

Long-term cost-effectiveness of transcatheter mitral valve repair in HF patients with secondary mitral regurgitation

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Abstract

Aims The long-term cost-effectiveness of MitraClip in heart failure patients with secondary mitral regurgitation is still unclear. This study aimed to evaluate the long-term cost-effectiveness of MitraClip added to guideline-directed medical therapy vs. guideline-directed medical therapy alone in heart failure patients with secondary mitral regurgitation from the perspective of the healthcare systems of mainland China, the United Kingdom, Germany, and the United States.

Methods and results A two-stage (decision + Markov) model was built. Health utilities were defined by the New York Heart Association class, heart failure re-hospitalization, and death and were calculated based on the 5 year follow-up results of the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation trial. Direct healthcare costs were derived from the nationally representative data. Future utilities and costs were discounted at country-specific rates. The primary outcome was the lifetime incremental cost-effectiveness ratio. The mean age of the base case in our model was 72.2 years. Over a lifetime horizon, treatment with MitraClip was associated with 829 fewer heart failure re-hospitalizations per 1000 treated patients. The MitraClip treatment was associated with incremental quality-adjusted life-year gains of 0.71, 0.76, 0.78, and 0.78, as well as incremental cost-effectiveness ratios of ¥468 462, £28 910, €26 045, and \$71 199 per quality-adjusted life-year for a lifetime horizon in mainland China, the United Kingdom, Germany, and the United States, respectively. In probabilistic sensitivity analysis, 0.2%, 59.4%, 99.6%, and 84.7% of patients were cost-effective in mainland China, the United Kingdom, Germany, and the United States at the country-specific willingness-to-pay thresholds.

Conclusions MitraClip + guideline-directed medical therapy was cost-effective in heart failure patients with secondary mitral regurgitation in the United Kingdom, Germany, and the United States, but not in mainland China from the perspective of the national healthcare system.

Keywords Heart failure; Mitral regurgitation; MitraClip; Quality-adjusted life-year; Cost-effectiveness

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Introduction

Heart failure (HF) has become a growing public health problem, with more than 64.3 million HF patients worldwide, including 13.7 million in China, 16 million in Europe, and 6.2 million in the United States.^{1–4} Approximately 43–77% of

the direct medical costs for HF were attributed to HF hospitalization.^{5–7} Appropriate treatments for HF can effectively improve patients' quality of life and reduce their risks of HF hospitalization and death, along with lowering the economic burden for patients and the national healthcare system.

The Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation (COAPT) trial demonstrated that among HF patients with moderate-to-severe or severe secondary mitral regurgitation (MR) who remained symptomatic despite guideline-directed medical therapy (GDMT), transcatheter edge-to-edge repair of the mitral valve resulted in a lower rate of HF hospitalization and a lower all-cause mortality than GDMT alone.^{8,9} Prior studies about the cost-effectiveness of MitraClip were based on the short-term results of the COAPT trial,^{10–13} and the estimated 5 year all-cause mortality was around 51.8% for patients with MitraClip.¹⁰ However, the recent published results of COAPT showed that the actual 5 year all-cause mortality was 57.3% in the device group,⁸ which indicated that previous cost-effectiveness studies had an unneglectable and large bias. Therefore, the long-term cost-effectiveness of the MitraClip treatment for HF patients is still unclear. In this study, we aimed to assess the long-term utility, costs, and cost-effectiveness of MitraClip added to GDMT compared with GDMT alone based on the 5 year follow-up results of the COAPT trial from the perspective of healthcare systems in mainland China, the United Kingdom, Germany, and the United States.

