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ORIGINAL ARTICLE

Are beta-blockers effective for preventing post-coronary artery bypass grafting atrial fibrillation? Direct and network meta-analyses

T. Ji[1] · C. Feng[2] · L. Sun[3] · X. Ye[4] · Y. Bai[2] · Q. Chen[2] · Y. Qin[2] · J. Zhu[2] · X. Zhao[2]

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Abstract

Background Atrial fibrillation is the most common arrhythmia in clinical practice and is a major contributor to mortality. Recently, several studies have reported different results for treatments aimed at reducing the risk of post-operative AF.

Aims The aim of this study was to evaluate the efficacy of beta-blockers (BBs) in preventing post-coronary artery bypass grafting (CABG) AF and to compare the efficacies of different BB treatments using a network meta-analytical approach.

Methods The PubMed, EMBASE and Cochrane Library databases were searched (Jan 1995 to May 2014) to identify randomized controlled trials. Two independent investigators separately extracted the data using a seven-point scoring system to assess randomization, allocation concealment, blinding, withdrawals and dropouts. A direct meta-analysis of these randomized controlled trials was conducted. Then, six trials comparing different BB treatments for the prevention of postoperative AF were added to perform a Bayesian network meta-analysis with mixed treatment comparisons.

Results Treatment with BBs was associated with a significant reduction in the postoperative incidence of AF compared with placebo/control [22.37 % compared with 34.45 %, relative risk (RR) = 0.53, 95 % confidence interval (CI): 0.37–0.75, $p < 0.00001$].

Conclusions The network meta-analysis revealed no significant differences among eight types of BB treatments but did provide a ranking. BB treatments could significantly reduce the occurrence of post-CABG AF. Insufficient evidence was available to show that one BB treatment was more effective than the others were. According to our network meta-analysis, bisoprolol and landiolol+bisoprolol are better alternatives compared with the other treatments.

Keywords Beta-blockers · Network meta-analysis · Atrial fibrillation · CABG

T. Ji, C. Feng, and L. Sun contributed equally to this work.

J. Zhu and X. Zhao also contributed equally to this work.

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✉ J. Zhu
zjq77324@126.com

✉ X. Zhao
13601713431@163.com

[1] Department of Geriatrics, Shanghai First People's Hospital Affiliated with Shanghai Jiaotong University, Shanghai, China

[2] Department of Cardiology, Changhai Hospital, Second Military Medical University, Shanghai, China

[3] Department of Nephrology, Shanghai Changzheng Hospital, Second Military Medical University, Shanghai, China

[4] Department of Health Statistics, Second Military Medical University, Shanghai, China

Introduction

Atrial fibrillation (AF) is the most common arrhythmia that occurs following coronary artery bypass grafting (CABG). The incidence of postoperative atrial fibrillation (POAF) ranges from 25 to 40 % after CABG surgery [1]. New-onset POAF significantly increases the cost and length of hospital stay [2] and is associated with a higher short-term mortality

after CABG [3] (3.6 % compared with 1.9 %; $p < 0.00001$), with mortality risks at 1 and 4 years of 2.56 [95 % confidence interval (CI) 2.14–3.08] and 2.19 (95 % CI 1.97–2.45; $p < 0.0001$), respectively. However, whether beta-blockers (BBs) can prevent POAF after CABG surgery remains unclear. Ebell [4], Wenke [5], Lucio [6], Connolly [7], Ogawa [8] and Sakaguchi [9] conducted trials supporting the effectiveness of BBs in preventing POAF after CABG. In contrast, Paull [10], Yazicioglu [11], Imren [12], Sezai [13] and Skiba [14] found that BBs are not effective; Bert [15] even concluded that BBs promote the occurrence of POAF. Additionally, an insufficient number of randomized controlled trials comparing different BBs for preventing post-CABG AF have been conducted, preventing a conclusion as to which BB functions best.

