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Cost-Effectiveness of Transesophageal Echocardiographic-Guided Cardioversion: A Decision Analytic Model for Patients Admitted to the Hospital With Atrial Fibrillation

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Objectives. **Using a decision-analytic model, we sought to examine the cost-effectiveness of three strategies for cardioversion of patients admitted to the hospital with atrial fibrillation.**

Background. **Transesophageal echocardiographic (TEE)-guided cardioversion has been proposed as a method for early cardioversion of patients with atrial fibrillation. The cost-effectiveness of this approach, relative to conventional therapy, has not been studied.**

Methods. **We ascertained the cost per quality-adjusted life-year (QALY) of three strategies: 1) conventional therapy—transthoracic echocardiography (TTE) and warfarin therapy for 1 month before cardioversion; 2) initial TTE, followed by TEE and early cardioversion if no thrombus is detected; 3) initial TEE, with early cardioversion if no thrombus is detected. With strategies 2 and 3, if a thrombus is seen, follow-up TEE is performed. If no thrombus is seen, cardioversion is then performed. All strategies utilized anticoagulation before and extending for 1 month after cardioversion. Life expectancy, utilities (quality-of-life weights) and event probabilities were ascertained from published reports. Cost estimates were based on published data and hospital accounting information.**

Results. **Transesophageal echocardiographic-guided early cardioversion (strategy 3: cost $2,774, QALY 8.49) dominates TTE/TEE-guided cardioversion (strategy 2: cost $3,106, QALY 8.48) and conventional therapy (strategy 1: cost $3,070, QALY 8.48) because it is the least costly with similar effectiveness. Sensitivity analyses demonstrated that TEE-guided cardioversion (strategy 3) dominates conventional therapy if the risk of stroke after TEE negative for atrial thrombus is slightly less than that after conventional therapy (baseline estimate 0.8%). The results also depend on the risk of major hemorrhage but are less sensitive to baseline estimates of morbidity from TEE, cost of TTE, cost of hospital admission for cardioversion and utilities for health states.**

Conclusions. **On the basis of a decision-analytic model, TEE-guided early cardioversion, without TTE, is a reasonable cost-saving alternative to conventional therapy for patients admitted to the hospital with atrial fibrillation. Such a strategy appears particularly beneficial for patients with an increased risk of hemorrhagic complications. Future clinical studies examining the TEE strategy should consider eliminating initial TTE and carefully assess both the thromboembolic and hemorrhagic risk.**

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Atrial fibrillation is the most common sustained arrhythmia, resulting in >179,000 hospital admissions in 1990 alone (1). The resultant loss of atrial mechanical function and associated blood stasis increases the risk of atrial thrombus formation and thromboembolism. Restoration of sinus rhythm relieves symptoms, improves hemodynamic variables and may lower thromboembolic risk. The likelihood of restoring sinus rhythm and the recovery of atrial systolic function are both inversely related to the duration of atrial fibrillation before cardioversion (2,3). Furthermore, the longer the course of anticoagulation, the greater the risk of hemorrhage. Therefore, it would be desirable to convert atrial fibrillation to sinus rhythm as early as possible.

Because transthoracic echocardiography (TTE) is not reliable for excluding left atrial thrombi (4–6), conventional therapy for patients presenting with atrial fibrillation >48 h in duration includes 3 to 4 weeks of warfarin therapy before cardioversion (7). Cardioversion in the absence of anticoagulation results in clinical thromboembolism in 5% to 7% of patients (8–11). Although no randomized trials have been reported, 3 to 4 weeks of warfarin therapy decreases the risk of cardioversion-related thromboembolism to 0% to 1.6% (8–11). One month of warfarin therapy is also prescribed after

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Abbreviations and Acronyms

ACUTE = Assessment of Cardioversion Using Transesophageal Echocardiography
CPT = current procedural terminology
DC = direct cardioversion
DEALE = Declining Exponential Approximation of Life Expectancy
QALY = quality-adjusted life-year
TEE = transesophageal echocardiography, transesophageal echocardiographic
TTE = transthoracic echocardiography

cardioversion for prophylaxis during recovery of atrial mechanical function (3) and to prevent reversion to atrial fibrillation. The downside of conventional therapy includes hemorrhagic complications associated with warfarin (10,12–17), increased use of outpatient services for monitoring, a delay in cardioversion for the majority of patients who would not experience thromboembolism and the need for a brief second hospital stay (or day visit) for cardioversion.