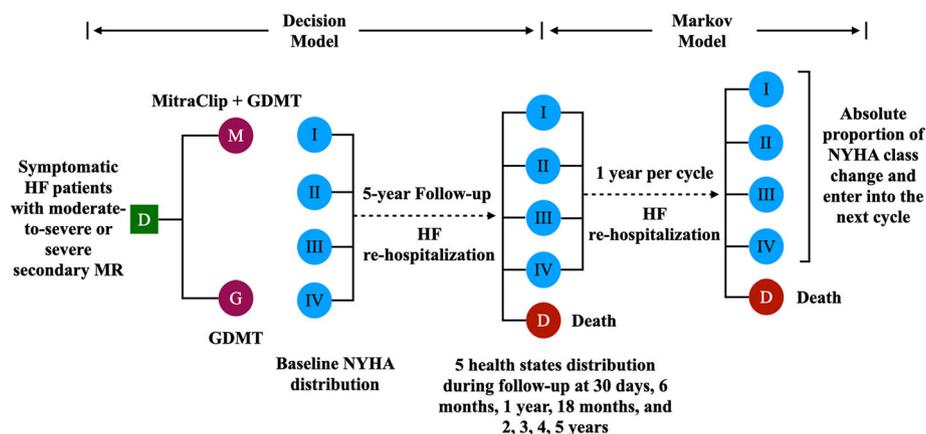
Materials and methods

Analytic overview

In this study, the cost-effectiveness analysis (MitraClip + GDMT vs. GDMT alone) was performed with a two-stage model

(decision + Markov model; *Figure 1*). A simulated cohort with 1000 patients in each arm was established, and the baseline characteristics were similar to those in the COAPT trial.^{8,9} In brief, the COAPT trial was a multicentre, randomized, controlled, parallel-group, open-label trial of transcatheter mitral valve repair with the MitraClip device in HF patients.^{8,9} Eligible patients suffered from ischaemic or non-ischaemic cardiomyopathy with a left ventricular ejection fraction of 20–50%, had moderate-to-severe or severe secondary MR, and remained symptomatic despite the use of stable maximal doses of GDMT. Details of the trial design, baseline characteristics, and results were published before.^{8,9} There were five health states in our model: New York Heart Association (NYHA) classes I–IV and death. The initial distribution of NYHA classes in the decision model was based on the baseline characteristics of HF patients in the COAPT trial.⁹ The proportion of five health states in each group would change during the first 5 year simulation, according to the 5 year follow-up results of COAPT.⁸ After a 5 year simulation, survivors would enter a Markov model to explore the long-term effects of different treatments. A lifetime horizon with a cycle length of 1 year was applied in the Markov model, consistent with previous HF economic studies.^{10–15} Patients would experience HF re-hospitalization, death, or no adverse events during the simulation, and all survivors would die at the end of the last cycle. The calculation of health utility was based on the health states, corresponding time spans, and the disutility of HF hospitalization. Only direct healthcare costs were calculated and expressed in 2022 renminbi/British pound/euro/US dollar (¥7.0 = £0.79 = €0.91 = \$1). Future utilities and costs were discounted using country-specific rates according to relevant

Figure 1 Structure of the two-stage model for cost-effectiveness assessment. The two-stage model for cost-effectiveness assessment for MitraClip contains a decision model and then a Markov model. Heart failure (HF) patients with mitral regurgitation (MR) would receive MitraClip + guideline-directed medical therapy (GDMT) or GDMT treatment at the beginning of the model. Health utility and adverse events would be calculated according to the 5 year follow-up results of the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation trial, along with the medical costs. At the end of the decision model, survivors would enter the Markov model, and health utility, medical cost, and adverse events would be estimated for a lifetime horizon. NYHA, New York Heart Association.



guidelines (Table 1).^{22–25} This work received local ethics committee approval (Guangdong Provincial People's Hospital).

Model inputs

Initial distribution and subsequent changes of five health states

According to the COAPT trial, the baseline distribution of NYHA classes I–IV was 0.2%, 39.0%, 52.5%, and 8.3%, respectively.⁹ From baseline to the end of the fifth year in the decision model, proportions of five health states in each group would change according to the follow-up data of the COAPT trial at 30 days, 6 months, 1 year, 18 months, and 2–5 years (Supporting Information, Table S1).⁸ Death from any cause through 5 years occurred in 162 patients (57.3%) in the device group and in 189 patients (67.2%) in the GDMT group, and the all-cause mortalities at 30 days, 6 months, 1 year, 18 months, and 2–4 years in each group were derived from the Kaplan–Meier curve in the COAPT trial.⁸ Because the detailed parameters of the proportions of NYHA classes were not reported in the trial, these data were approximated from the published results (Supporting Information, Methods S1).⁸

In the Markov model, we used proportions of different NYHA classes in survivors instead of transition probabilities between different NYHA classes. We assumed that the proportions of different NYHA classes in survivors of each group were constant every year. Relevant parameters were calculated as the averages of different NYHA proportions in survivors from the third year to the fifth year for each group (Supporting Information, Table S1). As for the estimated annual risk of mortality, relevant input was calculated as an average of the risk from the third year to the end of the fifth year for each group.

