*QALYs*) at age of presentation of **(A)** 50 to 70 years and **(B)** 70 to 90 years. Thresholds indicate change in preferred treatment strategy: open surgical repair (*OSR*), ≤60 years; thoracic endovascular aortic repair (*TEVAR*), 60 to ≤70 years; and optimal medical therapy (*OMT*) >70 years. OMT followed by TEVAR (*OMT-TEVAR*) and OMT followed by OSR (*OMT-OSR*) are exactly equal in panel **(B)**.

(95% CI, 9.38-9.88 QALYS) for OMT-OSR, a difference of 0.42 QALYs (95% CI, 0.01-0.81 QALYS), comparable with 5.5 months in perfect health, and 9.40 QALYs (95% CI, 9.11-9.69 QALYS) for OMT-TEVAR, a difference of 0.66 QALYs (95% CI, 0.17-1.12 QALYS) and comparable with 8 months in perfect health.

Age. Age at the time of the decision was an important factor in determining the optimal treatment strategy (Fig 2, *A* and *B*). OSR is the preferred treatment until the age of 60 years, TEVAR is preferred for patients between 60 and 70 years, and OMT should be considered after the age of 70 years for patients with medium perioperative mortality risks. The difference between OMT-OSR and OMT-TEVAR was ≤0.01 QALY along the entire range when patients were age ≥70 years. However, OMT as the initial treatment strategy in patients ≥70 years resulted in QALYs comparable with an additional 2.5 months in full health compared with TEVAR and nearly 6 months compared with initial OSR. Overall, age was the most important determinant for optimizing treatment decisions because it most frequently caused a change in preferred treatment strategy, although the choice was also dependent on sex, health of the patient, and initial maximum aortic diameter. The interaction between these four variables and the preferred treatment strategy for these patients is shown in Fig 3.

Sex. For 55-year-old women, all other variables being equal, OSR would yield higher QALYs (9.05 [95% CI, 8.61-9.45] QALYs) compared with TEVAR (8.94 [95% CI, 8.40-9.34] QALYs). The difference between OSR and TEVAR was 0.11 QALYs (95% CI, −0.19 to −0.41 QALYs), and therefore, this was a nonsignificant difference. Treating women with conservative management would diminish their life expectancy in full health by almost 1 year: OMT-TEVAR, 8.30 QALYs (95% CI, 8.04-8.56 QALYs), and OMT-OSR, 8.02 QALYs (95% CI, 7.71-8.32 QALYs). Compared with men, women generally have 1.0 QALY less to live at the moment of the treatment decision for chTBAD, mainly due to the higher excess mortality associated with chTBAD in women.

Perioperative mortality risk. Sensitivity analysis of different categories of perioperative mortality risks in the same reference-case patient showed that initial TEVAR had the highest expected QALYs if the RR for perioperative mortality was increased to 1.67. The benefit of TEVAR compared with OSR increased with higher RRs (Fig 4). For 75-year-old male patients, OMT was the optimal treatment strategy for all categories, including patients with low perioperative mortality risks.

Maximum initial aortic diameter and threshold for surgery. Size of the initial aortic diameter was an important predictor of rupture and dissection. Therefore, a sensitivity analysis was performed on the initial maximum aortic diameter. Overall, patients with larger initial aortic diameters had more benefit from immediate intervention than patients with smaller aortic diameters. The effect of initial aortic diameter on optimal treatment strategy was supported by the outcomes for the range of maximum aortic diameter thresholds for intervention that we evaluated in the analysis (range, 3.5-6.5 cm). A patient with an initial aortic diameter of 3.5 cm can expect 1.1 and 0.8 additional QALYs with initial OMT compared with immediate repair at the ages of 55 and 70 years, respectively. In contrast, patients with a very large initial aortic diameter (6.5 cm) should always be operated on immediately, which leads to an expected gain in QALYs of 1.1 (age, 55 years) and 0.7 (age, 70 years) compared with OMT (Fig 5). The outcomes for five different patient groups are reported in Table IV.

DISCUSSION

The current article presents a decision-analysis model that showed that there is no "one-size-fits-all" treatment for uncomplicated chTBADs. Choice of optimal treatment strategy depends on several important factors, including age, sex, maximum aortic diameter, and perioperative mortality risks. Overall, the model showed that very old patients (≥80 years) should receive OMT, unless the initial aortic diameter is >5.5 cm. Younger patients benefit more from immediate intervention, and particularly, the perioperative mortality risks (low risk, medium risk, or high risk) determine if OSR or TEVAR would be preferred.