Transesophageal echocardiography (TEE) offers superior visualization of the left atrium and its appendage (4–6,18) and thus offers the opportunity to perform early cardioversion if TEE results are negative for atrial thrombus (19–24). However, patients without evidence of atrial thrombi on TEE may still be at risk for embolization after cardioversion (25–28). Moreover, TEE does have associated morbidity and mortality (28–30), and the relative cost-effectiveness of a TEE-guided strategy for early cardioversion compared with conventional therapy has yet to be determined. Because patients who are admitted to the hospital for evaluation and initial therapy for atrial fibrillation (rate control, initiation of intravenous and oral anticoagulation) may benefit the most from a TEE-guided approach, we sought to examine the efficacy and cost-effectiveness of these treatment options using a decision-analytic approach.

Methods

Decision model. On the basis of the average age and gender of patients enrolled in recent studies of cardioversion for atrial fibrillation (19–24), we constructed a decision model (Fig. 1) for a prototypic 70-year old patient who is admitted to the hospital for initial treatment of atrial fibrillation >2 days in duration and for whom elective cardioversion is desired. The model does not pertain to patients with atrial fibrillation not admitted to the hospital or to those who spontaneously revert to sinus rhythm. The time frame of the model is 2 months—from index hospital admission through 1 month after elective cardioversion. Survival after 2 months was modeled using the Declining Exponential Approximation of Life Expectancy (DEALE) method (29–31). We used SMLTREE software (32) to compare the incremental cost-effectiveness of three strategies.

Strategy 1: conventional therapy. After hospital admission, intravenous heparin and oral warfarin therapy is started, and a TTE is performed to evaluate left atrial size and severity of mitral regurgitation, to exclude occult mitral stenosis and to assess left ventricular systolic function (33). Because TTE cannot reliably exclude a left atrial thrombus (4–6,19), once

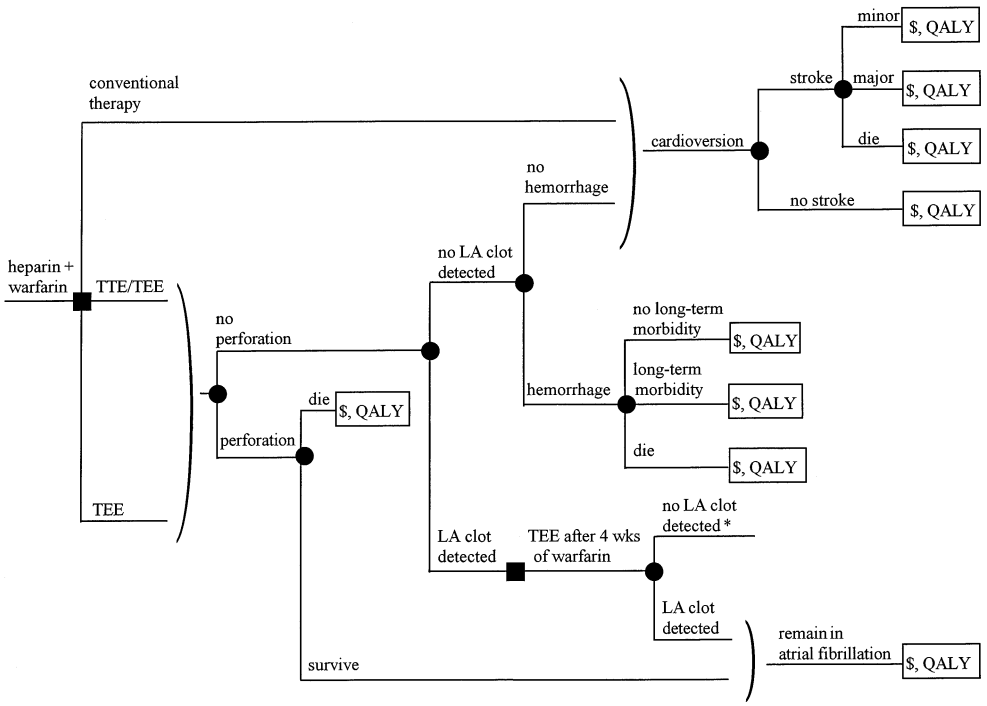

Figure 1. Decision tree model. Initial treatment strategy decision for patients with atrial fibrillation (**solid square at left**) and chance events (**solid circles**). Patients who undergo TEE have a risk of esophageal perforation and, if they survive, are assumed to remain in atrial fibrillation. Patients with left atrial clot detected receive anticoagulation for 4 weeks and return for follow-up TEE. If a left atrial clot is detected on follow-up TEE, then patients do not undergo cardioversion and remain in atrial fibrillation. Patients with no left atrial clot detected on follow-up TEE (**asterisk**) follow the same course as patients without left atrial clot detected on initial TEE. Not represented is the 4 weeks of anticoagulation after cardioversion. **Boxes** represent outcomes in terms of costs ($) and QALYs. LA = left atrial; perforation = esophageal perforation related to TEE.

warfarin anticoagulation is therapeutic, the patient is discharged in atrial fibrillation for an additional 1 month of outpatient warfarin therapy before elective cardioversion; anticoagulation has an attendant risk of major hemorrhage. During a second brief hospital stay or day visit, the patient undergoes elective cardioversion (pharmacologic or direct current), with an associated risk of neurologic impairment or death due to cardioversion-related thromboembolism. Patients who did not have a hemorrhagic complication receive an additional 1 month of warfarin therapy after cardioversion as prophylaxis against thrombus formation during the recovery of atrial mechanical function and in case of recurrent atrial fibrillation (3,7,24,34–36), with attendant cost and morbidity.