Probabilities of heart failure re-hospitalization

We assumed that the annualized risk of HF re-hospitalization for survivors in each group was constant in our two-stage model. Because HF hospitalization could happen repeatedly, the probabilities of HF re-hospitalization were calculated according to the total number of HF hospitalizations during follow-up. In the COAPT trial, the total number of hospitalizations for HF within 5 years was 314 in the device group and 447 in the GDMT group.⁸ Therefore, the annualized rate of HF re-hospitalization was 33.1% per year in the device group and 57.2% per year in the GDMT group.⁸ Because the risks of hospitalization unrelated to HF (including cardiovascular causes not related to HF and non-cardiovascular causes), per-

Table 1 Inputs in the two-stage model

Variables	China	United Kingdom	German	United States	Reference
Utilities					
NYHA I		0.815 (0.781, 0.850)			[16]
NYHA II		0.720 (0.693, 0.749)			[16]
NYHA III		0.590 (0.551, 0.629)			[16]
NYHA IV		0.508 (0.412, 0.605)			[16]
Disutility for HF re-hospitalization ^a		−0.321 (−0.10, −0.01)			[15]
Annualized risks of HF re-hospitalization in the two-stage model					
Device group		33.10% (27.79%, 38.41%)			[8]
GDMT group		57.20% (51.71%, 62.69%)			[8]
Annualized risk of all-cause death in the Markov model ^b					
Device group		16.30% (11.20%, 21.36%)			
GDMT group		17.40% (11.47%, 23.33%)			
Cost					
MitraClip device	¥322 000	£16 500	€16 000	\$30 000	Provided by Abbott
Index hospitalization (not including the MitraClip device)	¥18 062.9	£7516.0	€6430.2	\$28 657.0	[17–20]
HF re-hospitalization per episode	¥9031.5	£3758.0	€3215.1	\$14 328.5	[17–20]
Background resource use (annual per capita)	¥2326.1	£936.2	€595.1	\$2126.0	[6,15,17,18]
Drug (annual per capita)	¥5032.8	£480.0	€324.4	\$7063.0	[6,8,15,17,21]
Discounted rate	5%	3.5%	3%	3%	[22–25]
Life expectancy (years)					
Total	78.1	80.9	80.9	77.3	[26]
Male	75.3	79.0	78.6	74.5	[26]
Female	81.1	82.9	83.4	80.2	[26]
WTP	¥257 094	£30 000	€138 447	\$100 000	[22–25]

GDMT, guideline-directed medical therapy; HF, heart failure; NYHA, New York Heart Association; WTP, willingness to pay. Intervals in parentheses were tested in a one-way sensitivity analysis; as for inputs of costs, a range of half to twice of the cost was tested in a one-way sensitivity analysis, except for the cost of the MitraClip device.

^aSuch an input was scaled to represent estimated quality-adjusted life-year lost due to HF re-hospitalization and was applied for 1 month only.

^bThese inputs were calculated as an average of risk from the third year to the end of the fifth year for each group according to the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation trial.

cutaneous coronary intervention or coronary artery bypass grafting, myocardial infarction, new-onset permanent atrial fibrillation, stroke, new cardiac resynchronization therapy, a new pacemaker, and left ventricular assist device implantation or heart transplantation were not statistically different between the two groups,⁸ we did not introduce these parameters into our model.