The Society for Vascular Surgery/American Association for Vascular Surgery medical comorbidity grading system can be used to categorize patients into the different risk profiles. Initial aortic diameters of ≤3.5 cm should generally be managed with OMT, independent of age of the patient. Interestingly, female patients benefit more from immediate interventions than male patients. This benefit is mainly due to the higher aortic growth rate in female patients, whereby women reach the threshold for intervention earlier than men do. Although this decision model can provide more insight in the preferred treatment for patients with chTBADs, several combinations of these variables give a difference in treatment strategies of <2 months, and patient preference should play a major role in treatment decisions.

Decision analysis is an elegant method to study diseases that involve different health states, can progress, and transition requiring treatment or interventions. The strength of decision models is that one can perform a probabilistic sensitivity analysis by using a wide range of the variables instead of one fixed number, which is particularly useful in problems with uncertainty around the variables. Limitation of most of the clinical studies is that these studies mostly focus on one or two main outcomes such as overall survival or adverse events. Although these are certainly highly important outcomes, one must not only focus on survival and adverse events. Other important factors, such as QOL for long-term morbidities, rupture, and dissection risks after >5 years, and the risk-profile of the patient should also be taken into account. These data are lacking in most of these articles, although these results could highly affect the decision of treatment for a patient with a chTBAD.

This decision-analysis model considers all clinically relevant basic patient characteristics that should be taken into account before contemplating a decision about the treatment. First, we assessed the variables that mostly influenced the decision: age, sex, perioperative mortality risks, initial maximum aortic diameter, and size criteria for intervention during follow-up if OMT would initially be selected (threshold of 6.0 cm). The latter is not a fixed variable but a choice based on general consensus in current clinical practice. Subsequently, we selected subgroups and performed analyses for all of these subgroups. The outcomes in this model are fairly logical and compatible with consensus that intervention should be avoided for small maximum initial aortic diameters and old patients, whereas interventions are more beneficial for larger maximum initial aortic diameters and younger patients. One of the goals of this study was to create a treatment strategy decision tool in