Strategy 2: TEE-guided cardioversion with TTE. After hospital admission, intravenous heparin and oral warfarin therapy is started, and TTE is performed. If TTE does not detect an atrial thrombus, TEE is performed within 24 h of admission, with possible associated morbidity. If no thrombus is detected by either study, cardioversion is performed within 24 h with an attendant risk of neurologic impairment or death due to cardioversion-related thromboembolism. If a thrombus is detected by either TTE or TEE, the patient receives 4 weeks of warfarin therapy, and follow-up TEE is performed at 1 month, followed by cardioversion if no thrombus is seen. However, if the thrombus persists, the patient remains in atrial fibrillation and continues warfarin therapy. All patients receive 1 month of outpatient anticoagulation after cardioversion, with an attendant cost and morbidity.

Strategy 3: TEE-guided cardioversion. After hospital admission, intravenous heparin and oral warfarin therapy is started, and TEE is performed within 24 h. If no thrombus is detected, cardioversion is performed within 24 h, with the risk of neurologic impairment or death due to cardioversion-related thromboembolism. If a thrombus is seen by TEE, the patient receives 4 weeks of warfarin therapy and follow-up TEE is performed at 1 month followed by cardioversion if no thrombus is seen. If the thrombus persists, then the patient remains in atrial fibrillation and continues warfarin therapy. All patients receive 1 month of outpatient anticoagulation after cardioversion with attendant cost and morbidity.

Assumptions. We made several simplifying assumptions in the analysis.

Anticoagulation and hemorrhage. 1) All patients receive anticoagulation from the time of admission through 1 month after cardioversion. Those with a hemorrhage before cardioversion have their anticoagulant therapy stopped and remain in atrial fibrillation for the observation period. 2) The only complication of warfarin therapy considered is *major hemorrhage*, defined as a hemorrhage that requires a transfusion or that is life-threatening and requires hospital admission. Cost and morbidity related to non-major hemorrhagic complications are not considered. This assumption favors conventional therapy (strategy 1) because patients in that strategy receive warfarin for twice as long as others, and thus their risk of a non-major hemorrhagic complication would be expected to be higher. 3) For patients in strategy 1, cardioversion is attempted after 1 month of warfarin therapy for all patients. This assumption favors conventional therapy (strategy 1) because data suggest that 25% of patients scheduled for cardioversion of atrial fibrillation after 1 month of warfarin have cardioversion delayed due to inadequate anticoagulation or hemorrhagic complications (24).

Cardioversion. 1) Patients undergoing conventional therapy (strategy 1) undergo initial TTE to evaluate left atrial size, ascertain the presence and severity of mitral regurgitation, exclude occult mitral stenosis and assess left ventricular systolic function (33). Because patients in clinical practice might not undergo initial TTE as part of their management, we performed a sensitivity analysis comparing TEE-guided cardioversion (strategy 3) versus conventional therapy without initial TTE (i.e., anticoagulation and cardioversion without echocardiography). 2) All cardioversions are successful in restoring sinus rhythm, and sinus rhythm is maintained at equal rates under all strategies. This assumption favors conventional therapy (strategy 1) because patients who undergo TEE-guided early cardioversion (strategies 2 and 3) have a shorter (by 1 month) duration of atrial fibrillation before cardioversion and thus have a more rapid recovery of atrial mechanical function (3) and a greater chance of maintaining sinus rhythm (3). 3) The only morbidity from cardioversion considered is cerebral embolism/stroke. 4) Patients with esophageal perforation or a persistent thrombus detected on follow-up TEE (after 4 weeks of anticoagulation) do not undergo cardioversion and are assumed to remain in atrial fibrillation. This assumption favors conventional therapy (strategy 1) because we assumed that patients who remained in atrial fibrillation had a shorter life expectancy than those in sinus rhythm. 5) After 4 weeks of warfarin therapy for an atrial thrombus, a patient who has repeat TEE showing no atrial thrombus has the same risk of cardioversion-related clinical thromboembolization as a patient who did not have a thrombus seen on the initial study. 6) All cardioversions are elective.