The observed relationships between BBs and AF morbidity in post-CABG studies are subject to appreciable random error, particularly due to the low number of cases in each study. Thus, to limit purely random errors and to minimize selective biases, meta-analyses of the studies are needed. The present meta-analysis differs from a previously conducted meta-analysis [16] in the following two ways that could possibly increase the reliability and informativeness of the analysis: (1) the present meta-analysis includes several new randomized controlled trials that used new BB treatments to prevent post-CABG AF and (2) a Bayesian network meta-analysis with mixed treatment comparisons using several indirect lines of evidence was conducted to identify which drug is more effective.

The aim of this study was to identify whether BB treatments were effective in preventing POAF after CABG and to then investigate the comparative efficacy of eight different types of BB treatments (bisoprolol, atenolol, betaxolol, carvedilol, landiolol, landiolol+bisoprolol, metoprolol, and propranolol) for the prevention of POAF. Because of the small number of randomized controlled trials that directly compared these drug classes, we performed a network meta-analysis to integrate both direct and indirect lines of evidence across multiple trials. Network meta-analyses provide a unified, coherent analysis of all randomized controlled trials that compare these agents with placebo/control. Therefore, we conducted the present meta-analysis of all available RCTs to determine the overall effectiveness of BB treatments in the prevention of post-CABG AF.

Methods

Study selection

We conducted a comprehensive literature search using the PubMed, EMBASE and Cochrane Library databases (1995 to May 2014) to identify randomized, placebo-controlled trials reporting the effect of BB treatments on perioperative prophylaxis for AF. We restricted our search to begin in 1995 for two primary reasons: first, off-pump (OP) CABG was introduced in the late 1990s, and second, the widespread use of peri-CABG cardio-protective medications (including acetyl salicylic acid, statins and angiotensin-converting enzyme inhibitors) began in the late 1990s.

We also used MeSH and TIAB terms for the MEDLINE search. The format used for the PubMed search was as follows:

#1: Atrial fibrillation
#2: Cardiac surgery
#3: Beta-blockers
#4: #1 and #2 and #3

Two investigators (Feng C. and Ji T.) independently reviewed a list of potentially relevant retrieved articles. When multiple articles for a single study had been published, we used the most recent publication and supplemented it with data from earlier publications when necessary. Only studies that clearly identified morbidity in tables or text for both the new-onset AF and non-new-onset AF groups were included in the final data set. We excluded studies on atrial flutter or tachycardia, off-pump CABG procedures, research studies on sotalol or isolated valve surgery (patients with CABG and valve replacement were excluded except for those patients in four studies by Bert, Connolly, Sakaguchi, and Skiba). Studies with the primary aim of evaluating a treatment or intervention were also excluded unless the preoperative or intraoperative data were useful for the purpose of our study. The cut-off left ventricular ejection fraction (LVEF) values for heart failure varied from one study to another as shown in Table 1 (from 20 to 40 %).

Studies were included if they met all of the following criteria: (1) included patients who underwent CABG surgery, (2) compared BBs with placebo or control treatment, (3) included new-onset AF in each group as an outcome, and (4) were randomized controlled human trials.

Date extraction, outcome measures and quality evaluation

Two investigators (Feng C. and Ji T.) separately extracted the data. Disagreement was resolved by consulting a third investigator (Zhu JQ.). Using a standardized data extraction form, we collected information on the first author, country, publication year, number of centers, inclusion criteria, exclusion criteria, drug regimen, time of BB administration, and AF definition. Two independent reviewers (Feng C. and Ji T.) evaluated the methodological quality of individual studies using the Jadad scale, which is a seven-point scoring system for randomization, allocation