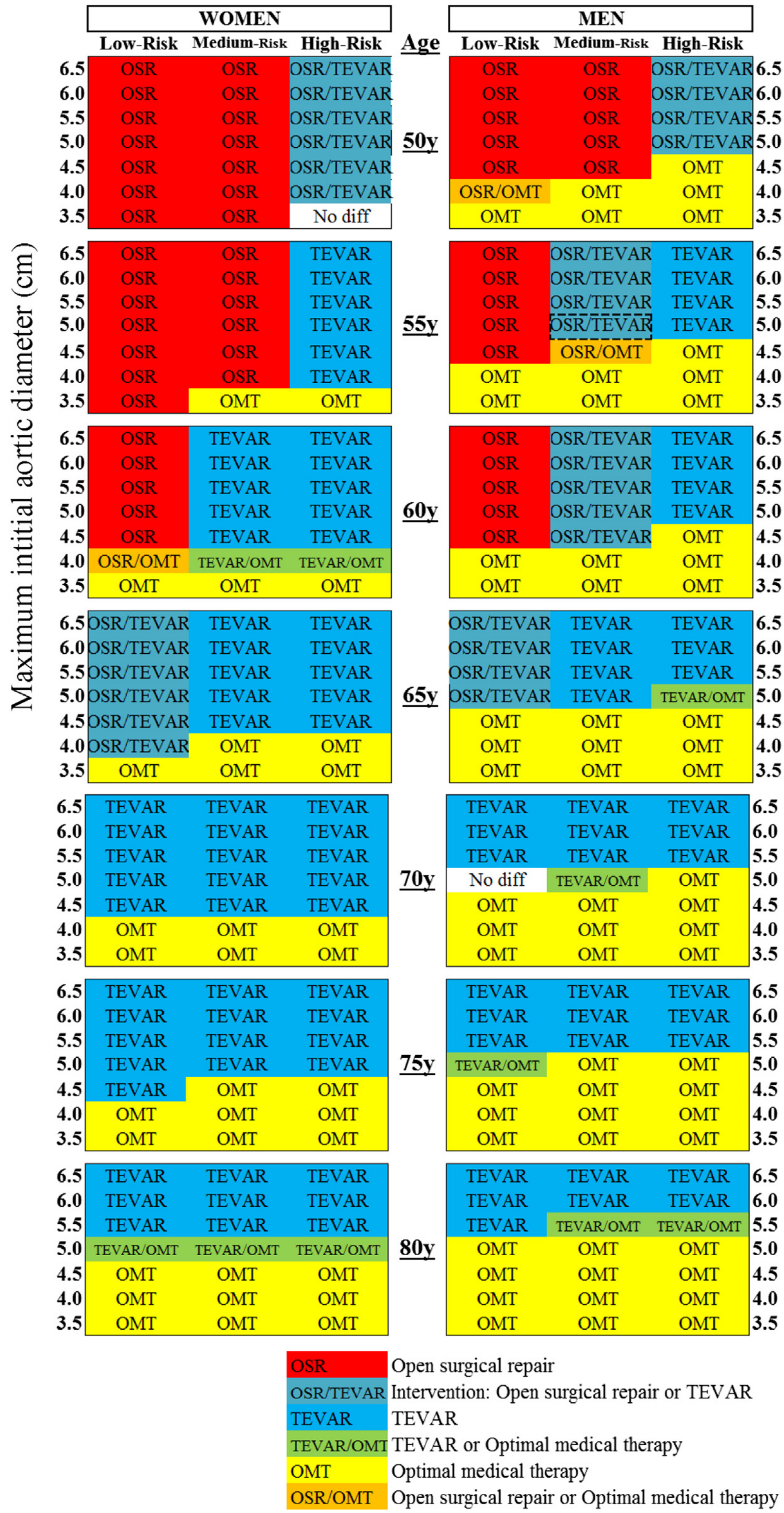

Fig 3. This treatment strategy decision chart indicates optimal treatment strategy on the basis of four basic characteristics: age, sex, surgical risk profile, and maximum initial aortic diameter. Two treatment strategies in the same cell (OSR/TEVAR, TEVAR/OMT, and OSR/OMT) indicate a difference of <2 months in quality-adjusted life-years (QALYs). *No diff* indicates a difference of <2 months for all the treatment groups. The *dotted box* is the reference case. *TEVAR,* Thoracic endovascular aortic repair.

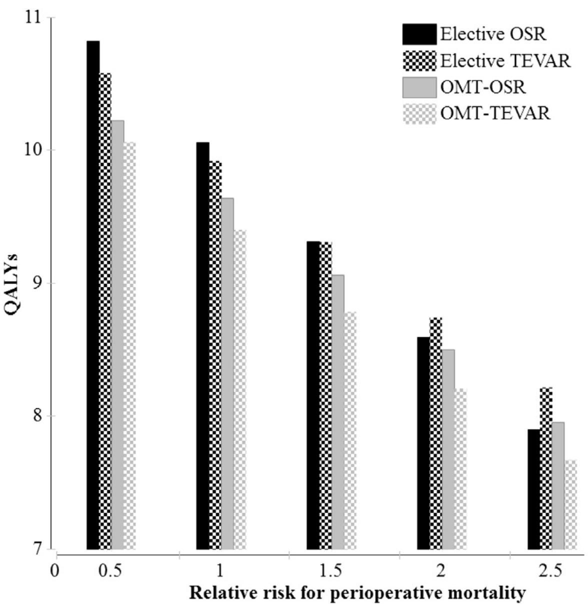

Fig 4. Total expected quality-adjusted life-years (*QALYs*) per risk profile of reference-case patient, a 55-year-old man. Low-risk patient: relative risk (RR), 0.5; medium-risk: RR, 1.0; high-risk: RR, 2.0. Increase of the patient's risk profile shows a shift from open surgical repair (*OSR*) to thoracic endovascular aortic repair (*TEVAR*). *OMT-OSR,* Optimal medical therapy followed by OSR; *OMT-TEVAR*, OMT followed by TEVAR.

the form of a chart, shown in Fig 3. This clinical decision model, requiring only basic patient characteristics, may guide treatment strategies for patients with chTBADs. However, other factors, such as extent of the dissection, including its complexity and proximity to the origin of the left common carotid and subclavian arteries, the number of fenestrations and potential compromise of the visceral vasculature and aortoiliac bifurcations, may be important determinants of whether TEVAR is feasible. In addition, there will be patients who are not appropriate candidates for aortic surgery of any kind. Finally, there are patients in the OMT group who never have enlargement of the dissected aorta or complications during follow-up. Therefore, treatment should be tailored to the patient, and a patient-specific approach should be performed.

Although decision analysis is a sophisticated method to synthesize the best available evidence, this type of analysis has some limitations. In this particular setting, one of the limitations is that data were extracted from published articles. We also observed that reporting was subject to heterogeneity in the array and detail for interventions, outcomes, and the quality of reporting overall. Although the data are not consistent across the entire range of these studies, we tried to overcome this by checking for consistency and integrating the evidence into weighted means. Furthermore, we explored the influence of the variables over wide ranges as determined from results in literature.