Cost. 1) All patients are initially admitted to the hospital for 3 nights, corresponding to Diagnostic Related Group (DRG) 139-Cardiac Arrhythmia and Conduction Disorders without Complication, which allows an average length of stay of 3.3 nights (37). While in the hospital, the patient typically undergoes evaluation and treatment to control the ventricular rate, anticoagulation with heparin and warfarin, echocardiography and cardioversion (for strategies 2 and 3). Elective cardioversion after 4 weeks of warfarin therapy for patients undergoing conventional therapy (strategy 1) and for patients with evidence of thrombi on TEE requires a 1-day hospital stay or day visit. Because some physicians may choose to perform this elective cardioversion on an outpatient basis, we varied the cost of this second hospital visit to determine its effect on the analysis. 2) The cost of death from esophageal perforation is the same as that for death from major hemorrhage.

Risk of TEE. 1) The only major complication of TEE is esophageal perforation. Other complications, such as arrhythmias, hypoxia and hoarseness are transient (24,38–40), and thus were not considered in our baseline analysis. In our

Table 1. Baseline Probability Estimates

Variable	Baseline (%)	Reference No.
Hemorrhage in pts taking warfarin		
Annual rate	1.7	12–17
1st-mo rate	0.36	41–43
2nd-mo rate	0.12	41–43
Thrombus detected in pts with AF		
By TTE	2	23
By TEE	15	23
By TEE if none seen on TTE	14	23
By TEE after 4 wk of anticoagulation if thrombus detected on initial TTE or TEE	15	45
Complications from hemorrhage		
None	92	44
Long-term morbidity	2	44
Death	6	44
Stroke after cardioversion		
After 4 wk of anticoagulation (strategy 1)	0.8	8–11
If no thrombus detected by TEE (strategies 2 and 3)	0.5	22–24
Neurologic sequelae of stroke		
Minor	46	44
Long-term morbidity	30	44
Death	24	44
Esophageal perforation		
Incidence	0.02	46, 47
Mortality	8.0	48

AF = atrial fibrillation; pts = patients; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

sensitivity analysis, we varied the major complication rate of TEE over a wide range to account indirectly for these other complications.

Probabilities. Event probabilities were ascertained from published reports and are summarized in Table 1.

Risks of hemorrhage. Published estimates of the risk of hemorrhage associated with anticoagulation vary widely. Recent large, prospective, multicenter clinical trials of warfarin for nonvalvular atrial fibrillation (12–17) found major hemorrhage rates of 0.8% to 2.5%/year. For our baseline analysis, we selected the midpoint of this range, 1.7%/year, as the major hemorrhage rate.

On the basis of evidence that the risk of major hemorrhage from anticoagulation is greatest during the initial month of therapy (41–43), we estimated that the risk of major bleeding was three times greater during the first month of therapy compared with subsequent months. Thus, our baseline estimates for the rate of major hemorrhage were 0.36% for those receiving 1 month of warfarin therapy (strategy 2 and 3) and 0.48% for those receiving 2 months of warfarin therapy (strategy 1). This assumption favors conventional therapy (strategy 1) because the monthly risk of hemorrhage during the second month was estimated to be lower than the first. Our baseline estimate is much lower than the 1-month major hemorrhage rate of 1.6% reported in a recent population-based study of anticoagulant therapy (41). Our estimate is also conservative with respect to the 2-month hemorrhagic complication rate of 1.6% among patients in the Assessment of Cardioversion Using Transesophageal Echocardiography (ACUTE) pilot study randomized to strategy 1 (24).

Of patients with a major hemorrhage, we estimated that 6% die, 2% have long-term morbidity, and 92% recover after a short hospital stay (44).

Probability of detecting a left atrial thrombus by TTE or TEE. The true sensitivity and specificity of TTE and TEE in detecting left atrial thrombi in patients with atrial fibrillation are unknown. Rather than estimating this directly, we estimated the probability that a patient with new atrial fibrillation will have a thrombus detected by TTE or TEE. On the basis of published data, our baseline analysis assumes that, of patients presenting with new atrial fibrillation, TTE detects thrombi in 2%, TEE detects thrombi in 15%, and among those with a negative TTE, TEE detects thrombi in 14% (21–23). The probability of seeing a persistant thrombus by TEE on the follow-up examination at 1 month was estimated at 15% (45).

Probability of stroke after cardioversion. Several retrospective studies (9–11) and one nonrandomized, prospective study (8) of elective cardioversion have shown an incidence of cardioversion-related thromboembolism of 0% to 1.6% for patients receiving warfarin for 2 to 4 weeks before cardioversion (strategy 1) (8–11). On the basis of these data, we assumed a baseline risk of stroke of 0.8% after 1 month of anticoagulation. For the risk of stroke after cardioversion among patients without evidence of atrial thrombi on TEE, we assumed a baseline risk of 0.5% (or relative risk of 0.625 [= 0.5/0.8]) based on the approximate midpoint of the 95% confidence interval from prospective data gathered from three trials (n = 340) utilizing a protocol similar to strategy 2 (22–24) (combined stroke rate 0%, 95% confidence interval 0% to 0.9%). Because the stroke rates after TEE-guided cardioversion and conventional therapy are not firmly established, we linked them to each other (ratio) to examine how the relative risk of stroke after TEE-guided cardioversion versus conventional therapy affected the cost-effectiveness ratio. Of those with clinical cerebral embolization, we estimated that 24% die, 30% have long-term morbidity, and 46% have only a minor stroke with full recovery (44).