Table 1 Characteristics of the included trials

First author	Country	Year	Timing	No. of centers	Drug regimen	Exclusion criteria	AF definition
Ebell [4]	Germany	1996	Postop	1	Propranolol	EF < 40 %	NK
Paull [10]	USA	1997	Postop	1	Metoprolol	EF < 30 %	NK
Wenke [5]	Germany	1999	Postop	1	Metoprolol	EF < 30 %	NK
Bert [15]	USA	2001	Postop	1	Propranolol	EF < 20 % AVR included	Sustained >5 min
Yazicioglu [11]	Turkey	2002	Preop	1	Atenolol	EF < 30 %	NK
Connolly [7]	Canada	2003	Postop	1	Metoprolol	CHF, valve surgery included	NK
Lucio [6]	Brazil	2004	Postop	1	Metoprolol	EF < 35 %	NK
Imren [12]	USA	2007	Preop	1	Metoprolol	CHF included	NK
Sezai [19]	Japan	2011	Periop	1	Landiolol	Cardiogenic shock	Persistence ≥5 min
Sezai [13]	Japan	2012	Postop	1	Landiolol	Cardiogenic shock	Persistence ≥5 min
Sakaguchi [9]	Japan	2012	Postop	1	Landiolol	EF < 40 %, valve surgery included	Persistence ≥1 min
Ogawa [8]	Japan	2013	Periop	1	Landiolol	EF < 30 %	Persistence ≥10 min
Skiba [14]	Australia	2013	Periop	1	Metoprolol	valve surgery included	NK

Postop postoperative, *Periop* perioperative, *Preop* preoperative, *EF* ejection fraction, *AVB* atrial ventricular block, *AVR* aortic valve replacement, *NK* not known, *CHF* congestive heart failure

concealment, blinding, withdrawals and dropouts. The rate of AF occurrence was investigated and summarized through all studies.

Statistical analysis

We used Review Manager (RevMan, version 5.0 for Windows, Oxford, United Kingdom; The Cochrane Collaboration, 2008) for statistical analysis. To summarize all available evidence, we conducted direct and network meta-analyses to compare the efficacy of BB treatments. In the conventional direct meta-analysis, two or more studies that compared two interventions of interest were statistically combined. We calculated the pooled risk ratio (RR) with a 95 % CI using a random-effects model. We used funnel plots and Egger's regression test to examine the potential publication bias, and we defined its significance as a p value of less than 0.05. A network meta-analysis was conducted using a Bayesian Markov chain Monte Carlo method and fitted in ADDIS software (Version 1.16.3; Drug Information Systems) together with the *R* package. Analytical results are presented as RR with 95 % credible intervals (CrIs). In the presence of minimally informative prior probabilities, the CrI can be interpreted as a conventional CI [17]. Rankings for the treatment efficacy of the 8 BB treatments and placebo were originally derived from Monte Carlo simulations and presented as the probability of possessing a specific ranking; the probabilities of different rankings of the same treatment were summed to 100 % [18]. Pooled results were considered statistically significant for $p < 0.05$ or if the 95 % CI (CrI) did not contain the value 1. The Bayesian p value was reported to measure the level of agreement between the direct and indirect evidence for each split node. Bayesian probability is one interpretation of the concept of probability and specifies some prior probability, which is then updated in the light of new data. After computing the prior information and sample information, a Bayesian p value was obtained. In addition, sensitivity analysis was conducted using the same computations with a fixed-effects model.

Results

Search results

A total of 401 citations were identified and screened. Of the 401 citations, 363 articles did not fulfill our selection criteria. The majority of excluded articles were review articles (131) and irrelevant articles (148). Finally, 13 randomized controlled trials that provided data regarding a total of 2357 patients were included in the direct meta-analysis (Fig. 1), and 18 trials were included in the network meta-analysis.

Study and patient characteristics

The randomized trials included in this meta-analysis are summarized in Table 1. Individual records for each of the 2357 participants in 13 studies were included in this meta-analysis; 55.54 % of the participants were from North America, 11.2 % were from Europe, and the remaining participants were from Turkey, Japan, Australia or South America. The trials were published from 1996 to 2013 and varied in sample size (range 60–1000; median 100). All studies were from a single center, and the major exclusion