Inputs of utility

The NYHA class reflected the activity of daily living and was regarded as a marker of health status. The utilities for NYHA classes were based on the result of the Cardiac Resynchronization—Heart Failure (CARE-HF) trial,¹⁶ which was a multicentre, international, randomized trial that compared a combination of pharmacologic therapy and cardiac resynchronization with pharmacologic therapy alone. Utilities of different NYHA classes were estimated from quality-of-life assessments using the EQ-5D at baseline and 90 days.¹⁶ Additionally, the disutility associated with HF re-hospitalization was 0.321, which was derived from the Dapagliflozin And Prevention of Adverse outcomes in Heart Failure (DAPA-HF) trial.¹⁵ Such an input was scaled to represent estimated quality-adjusted life-year (QALY) lost due to HF re-hospitalization and was applied for 1 month.¹⁵

Inputs of costs

There were four components of the inputs of costs (index HF hospitalization, HF re-hospitalization, background resource use, and drugs) in our model. Index HF hospitalization cost included the MitraClip device cost, ancillary procedural cost, complication management cost, and remaining non-procedural cost, and such costs were only calculated in the device group. The cost of the MitraClip device per procedure in our model, which did not vary with the number of clips used or implanted, was calculated according to the recommended price provided by the manufacturer (Abbott) and the result of the COAPT trial, which found that MitraClip was attempted in 293 of 302 (97.0%) patients in the device group.⁹ Because there were no nationally representative cost data for the hospitalization with MitraClip treatment, we used twice the HF re-hospitalization cost (higher than those in previous studies^{10–12}) as the point estimation for the non-device cost of the index HF hospitalization, which would make our estimation conservative.

Inputs of costs during follow-up (HF re-hospitalization, background resource use, and drugs) in our model were derived from the up-to-date studies, which were national representative for China, the United Kingdom, Germany, and the United States if available, public data of national websites, or other sources wherever possible,^{17–21,26} and details were shown in *Table 1* and Supporting Information, *Methods S1*. The costs of background resource use associated with HF were applied to patients in both groups and included contact

with primary care, a cardiologist visit, accident and emergency referrals (for the United Kingdom and Germany), or outpatient care (for mainland China and the United States). Because medication use during follow-up in both groups appeared to be similar and major medication changes during follow-up were not frequent,⁸ we assumed that the costs of drugs were similar and constant in both groups in our model. All costs from years before 2022 were converted to 2022 currency using a country-specific consumer price index (*Table 1* and Supporting Information, *Methods S1*).

Statistical analysis

In the base-case analysis, accumulated health utility, cost, and the incremental cost-effectiveness ratio (ICER) were calculated for a lifetime horizon (Supporting Information, *Methods S1*). The accumulated health utility was calculated as a time-weighted average of utility values, with the midpoint between assessments used as the transition between different health states, along with disutilities if HF re-hospitalization occurred. The accumulated cost was calculated as the sum of the costs of index HF hospitalization (only for the device group), HF re-hospitalization, background resource use, and drugs. We also reported the number of adverse events and cost components based on our simulated cohort of 1000 patients. The primary outcome was the lifetime ICER, which was calculated by dividing the differences in accumulated costs and accumulated health utilities between groups. When a treatment was both more expensive and more effective than another, ICER was used to determine the magnitude of the incremental cost for each unit of health improvement. An intervention was considered cost-effective if the ICER was lower than the willingness-to-pay (WTP) threshold. Country-specific WTP thresholds according to relevant guidelines were used to assess the cost-effectiveness of our study.^{23–25,27}

In order to test the impact of the uncertainty of a single input on our model results, a one-way sensitivity analysis with an interval for each input (*Table 1*) was performed, and the results were displayed with tornado diagrams. The effects of the simulation time span on ICER were also tested, and the ICERs were shown according to the country-specific life expectancy from the World Bank.²⁶ Additionally, the influence of the cost of MitraClip on ICER was also assessed for countries where the base case was not considered cost-effective. Furthermore, to assess the influence of simultaneous variation of the inputs on ICER, a probabilistic sensitivity analysis (PSA) was performed using specific variable distributions (Supporting Information, *Table S2*). A second-order Monte Carlo simulation was performed at random 1000 times. We displayed the results of PSA with scatter plots and country-specific cost-effectiveness acceptability curves.