In our analysis, patients with major hemorrhagic complications before cardioversion remain in atrial fibrillation and do not take warfarin. Because such patients are at an increased risk of thromboembolism, we assumed an embolic risk of 4.3%/year (0.004%/month) based on data from randomized trials of warfarin versus placebo for patients in atrial fibrillation (12–17). In our baseline model, patients with a thrombus detected on initial echocardiography and repeat TEE after 4 weeks of warfarin do not undergo cardioversion and therefore remain in atrial fibrillation. Because these patients might have a higher embolic risk than patients without a thrombus detected on TEE, they were given an additional stroke risk of 0.05% during the observation period.

Risks of TEE. Life-threatening complications associated with TEE are rare. In a review of 10,419 examinations, Daniel

et al. (38) reported only one death (0.0098%), which was caused by laceration of a malignant lung tumor penetrating into a patient's esophagus. Other complications, such as bronchospasm, arrhythmias and hoarseness, are rare and transient (38–40). Chan et al. (34) reviewed 1,500 consecutive TEE examinations and reported no deaths. Reversible complications, such as stridor, wheezing or transient, asymptomatic atrial fibrillation, occurred in five (0.3%) patients (39). In a preliminary report, the Value of Transesophageal Echocardiography (VOTE) study (40) also reported no deaths among 3,003 examinations. Esophageal perforation is the most serious, life-threatening complication of TEE. The risk of esophageal perforation for diagnostic endoscopy ranges from 0.01% to 0.03% (46,47). These data most likely overestimate the risk of perforation during TEE because patients in the endoscopic studies had esophageal disease. To be conservative, we assumed a baseline risk of esophageal perforation of 0.02% and also assumed that patients who experienced esophageal perforation would not undergo cardioversion. The mortality rate from esophageal perforation related to diagnostic endoscopy has been estimated to be 8.0% (48), which is the rate we used in our analysis.

Effectiveness. Effectiveness was measured in terms of quality-adjusted life-years (QALYs), which was calculated for each outcome by multiplying the life expectancy by its utility (quality of life weight ranging from 0 to 1). For patients surviving the 2-month time horizon, we first estimated the expected mortality rate as the sum of the age-adjusted annual mortality rate plus the disease-specific mortality rate and then calculated life expectancy by taking the reciprocal of the overall mortality rate, according to the DEALE method (29–31).

The baseline annual mortality rate for a 70-year old person is 0.072 (49). The annual disease-specific mortality rate due to major stroke and major hemorrhage has been estimated to be 0.49 and 0.52, respectively (44,50). In addition, due to the possible recurrence of atrial fibrillation after cardioversion, we estimated the disease-specific postcardioversion mortality rate to be 0.016 (50). Thus, the annual disease-specific mortality rate of patients in chronic atrial fibrillation was estimated to be 0.027 for patients receiving long-term warfarin therapy and 0.043 for those not receiving anticoagulation (12–16).

Because patients with esophageal perforation do not undergo cardioversion and do not receive anticoagulation, these patients were assigned the disease-specific mortality rate of those with chronic atrial fibrillation, 0.043 (12–16). Thus, for example, the expected mortality rate of a 70-year old man with a major stroke is 0.562 (= 0.072 + 0.49), and the life expectancy is 1.78 (= 1/0.562) years.

The utility of death was set at 0.0 and that of successful cardioversion without stroke or major hemorrhage (using any strategy) equal to 1.0. Utility estimates for embolization and hemorrhage were based on published data (44). The utility resulting from stroke with long-term morbidity was assumed to be 0.5, whereas that of minor stroke was assumed to be 0.7 for the first month only (44). For hemorrhage, the utility associated with long-term morbidity was 0.6, whereas that of hemorrhage without long-term morbidity was 0.9 for 1 month (44). The utility of esophageal perforation was assumed to be the same as that for major hemorrhage with resolution. If more than one condition was present, the lowest utility was used. All life-years were discounted at 5%.