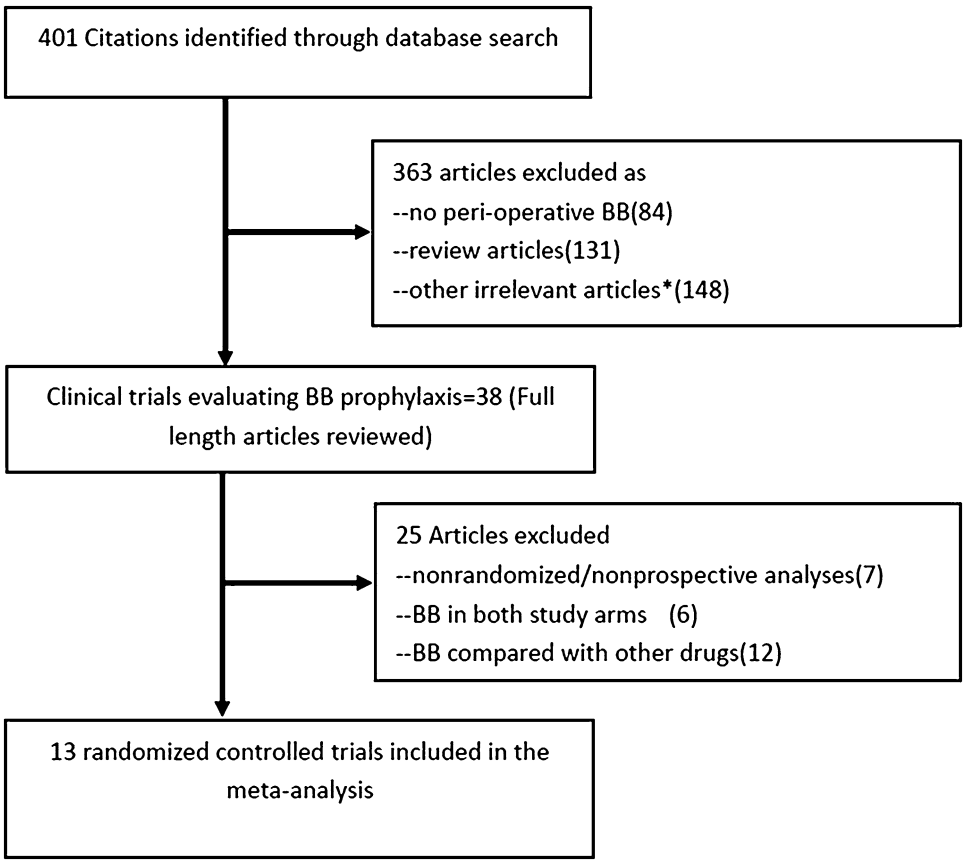

Fig. 1 Flow diagram of the selection process *Asterisk* including risk factors for post-CABG AF, treatment of AF, *letters* to editor, noncardiac surgery patients; *Dragger* all of these studies were included in the network meta-analysis

criterion for all of the studies was heart failure (EF <30 %). All Jadad scores were above 4 points, indicating that the quality of the trials was reliable (Table S1).

Direct meta-analysis

The results of the meta-analysis based on direct comparisons are presented in Fig. 2. We made the following assumptions: that the effect sizes differed from each other, that the baseline in all included studies was similar, and that the usage and dosage of each treatment in different studies were similar. Thus, we used a random-effects model for the direct meta-analysis. Overall, patients on prophylactic BBs had a 53 % reduced risk of developing post-CABG AF (RR = 0.53; 95 % CI 0.37–0.75 with $p = 0.0004$; $I^2 = 74$ %; $p < 0.0001$). Publication bias was assessed graphically with funnel plots (Figure S2) and using Egger's test ($p = 0.055$). Publication bias was statistically insignificant according to the results, indicating that there was no evidence to support publication bias in the direct meta-analysis. The BB group included 1158 patients, and POAF events were observed in 259 patients; the control group included 1199 patients, and POAF events were observed in 413 patients. The POAF incidence rate ranged from 14.1–36.7 % for each trial.

Network meta-analysis

After conducting the direct meta-analysis, we included 6 additional randomized controlled trials (2157 patients in total) that were excluded from the direct meta-analysis because BBs were used in both study arms. The total number of articles included in the network meta-analysis was 18 [a portion of the data in the article by Sezai et al. [13] was used in the direct meta-analysis]. We processed a network meta-analysis to investigate which BB was the most effective in preventing POAF. Table 2 shows the characteristics of these added trials.