Results

Base-case results for a lifetime horizon

The mean age of the base case in our model was 72.2 years. Over a lifetime horizon, treatment with MitraClip was estimated to be associated with 829 fewer HF re-hospitalizations per 1000 treated patients. In the device group, the cost of MitraClip accounted for 82.34%, 43.18%, 48.02%, and 22.49% of the lifetime total direct medical cost in mainland China, the United Kingdom, Germany, and the United States, respectively. The estimated proportions of different costs according to the results of our models are displayed in Supporting Information, *Table S3*. The MitraClip treatment was associated with fewer costs for HF re-hospitalization but more costs for background resources and drugs, which resulted in decreased total medical costs during follow-up of ¥187, £1495, €1558, and \$2012 per patient for a lifetime horizon in mainland China, the United Kingdom, Germany, and the United States, respectively. The MitraClip treatment was associated with incremental QALY gains of 0.71, 0.76, 0.78, and 0.78, as well as ICERs of ¥468 462, £28 910, €26 045, and \$71 199 per QALY gained for a lifetime horizon in mainland China, the United Kingdom, Germany, and the United States, respectively. The ICERs were lower than the country-specific WTP thresholds in all countries except mainland China (*Table 2*). As the ICER of mainland China was higher than the WTP, we evaluated the influence of the device cost on ICER, and the result showed that the ICER would be less than the WTP if the price was lower than ¥168 401 (Supporting Information, *Figure S1*).

Effect of life expectancy on incremental cost-effectiveness ratio

The effect of the simulation time span on the ICER was shown in Supporting Information, *Table S4*, indicating that patients with a longer life expectancy would have a lower ICER. Additionally, analyses based on the country-specific life expectancy by gender showed that the ICERs in females were lower than those in males across four countries (Supporting Information, *Table S5*).

Results of sensitivity analysis

In one-way sensitivity analyses, the variations of ICER were largely driven by the annual risk of mortality in the Markov model, index hospitalization cost, HF re-hospitalization cost, discount rate, and disutility of HF re-hospitalization (Supporting Information, *Figure S2*). The results of one-way sensitivity analyses were robust. Results of the PSA showed that the ICERs were ¥566 698, £27 448, €25 824, and \$67 877 in mainland China, the United Kingdom, Germany, and the United States, respectively (*Table 3* and *Figure 2*). In the second-order Monte Carlo simulation, 59.4%, 99.6%, and 84.7% of patients with the MitraClip treatment were considered cost-effective in the United Kingdom, Germany, and the United States according to the country-specific WTPs, while only 0.2% were in mainland China. The country-specific cost-effectiveness acceptability curves are displayed in *Figure 3*.

Table 2 Base-case results for lifetime horizon

Variables	Device group	GDMT group	Incremental
China			
Total costs	¥379 423	¥49 143	¥330 280
Total life years	4.60	3.75	0.85
Total QALYs	3.17	2.46	0.71
ICER	—	—	¥468 462/QALY
United Kingdom			
Total costs	£37 070	£15 041	£22 029
Total life years	4.89	3.96	0.93
Total QALYs	3.36	2.60	0.76
ICER	—	—	£28 910/QALY
Germany			
Total costs	€32 325	€11 930	€20 395
Total life years	4.99	4.03	0.96
Total QALYs	3.43	2.65	0.78
ICER	—	—	€26 045/QALY
United States			
Total costs	\$129 419	\$73 669	\$55 750
Total life years	4.99	4.03	0.96
Total QALYs	3.43	2.65	0.78
ICER	—	—	\$71 199/QALY
Clinical events			
Number of HF re-hospitalization (per 1000 treated patients)	2062	2891	829

GDMT, guideline-directed medical therapy; HF, heart failure; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

Table 3 Results of probabilistic sensitivity analysis

Variables	Device group	GDMT group	Incremental
China			
Total costs	¥373 937	¥48 385	¥325 552
Total QALYs	3.17	2.60	0.57
ICER	—	—	¥566 698/QALY
United Kingdom			
Total costs	£38 972	£20 948	£18 024
Total QALYs	3.32	2.66	0.66
ICER	—	—	£27 448/QALY
Germany			
Total costs	€33 924	€13 747	€20 177
Total QALYs	3.44	2.66	0.78
ICER	—	—	€25 824/QALY
United States			
Total costs	\$103 131	\$53 385	\$49 746
Total QALYs	3.41	2.68	0.73
ICER	—	—	\$67 877/QALY