Table 2. Costs and Utilities

Variable	Baseline Cost ($)	Source
Echocardiography		
TTE	321	Hospital accounting and
TEE	432	Medicare reimbursement
Embolization after cardioversion		
Minor stroke	4,438	Eckman et al. (44)
Major stroke	22,939	Eckman et al. (44)
Death due to stroke	5,980	Eckman et al. (44)
Complication of TEE		
Esophageal perforation	1,602	Hospital accounting
Death due to perforation	5,980	*
Hemorrhage		
No morbidity	3,172	Eckman et al. (44)
Morbidity	24,546	Eckman et al. (44)
Anticoagulation/mo		
Warfarin therapy (4 mg/day)	15	Wholesale cost
Prothrombin time test (1/wk)	42	Wholesale cost
Hospital stay		
Initial stay	1,856	Hospital accounting
Second stay	464	Hospital accounting
Elective cardioversion	213	Hospital accounting

*Assumed to be the same as death due to stroke.

Costs. Because hospital and physician charges may not reflect true economic costs (51), we used costs rather than charges and based our estimates on both published data and actual cost estimates at our institution (Table 2) in 1993. For costs of hemorrhagic complications and stroke, including the cost of hospital admission and long-term care, we used the variable cost estimates of Eckman et al. (44). The variable costs of esophageal perforation, hospital admission for atrial fibrillation and elective cardioversion were obtained from our hospital cost accounting information.

We estimated the cost of a month of warfarin therapy using the wholesale cost of 4 mg/day of warfarin and the laboratory cost of four prothrombin time tests (the rate charged to institutions by a private laboratory in Boston). No cost was assumed for physician/nurse interpretation and management of warfarin therapy. This would favor strategy 1 (conventional therapy) because more prothrombin time assessments are made under that strategy. To obtain the physician costs for performing and interpreting echocardiography, we converted the current procedural terminology (CPT) codes (52,53) for TTE (CPT code 93307) and TEE (CPT code 93312) into resource-based relative value units (RBRVUs) and then used the Medicare reimbursement rate to convert these into dollars (54). The remainder of the TTE and TEE costs included technician fees, probe depreciation and equipment mainte-

Table 3. Baseline Results

Strategy	Cost ($)	QALY	Incremental Cost-Effectiveness
TEE-guided cardioversion (strategy 3)	2,774	8.49	—
Conventional therapy (strategy 1)	3,070	8.48	Dominated
TEE-guided cardioversion with TTE (strategy 2)	3,106	8.48	Dominated

Dominated = more costly and less effective than transesophageal echocardiographic (TEE)-guided cardioversion; QALY = quality-adjusted life-year; TTE = transthoracic echocardiography.

nance. We subsequently varied the cost of TEE in our sensitivity analysis.

Costs were discounted at 5%/year, and future outpatient costs were obtained by summing annual discounted outpatient costs over the predicted life expectancy (44). All costs are expressed in 1993 dollars, with costs from previous years inflated using the medical care component of the consumer price index.

Sensitivity analysis. We performed sensitivity analyses by varying the baseline probabilities, utilities and costs over wide ranges. We also performed threshold analyses to identify values for model variables that would result in an incremental cost-effectiveness ratio >$50,000/QALY, an often cited threshold for cost-effective care (55–57).

Results

Baseline analysis. Using our baseline assumptions, the cost and QALYs for each strategy are summarized in Table 3. TEE-guided cardioversion (strategy 3) is the least costly strategy ($2,774) compared with $3,070 for conventional therapy (strategy 1) and $3,106 for TTE/TEE-guided cardioversion (strategy 2). There is no meaningful difference in effectiveness between the three strategies (Table 3). Thus, TEE-guided cardioversion (strategy 3) dominates in that it is the least costly with similar effectiveness.

Sensitivity analyses. Most centers that use TEE to guide cardioversion of atrial fibrillation have followed a TTE/TEE-guided cardioversion strategy (20–24) (strategy 2). In our sensitivity analyses, this strategy is always dominated by TEE-guided cardioversion (strategy 3) because strategy 2 has the additional cost of TTE without added measurable effectiveness for guiding early cardioversion. Thus, our sensitivity analyses focus on comparing TEE-guided early cardioversion (strategy 3) with conventional therapy (strategy 1).

Probability of thromboembolism. We varied the relative risk of stroke (ratio of stroke risk after TEE-guided cardioversion to the stroke risk after conventional therapy) to analyze how the probability of thromboembolism affects the incremental cost-effectiveness of TEE-guided cardioversion (strategy 3) compared with conventional therapy (strategy 1). If the relative risk of stroke using TEE-guided cardioversion is <0.95, TEE-guided cardioversion is both more effective and less costly than conventional therapy. At a relative risk >0.95, TEE-guided cardioversion remains less costly but is also less effective. At a relative risk of 1.1, the incremental cost-effectiveness for TEE-guided cardioversion is $50,000/QALY.