As the trials between different BBs were few, we did not construct funnel plots for the network meta-analysis. As in the direct meta-analysis, we made the following assumptions: that the effect sizes differed from each other, that the baseline in all included studies was similar, and that the usage and dosage of each treatment in different studies were similar. Thus, a random-effects model was used in the Bayesian network meta-analysis. We assessed heterogeneity and found heterogeneity between propranolol and control ($I^2 = 90.50$ %; $p = 0.001$) and between metoprolol and control ($I^2 = 74.90$ %; $p = 0.001$). We did not find heterogeneity between landiolol and control ($I^2 = 0.00$ %; $p = 0.705$) or between carvedilol and metoprolol

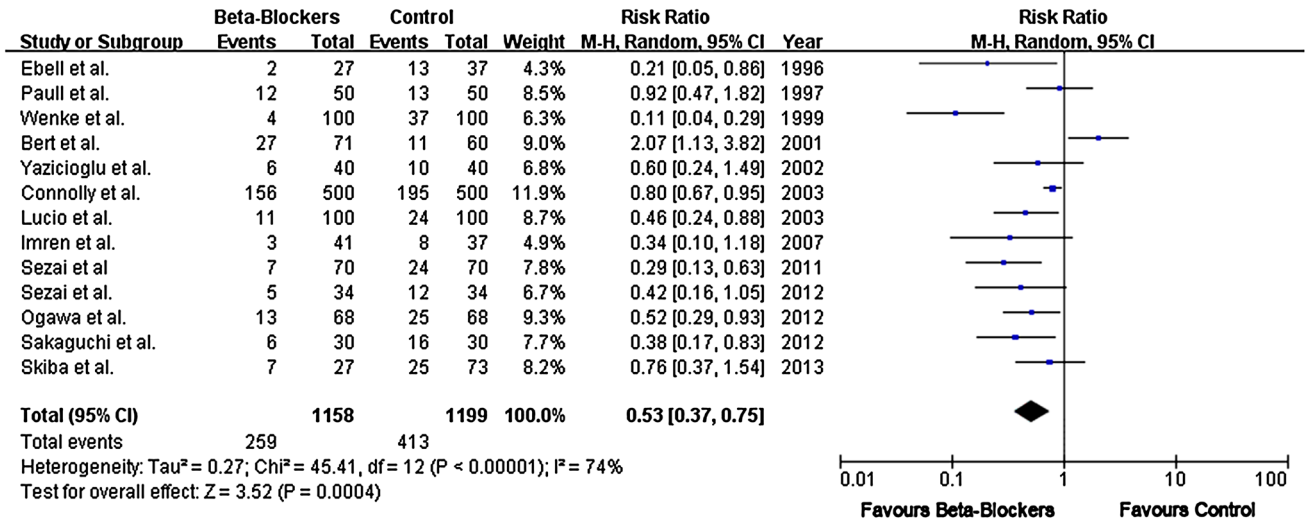

Fig. 2 Direct meta-analysis of BBs for preventing post-CABG AF

Table 2 Characteristics of the trials added to the network meta-analysis

First author	Country	Year	Timing	No. of centers	Drug regimen	Exclusion criteria	AF definition
Haghjoo [20]	Iran	2007	Periop	1	Carvedilol, metoprolol	CHF	sustained >5 min
Acikel [21]	Turkey	2008	Periop	1	Carvedilol, metoprolol	EF < 35 %	sustained >30 s
Iliuta [22]	Romania	2009	Periop	1	Betaxolol, metoprolol	CHF	NK
Marazzi [23]	Italy	2010	Postop	1	Bisoprolol, carvedilol	COPD	sustained >5 min
Sezai [13]	Japan	2012	Periop	1	Landiolol, landiolol+bisoprolol	Cardiogenic shock	persistence ≥5 min
Ozaydin [24]	Turkey	2013	Periop	1	Carvedilol, metoprolol	EF < 25 %	sustained >5 min

Postop postoperative, *Periop* perioperative, *Preop* preoperative, *EF* ejection fraction, *COPD* chronic obstructive pulmonary disease, *NK* not known, *CHF* congestive heart failure

($I^2 = 0.00$ %; $p = 0.572$). We evaluated the coherency between direct and indirect comparisons by the nod-split method and found no difference between the direct and indirect comparisons ($p > 0.05$). Thus, the data were combined using a consistency model.