GDMT, guideline-directed medical therapy; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

Discussion

To the best of our knowledge, our study is the first to evaluate the long-term cost-effectiveness of the MitraClip treatment based on the 5 year follow-up result of the COAPT trial. By using NYHA classes at a series of time points during a 5 year follow-up to calculate health utility instead of NYHA transition probabilities as reported in previous studies,^{12–15} our study makes the estimation of health utility more precise because NYHA transition probabilities may not be uniformly distributed. A study reported by Baron *et al.* estimated that the 5 year probability of all-cause death was 51.8% in the MitraClip group and 68.3% in the GDMT group.¹⁰ However, the recent published results of the COAPT trial showed that the actual 5 year all-cause mortality was 57.3% in the MitraClip group and 67.2% in the GDMT group.⁸ Such differences indicated that the estimation of mortality was underestimated not only in the MitraClip group but also in the GDMT group because the mitral transcatheter edge-to-edge repair was performed in 62 patients, representing 44.9% of the 138 patients after 2 years.⁸ Thus, there was a potentially large bias about the long-term cost-effectiveness evaluation in previous studies.^{10–13}

Although the use of MitraClip was associated with less HF re-hospitalization and death, which contributed to more QALYs gained and important cost savings during follow-up, our study showed that the cost-effectiveness of MitraClip was different across countries. The base-case analyses for three developed countries (the United Kingdom, Germany, and the United States) indicated that MitraClip + GDMT was cost-effective for HF patients with moderate-to-severe or severe secondary MR compared with GDMT alone, and both the one-way sensitivity analysis and the PSA showed that most results were robust. In contrast, the MitraClip treatment was not considered cost-effective in mainland China (the only developing country in our study). The results

of one-way sensitivity analyses showed that all inputs had limited influences on the ICERs, while the cost of the MitraClip device might have the most important impact on the ICER in mainland China. The present cost of the MitraClip device in China provided by Abbott [¥322 000, equal to around \$46 000 (¥7 = \$1 in 2023)] was higher than those in the other three countries (£16 500 in the United Kingdom, €16 000 in Germany, and \$30 000 in the United States). We found that only when the cost of MitraClip was less than ¥168 401 (equal to around \$24 057) would the MitraClip treatment be considered cost-effective in mainland China. Such a price is far less than the present one. This situation indicated that it is necessary to develop domestic devices for MR treatment and to lower the device price in China. At present, there are several domestic devices in China, such as the ValveClamp system (Hanyu Medical Technology, Shanghai),²⁸ the DragonFly system (DeJin Medtech Co., Hangzhou),²⁹ and the NovoClasp system (Yingmai Medical Technology, Shanghai),³⁰ which are under development and being tested in clinical trials. Recently, a first-in-human study demonstrated encouraging results in terms of safety and efficacy of the domestic DragonFly system for the treatment of severe MR in different aetiologies, and a larger pivotal trial with longer term follow-up is ongoing.²⁹

Potential burden of mitral regurgitation in heart failure

A recent cohort study indicated that the prevalence of moderate or severe secondary MR rose with advancing age.³¹ Severe secondary MR accounted for 25% of patients with reduced ejection fractions, 10% of patients with mid-range ejection fractions, and 4.5% of patients with preserved ejection fractions.³¹ Given an overall HF prevalence of 1–2%, it is estimated that there are 2.6–5.2 million Europeans with HF and moderate or severe secondary MR.³¹ In the United States, Carpentier IIIb was the largest group, leading to MR.³² The prevalence of Carpentier IIIb in the US adult population was 16 250 per million, and it was estimated that there were around 3.25 million patients with secondary MR in the United States in 2010.³² Although the epidemiological characteristics of MR in China are still unclear, it is estimated that ~7.5 million patients with MR need intervention in China, including 5.5 million patients with severe MR.³³ These modern epidemiological data on MR indicate an exponential public health threat and economic burden. And our study would not only help doctors and patients to make decisions in clinical practice but also help governments to make relevant healthcare policies for HF management to improve the allocation and application of limited medical resources in a certain region.