In our analysis, we assumed that patients with a thrombus detected on follow-up TEE after 4 weeks of anticoagulation would not undergo cardioversion. Because such patients may have a higher risk of embolism than those without a thrombus, their risk of embolism was increased by 0.05%. TEE-guided cardioversion is still less costly and more effective than conventional therapy if this added risk of stroke were as high as 13%.

Probability of hemorrhage. We varied the risk of major hemorrhage from its baseline of 1.7%/year (0.36% first-month risk) while varying the relative risk of postcardioversion stroke (risk of postcardioversion stroke with strategy 3 vs. strategy 1) from 0 to 1.25 (Fig. 2). Assuming that the risk of hemorrhage during the first month of anticoagulation is three times as great as that in the subsequent month (42), we varied the annual risk of hemorrhage from 0.8%/year (0.2% first-month risk) to 11%/year (2.4% first-month risk). Using the 0.8%/year risk of hemorrhagic complication, TEE-guided cardioversion (strategy 3) remains more effective than conventional therapy (strategy 1) if the relative risk of postcardioversion stroke is <0.56. If the relative risk of stroke after TEE-guided cardioversion is >4.7, then conventional therapy is more effective, even at a risk of hemorrhage as high as 11%/year (2.4% first-month risk).

Complications of TEE. The reported risk of esophageal perforation for diagnostic endoscopy ranges from 0.01% to 0.03% (24,46,47). Within this range, TEE-guided cardioversion (strategy 3) dominates conventional therapy (strategy 1). To estimate how a higher overall complication rate of TEE might affect our results, we varied the risk of perforation to find the value at which TEE-guided cardioversion becomes less effective than conventional therapy. The risk of TEE-related esophageal perforation would have to be >0.30% before conventional therapy is more effective than TEE-guided cardioversion.

Costs and utilities. Holding the cost of TTE at its baseline of $321, we varied the cost of TEE. If the cost of TEE increases to $1,100, the incremental cost-effectiveness of TEE-guided cardioversion (strategy 3) compared with conventional therapy (strategy 1) is $50,000/QALY.

In the model, all patients undergoing conventional therapy (strategy 1) return after 1 month of warfarin therapy for a 1-day hospital stay for elective cardioversion, as do patients

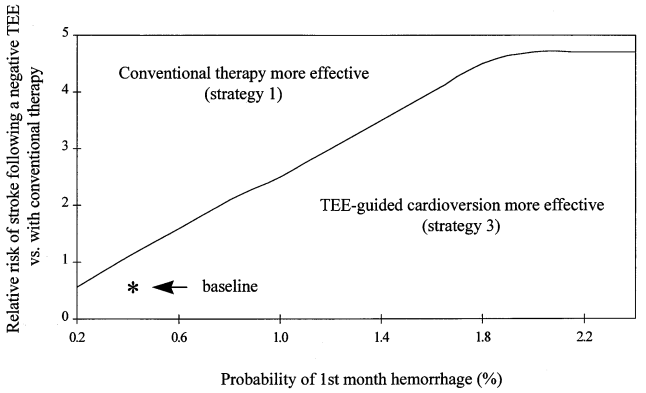

Figure 2. Two-way sensitivity analysis: relative risk of stroke after cardioversion versus risk of hemorrhage during the first month of warfarin therapy. The relative risk of stroke after cardioversion is plotted against the risk of hemorrhage during the first month of warfarin therapy, which varied from 0.2% (0.8%/year) to 2.4% (11%/year). The relative risk of stroke is the ratio of the risk after TEE-guided cardioversion (strategy 3) to the stroke risk after conventional therapy (strategy 1). **Solid line** represents the values at which the effectiveness of TEE-guided cardioversion (strategy 3) and conventional therapy (strategy 1) are equivalent. **Values above the line** favor conventional therapy, and **values below the line** favor TEE-guided cardioversion. If the relative risk of postcardioversion stroke is <0.56, then TEE-guided cardioversion (strategy 3) is more effective than conventional therapy, even if the risk of first-month hemorrhage is as low as 0.2%. If the relative risk of stroke after cardioversion is >4.7, then conventional therapy is more effective, even with a first-month hemorrhage risk as high as 2.4%. **Asterisk** represents baseline estimates of hemorrhage risk (0.32%) and relative risk of stroke (0.625).

who had a thrombus detected by initial TEE. Because some physicians may elect to perform cardioversion on an outpatient basis, we varied the cost of this second hospital stay. Even if there were no cost for this elective hospital stay, TEE-guided cardioversion (strategy 3) costs only $110 more than conventional therapy ($2,718 vs. $2,608) and remains slightly more effective, with an incremental cost-effectiveness of $11,512/QALY.

The results are insensitive to both the cost of esophageal perforation and the cost of death due to esophageal perforation. For the TEE strategy not to dominate, the cost of perforation (or other complications with similar mortality) would have to exceed $1.2 million, or the cost of death due to perforation would have to exceed $13 million.