Regarding the priors in the Bayesian network meta-analysis, we used three chains. The parameters were as follows:

```
#chain 1
  list(d=c(NA, 0, 0, 0, 0, 0, 0, 0, 0), sd=1,
       mu=c(0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0))
  #chain 2
  list(d=c(NA, -1, -1, -1, -1, -1, -1, -1, -1), sd=4,
       mu=c(-3, -3, -3, -3, -3, -3, -3, -3, -3, -3, -3,-3, -3, -3, -3,-3, -3, -3))
  #chain 3
  list(d=c(NA, 2, 2, 2, 2, 2, 2, 2, 2), sd=2,
            mu=c(-3, 5, -1, -3, 7, -3, -4, -3, -3, 0,-3, -3, 0, 3, 5, -3, -3, -1))
```

The network meta-analysis of comparisons for each outcome of interest is shown in Fig. 3 and Table 3. The numbers shown in Table 3 are RRs (95 % CI). Significant differences were found between the following groups in the

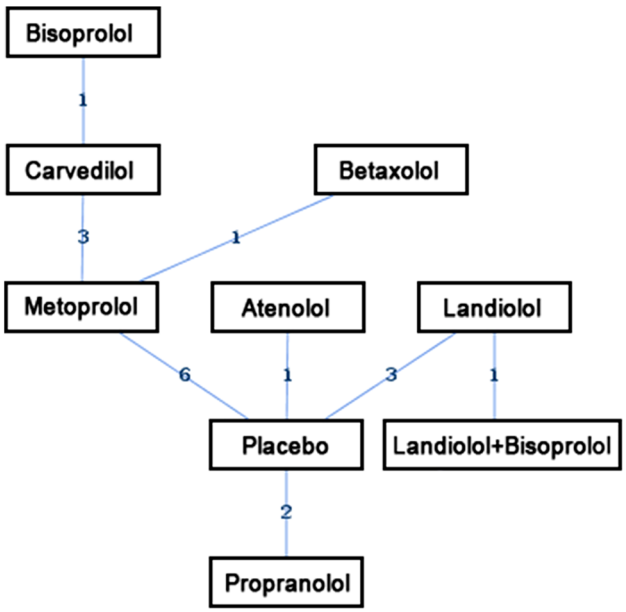

Fig. 3 Network of comparisons included in analyses. *Solid lines* represent direct comparisons within randomized controlled trials

Table 3 Network meta-analysis comparing the effects of bisoprolol, atenolol, betaxolol, carvedilol, landiolol, landiolol+bisoprolol, metoprolol, and propranolol on each outcome

Treatment	Bisoprolol	Atenolol	Betaxolol	Carvedilol	Landiolol	Landiolol+bisoprolol	Metoprolol	Propranolol	Placebo/control
Bisoprolol	–	–	–	–	–	–	–	–	–
Atenolol	0.17(0.01, 5.8)	–	–	–	–	–	–	–	–
Betaxolol	2.23(0.10, 51.02)	0.39(0.02, 8.74)	–	–	–	–	–	–	–
Carvedilol	1.80(0.24, 14.28)	0.32(0.02, 5.23)	0.81(0.07, 8.81)	–	–	–	–	–	–
Landiolol	2.84(0.18, 51.81)	0.50(0.03, 7.02)	1.31(0.11, 17.12)	1.59(0.21, 12.02)	–	–	–	–	–
Landiolol+bisoprolol	1.55(0.03, 69.63)	0.26(0.01, 9.96)	0.68(0.02, 24.96)	0.84(0.03, 21.29)	0.53(0.04, 6.83)	–	–	–	–
Metoprolol	4.38(0.41, 50.28)	0.78(0.06, 8.80)	1.99(0.26, 14.85)	2.43(0.70, 8.54)	1.53(0.32, 7.43)	2.90(0.14, 58.64)	–	–	–
Propranolol	9.21(0.42, 184.95)	1.60(0.08, 25.11)	4.17(0.25, 59.31)	5.02(0.53, 43.74)	3.13(0.38, 23.16)	5.80(0.22, 151.92)	2.05(0.30, 12.72)	–	–
Placebo/control	10.92(0.86, 147.92)	1.95(0.19, 18.94)	4.97(0.56, 44.98)	6.05(1.29, 29.48)	3.82(1.08, 13.71)	7.23(0.42, 126.10)	2.49(1.05, 6.23)	1.21(0.25, 6.68)	–