Figure 2 Scatter plots of probabilistic sensitivity analysis (PSA) in (A) China, (B) the United Kingdom, (C) Germany, and (D) the United States. Dots represent 1000 simulation patients in the PSA with different incremental cost-effectiveness ratios (ICERs) and costs between MitraClip added to guideline-directed medical therapy vs. guideline-directed medical therapy alone in four countries. Dotted lines represent the country-specific willingness-to-pay thresholds. Dots below the dotted lines mean these simulation patients are considered cost-effective if they receive MitraClip therapy, and vice versa. QALY, quality-adjusted life-year.

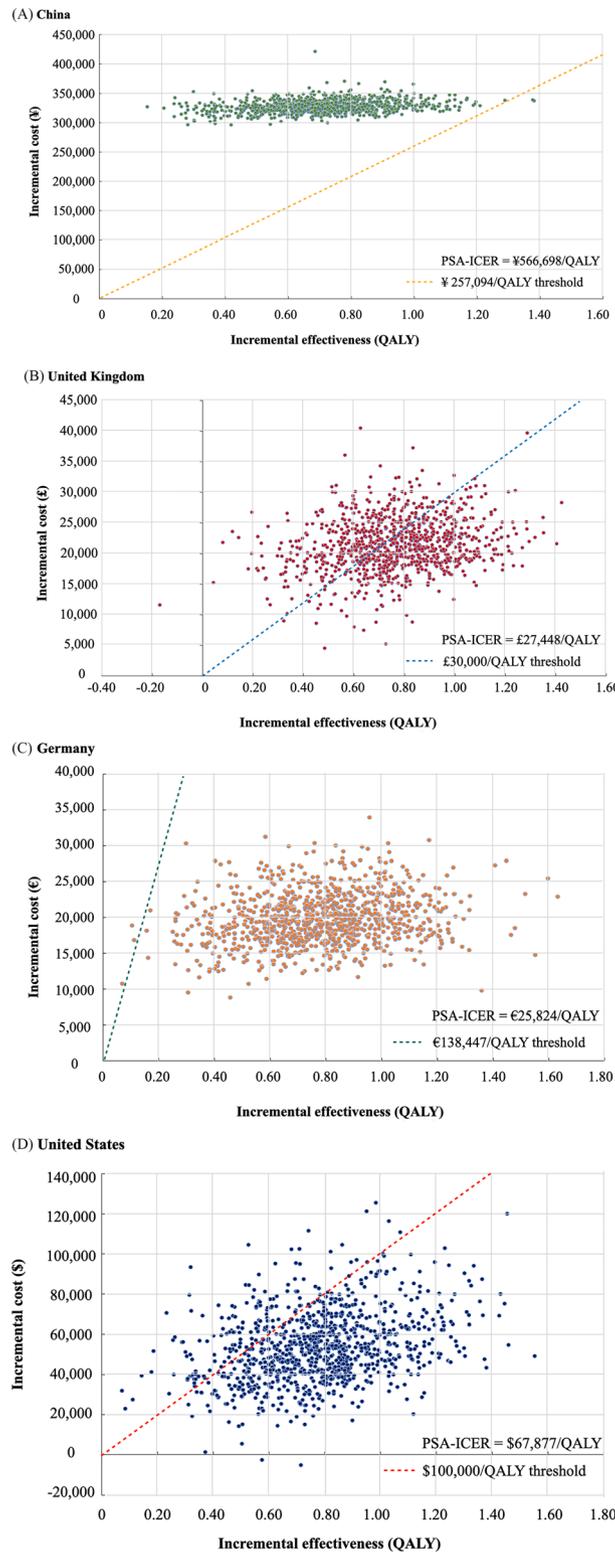
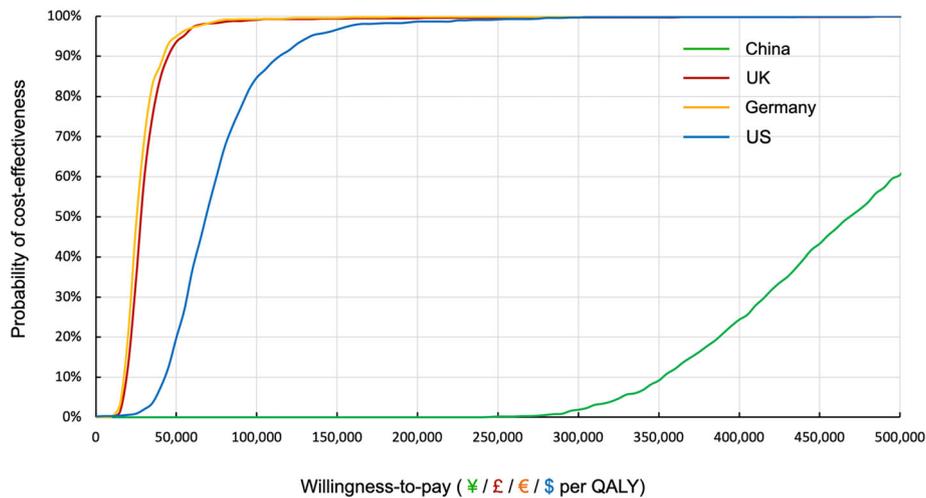