Second, the growth rates of aortic diameters are difficult to predict, and a wide range of yearly growth rates across patient groups has been described.[31-34] Furthermore, prediction of dissection-related complications is relatively complex, and only absolute aortic diameters were used in the analysis. In general, the faster the aortic diameter is expanding, the earlier the intervention should be performed. Patients who receive OMT should be assessed every 6 months and should undergo an intervention if a predefined threshold for intervention is reached or when the aorta grows relatively fast (≥1 cm per year by consensus).[40] However, until the exact role of growth rates and dissection-related complications are known, we should use currently available evidence to its fullest extent to optimize current treatment strategies.

QOL values were obtained from published articles, and conservatively treated patients reported lower QOL values than patients who received an intervention. However, sensitivity analysis of this showed that even if QOL for conservatively treated patients was higher for patients who received an intervention, elective OSR and TEVAR were still preferred over OMT (Fig 6). This emphasizes the strength of this decision model. Finally, no QOL values have been published for the health state "multiple morbidities." This QOL value was assumed to be lower than for patients with one major morbidity and was tested over a wide range (0-1), which did not result in a change of conclusions because only a very small percentage of patients will end up in this health state.

Although several patient groups in the model had a difference of >1.0 QALYs, the small difference in QALYs for different treatment strategies for the reference-case cohort is noteworthy. How much does a difference of ≤2 months during long-term follow-up mean? Is it worth surgical or endovascular intervention and associated costs? Does this mean there is no preferred strategy in these specific categories? This will also depend on patient preferences. However, sensitivity analysis of the tested variables showed a robust model and did not significantly change the recommended treatment strategies. It is important to realize that a small difference in QALYs is an average for the group; whereas, some patients may have a small benefit, and others may have a large benefit. A mean difference of 0.14 QALY per patient is 1400 QALYs extra for a group of 10,000 patients; thus, 1400 additional life-years in perfect health for the whole group.

Decision analysis is a powerful tool to distinguish preferred treatment strategies based on QALYs. Other decision-analysis studies on surgical topics show similar results, with small differences between treatment strategies. Examples include evaluation of the benefit of carotid endarterectomy in asymptomatic patients compared with symptomatic patients with severe carotid artery stenosis (maximum <0.07 QALYs benefit)[41] and bare-metal vs drug-eluting stents in percutaneous coronary interventions (<0.014 QALYs).[42] Decision analysis is especially helpful for informed decisions in situations of uncertainty

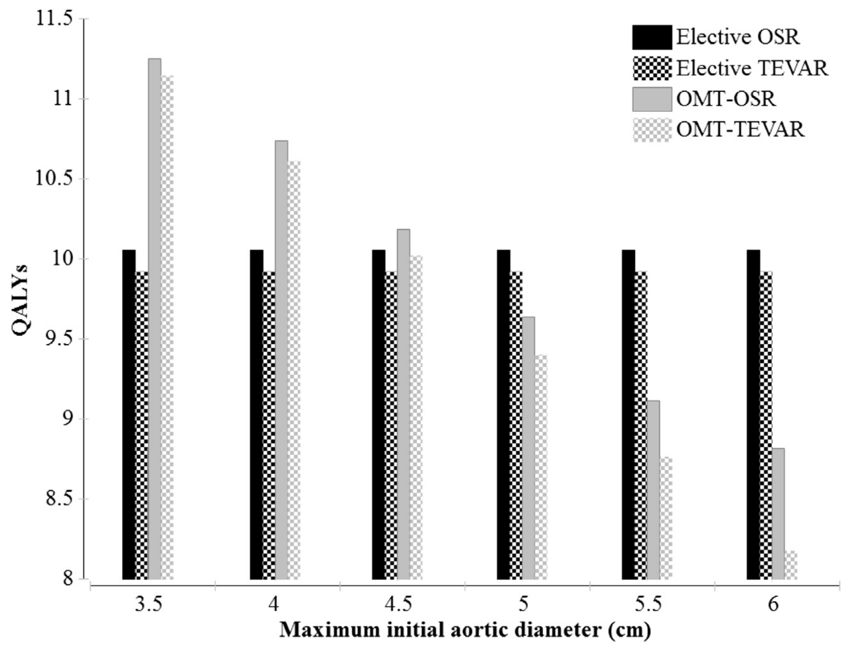

Fig 5. Total expected quality-adjusted life years (*QALYs*) for maximum initial aortic size (in cm) of reference-case patient, a 55-year-old man with chronic type B aortic dissection (chTBAD). Increase of the maximum initial aortic diameter shows shift from optimal medical therapy (*OMT*) to intervention by open surgical repair (*OSR*) or thoracic endovascular aortic repair (*TEVAR*). *OMT-OSR,* OMT followed by OSR; *OMT-TEVAR,* OMT followed by TEVAR.