network meta-analysis: carvedilol and placebo/control; landiolol and placebo/control; metoprolol and placebo/control; and propranolol and placebo/control. Carvedilol, landiolol and metoprolol had better efficacy than placebo/control in preventing post-CABG AF. No significant differences were found for all other comparisons.

We then summarized the estimated probability that a given drug class would be the next best treatment for preventing POAF, with a rank of 1 as the worst and a rank of *N* as the best. In terms of POAF prophylaxis, bisoprolol was ranked as 9, with the highest probability, followed by landiolol+bisoprolol, whereas the placebo/control group was ranked as 1, with the highest probability, followed by propranolol (Table 4, Fig. 4).

We also evaluated the publication bias of the additional studies included for indirect comparison in the network meta-analysis. Publication bias was not found in the indirect comparisons, except in the comparison between carvedilol and metoprolol (Egger's test, $p = 0.007$).

To test the stability of the results, we performed sensitivity analysis by switching from a random-effects model to a fixed-effects model. We found that the results did not change (Table S3). Numbers shown in Table S3 are RRs (95 % CI).

Discussion

The updated American College of Cardiology Foundation/American Heart Association (ACCF/AHA) 2011 guidelines recommend the preoperative or postoperative initiation of BB therapy for preventing post-CABG AF (size of treatment effect: Class I; Level of Evidence: B). Due to recent debates regarding the perioperative use of BBs in non-cardiac surgery, we wanted to evaluate whether the ranking of BBs remains stable in the prevention of post-CABG AF. Therefore, we conducted this meta-analysis on cardiac surgery, particularly CABG, using the most recently published data to assess the efficacy of BBs and innovatively employed a network meta-analysis to evaluate the efficacy of different BB treatments.

Our results suggest that patients who develop POAF should undergo strict surveillance and routine screening for AF during follow-up after surgery. BBs are still useful for preventing POAF after CABG surgery. To the best of our knowledge, this is the first network meta-analysis of this evolving area that combines direct and indirect comparisons.

A prior meta-analysis of clinical trials performed by Khan et al. [16] indicated that the continuation of perioperative BB therapy in patients lacking contraindications to BB therapy is protective against post-CABG AF. We wanted to further confirm their conclusion and attempt to

Table 4 The estimated probability that a given drug class is the next best one for preventing post-CABG AF

Drug	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5	Rank 6	Rank 7	Rank 8	Rank 9
Bisoprolol	0.02	0.02	0.03	0.04	0.05	0.07	0.12	0.23	0.43
Atenolol	0.21	0.13	0.18	0.12	0.10	0.09	0.07	0.06	0.04
Betaxolol	0.04	0.04	0.06	0.10	0.13	0.16	0.18	0.17	0.12
Carvedilol	0.00	0.01	0.02	0.05	0.11	0.19	0.29	0.26	0.06
Landiolol	0.01	0.03	0.08	0.16	0.22	0.22	0.16	0.10	0.03
Landiolol+bisoprolol	0.05	0.04	0.06	0.06	0.08	0.10	0.12	0.17	0.31
Metoprolol	0.01	0.05	0.22	0.36	0.23	0.12	0.03	0.01	0.00
Propranolol	0.31	0.25	0.19	0.09	0.06	0.04	0.03	0.01	0.01
Placebo/control	0.37	0.43	0.16	0.03	0.01	0.00	0.00	0.00	0.00