Figure 3 Cost-effectiveness acceptability curves. The probability of cost-effectiveness is derived from the probabilistic sensitivity analysis that demonstrates economically attractive results across a range of willingness-to-pay thresholds. QALY, quality-adjusted life-year.



MitraClip and contemporary guideline-directed medical therapy

It should be emphasized that optimized medical treatment based on current HF management guidelines should be applied before delivering mitral transcatheter edge-to-edge repair to HF patients with secondary MR. Notably, although sacubitril–valsartan and sodium–glucose co-transporter-2 inhibitor (SGLT2i) were recommended by current guidelines for HF management,^{34,35} there were only <5% of patients treated with sacubitril–valsartan at baseline and only three patients using SGLT2i within the final year of the follow-up in the COAPT trial.⁸ Consequently, whether these two drugs would modify the benefit of MitraClip in HF patients is unclear, and the effect and cost-effectiveness of MitraClip with modern GDMT need to be explored in the future. Additionally, if HF patients with secondary MR are appropriate for transcatheter mitral repair, according to the result of our study, the health-economic differences by gender and life expectancy ought to be considered because the MitraClip treatment may be more cost-effective for females or patients with a long life expectancy.

Study limitations

The results of our study should be considered in light of several limitations. First, the requirement to extrapolate beyond the follow-up duration of 5 years in the COAPT trial introduced uncertainty. However, sensitivity analyses showed that most results remained robust. Second, the costs and events unrelated to HF were not included in our analyses. Because

there were no differences in adverse events unrelated to HF between groups in the COAPT trial, a lack of relevant parameters in our model might have limited effects on the estimation of ICER. Third, the cost of the MitraClip device per procedure in our model did not vary with the number of clips used or implanted, which might also influence the extrapolation of our results. Furthermore, the efficacy of MitraClip in HF patients in mainland China, the United Kingdom, and Germany might be different from that in the COAPT trial because all participants were enrolled in the United States and Canada. In addition, direct non-medical costs and indirect costs were not included in our study; therefore, our study could not provide a cost-effectiveness assessment of MitraClip from the perspective of society. Last, because the clinical inputs of our models were based on a randomized clinical trial (the COAPT trial), the extrapolation of the results of our study was limited, and cost-effectiveness studies of MitraClip in HF patients based on real-world data in the future were needed.

Conclusions

Our study showed that the health-economic performances of percutaneous transcatheter edge-to-edge repair were different across countries from the perspective of the national healthcare system. The benefits of MitraClip, added to GDMT, were considered cost-effective in HF patients with moderate-to-severe or severe secondary MR in the United Kingdom, Germany, and the United States, but not in mainland China.

Conflict of interest

Y.Y., Z.Z., T.G., A.C., T.L., J.Y., J.C., and L.L. declare that they have no conflict of interest.

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Table S1. Proportions of five health states in the two-stage model.

Table S2. Distributions of variables in probabilistic sensitivity analysis.

Table S3. Proportions of different costs for a lifetime horizon in the model.

Table S4. Effect of time span on ICER.

Table S5. ICER based on country-specific life expectancy by gender.

Figure S1. Impact of the cost of the MitraClip device on ICER in China.

Figure S2. Results of the one-way sensitivity analysis.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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