Our results were not significantly affected when utilities for major stroke, hemorrhage with long-term morbidity and esophageal perforation were varied individually over wide ranges.

Alternative strategy: conventional therapy without TTE. The initial TTE as part of conventional therapy (strategy 1) has little impact on the decision-making process but does have associated cost. We thus compared TEE-guided cardioversion (strategy 3) with a strategy similar to conventional therapy but without the initial TTE. If the initial TTE were eliminated from conventional therapy, TEE-guided cardioversion is slightly more expensive than conventional therapy ($2,774 vs. $2,750) but remains more effective, with an incremental cost-effectiveness of $2,539/QALY.

Discussion

In this decision analysis, we examined three clinical strategies for guiding cardioversion of patients admitted to the hospital with new atrial fibrillation. Using our baseline assumptions, TEE-guided cardioversion without initial TTE (strategy 3) is identified as an effective and cost-saving alternative to conventional therapy (strategy 1). In our sensitivity analysis we found that the results are dependent on the risk of postcardioversion stroke in TEE-negative patients being slightly lower than the risk of stroke after conventional therapy. Although several case reports or small series have reported thromboembolism after TEE-guided cardioversion in the absence of anticoagulation (25–28), three prospective trials, involving >340 patients and using an anticoagulation schedule similar to strategy 3, have reported a stroke rate of 0% (95% confidence interval 0% to 0.9%) (22–24). The importance of adequate anticoagulation from the time of TEE through 1 month after cardioversion is underscored by data demonstrating more pronounced atrial spontaneous contrast—a marker of stasis (58,59)—as well as new thrombus formation immediately after cardioversion (60).

The cost-effectiveness of TEE-guided cardioversion (strategy 3) is sensitive to the risk of major hemorrhage. Our baseline annual hemorrhage rate estimate was derived from data gathered from five large multicenter, prospective studies of warfarin therapy in patients with atrial fibrillation (12–17). This estimate most likely underestimates the true risk of hemorrhage in clinical practice for patients admitted to the hospital with atrial fibrillation because these long-term studies excluded many patients who might be considered candidates for short-term anticoagulation. Observational studies of warfarin therapy have noted a major hemorrhage rate of 0.6% to 7.4%/year (41,61–63). The discrepancy with the previously mentioned multicenter trials of long-term warfarin therapy for atrial fibrillation is most likely related to the exclusion of 60% to 90% of potential enrollees in the nonvalvular atrial fibrillation trials (15,16), including those patients with a higher propensity to bleed (64). Data from the ACUTE pilot study (24) demonstrated major hemorrhage rates of 1.6% during 2 months of observation for patients receiving conventional therapy and 0% for patients undergoing TTE/TEE-guided cardioversion. In addition, the ACUTE pilot study found that almost 25% of patients randomized to conventional therapy (strategy 1) did not undergo cardioversion after 1 month (as intended) due to transiently subtherapeutic anticoagulation. For those patients, cardioversion was delayed, and the actual duration of anticoagulation was extended, again suggesting that our baseline estimates for hemorrhagic complications were conservative. Although we did not formally include the possibility of subtherapeutic anticoagulation in the model, a prolonged course of warfarin for the conventional group

(strategy 1) would expose them to a higher risk of hemorrhagic complication.

Study limitations. Our analysis assumes that the duration of the initial hospital period is similar for all strategies, that TEE is performed by an experienced physician and that cardioversion is performed expeditiously (while the patient is receiving heparin and the prothrombin time is advancing toward therapeutic range). Our results are not generalizable to patients who are managed exclusively as outpatients. Our model also does not account for potential cost savings from patients treated in a conventional manner who spontaneously convert while awaiting elective cardioversion. Finally, we assumed that the initial TTE in the conventional therapy strategy provided no additional information to influence the decision to perform or withhold cardioversion. Because TTE is generally performed to exclude occult mitral stenosis, evaluate left atrial size and left ventricular function and assess the presence and severity of mitral regurgitation, we may have underestimated its clinical role in guiding the decision to perform cardioversion.

Conclusions. Our analysis demonstrates that TEE-guided early cardioversion, without initial TTE, is a reasonable and potentially cost-saving alternative to present-day conventional therapy for patients admitted to the hospital with new atrial fibrillation. Sensitivity analysis demonstrated that these conclusions are dependent on the risk of cardioversion-related thromboembolism after negative TEE being slightly lower than the risk associated with conventional therapy. By avoiding 1 month of anticoagulation, the TEE approach also appears particularly beneficial for those with an increased risk of hemorrhagic complications. Further studies examining the role of TEE in this population should consider eliminating the initial TTE in patients eligible for TEE-guided cardioversion, with careful assessment of hemorrhagic risk.

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