Table IV. Outcomes of different treatment strategies for five patient groups

Reference-case patient and changed variable[a]	*Initial and changed variable*	*OSR*[b]	*TEVAR*[b]	*OMT-OSR*[b]	*OMT-TEVAR*[b]
Male, 55 years, medium-risk, aortic diameter: 5.0 cm	NA	**10.06**	9.92	9.64	9.40
Age, years	55→80	3.28	3.57	**3.75**	**3.77**
Risk	Medium→high	8.59	**8.74**	8.41	8.12
Sex	Male→female	**9.05**	8.94	8.30	8.02
Initial aortic diameter, cm	5.0→3.5	10.06	9.92	**11.25**	11.14

chTBAD, Chronic type B aortic dissection; *NA,* not applicable; *OMT-OSR,* optimal medical therapy followed by open surgical repair; *OMT-TEVAR,* optimal medical therapy followed by thoracic endovascular aortic repair; *OSR,* open surgical repair; *QALYs,* quality-adjusted life-years; *TEVAR,* thoracic endovascular aortic repair.

[a]Expected QALYs for the reference-case and subsequently for patients where the described parameter is changed compared with the reference case. Reference-case patient: 55-year-old, medium-risk, male patient with a chTBAD and aortic diameter of 5.0 cm.

[b]Outcomes are described in QALYS. Preferred treatment is printed in bold. A difference of <0.1 QALYs is described as indifferent.

and high complexity and especially when randomized controlled trials are lacking. Furthermore, decision analysis is particularly useful when the difference in outcomes between strategies is small.

The purpose of this study was to design a decision tool that can be used to guide the surgeon in determining the preferred treatment option tailored to the individual patient with maximum number of QALYs as primary outcome; therefore, associated costs were not analyzed. However, because health care costs are increasing nationwide and political and societal focus on controlling health care costs is increasing, a cost-effectiveness analysis should be performed, and future studies should assess the total costs and cost-effectiveness of the currently proposed treatment strategies for chTBADs.

The results of this model were based on the best available evidence in literature, and prospective evaluation of the model will be needed. However, because a higher level of evidence is currently lacking and treatment decisions need to be made, this model, based on the best available evidence, could guide treatment decisions for patients with chTBADs.

CONCLUSIONS

This decision-analysis model shows that there is no "one-size-fits-all" treatment for uncomplicated chTBADs. Age is the most important variable for determining preferred treatment, followed by initial aortic diameter. This clinical decision model can be used as a guide for the preferred treatment option for different patients with chTBADs.

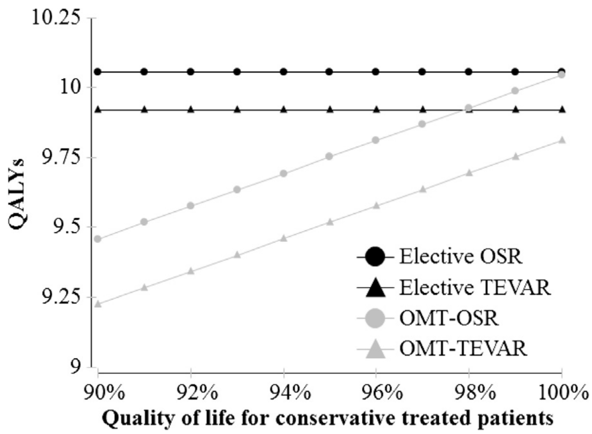

Fig 6. Total expected quality-adjusted life-years (*QALYs*) for treatment of chronic type B aortic dissection (chTBAD) in the reference-case patient (a 55-year-old man) with open surgical repair (*OSR*), thoracic endovascular aortic repair (*TEVAR*), and optimal medical therapy (*OMT*) per quality of life (QOL) for conservative treated patients. Expected QALYs for OSR are always higher than for TEVAR and OMT, and only OMT is affected by QOL for conservative treatment.

AUTHOR CONTRIBUTIONS

Conception and design: WH, MH, FM, BM
Analysis and interpretation: WH, MH
Data collection: WH, FS
Writing the article: WH, FS, BM
Critical revision of the article: MH, FS, FM, BS, BM
Final approval of the article: WH, MH, FS, FM, BS, BM
Statistical analysis: WH, MH
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Overall responsibility: WH

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