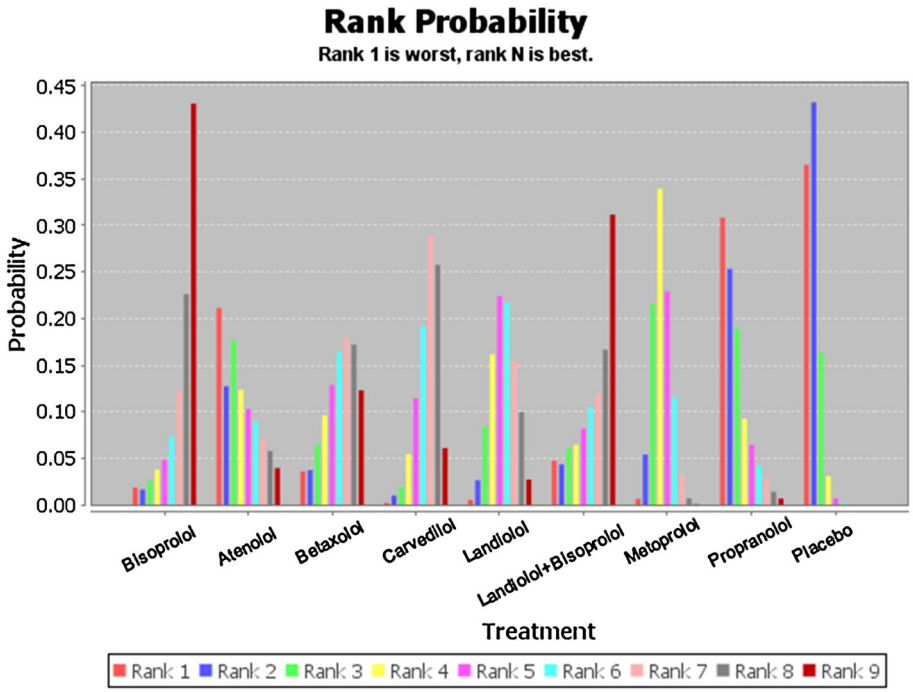

Fig. 4 Ranking of drug efficacy of BBs for preventing post-CABG AF

identify which BB has the best efficacy for preventing post-CABG AF. Our findings are in agreement with the conclusions of Khan et al. [16], with a few exceptions. First, compared with their study, our ten additional trials [5 in the direct meta-analysis, including Sezai [19], Sezai [13], Ogawa [8], Sakaguchi [9], and Skiba [14], and 6 in the network meta-analysis, including Haghjoo [20], Acikel [21], Iliuta [22], Marazzi [23], Ozaydin [24], and Sezai [13]. Notably, the study by Sezai was used both in the direct and network meta-analyses], which add new evidence to this field, were included in our analysis. Second, we employed a network meta-analysis to compare the efficacy of the following BB treatments: bisoprolol, atenolol, betaxolol, carvedilol, landiolol, landiolol+bisoprolol, metoprolol, propranolol, and placebo. According to our network meta-analysis, although no significant differences were found among the 8 BB types, the preventive effects of three regimens (carvedilol, landiolol and metoprolol) compared with placebo were demonstrated (Table 3). Additionally, the network meta-analysis allowed us to rank the different BB treatments. Table 4 shows the probability that each alternative will obtain each rank; the results are also visualized in Fig. 4. The rank probabilities sum to one, both within a rank for all treatment and within a treatment for all ranks. Rank 1 is the worst, indicating the highest AF incidence, and rank 9 is the best, indicating the lowest AF incidence. According to this rank probability (Table 4), bisoprolol and landiolol+bisoprolol are better alternatives compared with the other treatments because they have much higher scores for rank 9 (0.43 and 0.31, respectively), indicating that these BBs are associated with a lower AF incidence. In contrast, placebo is the worst, with the

highest probability in rank 1 (0.37) and the lowest probability in rank 9 (0.00). Propranolol has the second highest probability in rank 1 (0.31), indicating its lower effect. The other non-significant differences may due to the limited numbers of trials and the small sample size in this study. Moreover, Table 4 shows which drug is considered the best by the Bayesian probability method, while Table 3 provides a comparison of the effects between each two drug regimens. Notably, the conclusions of Tables 3 and 4 are not consistent because of the limited number of studies.

Based on the available information, it is difficult to evaluate the relationship between BB doses and the incidence of post-CABG AF. Different trials used different doses, and the doses were adjusted according to the heart rate and other characteristics of the patients. Therefore, the dose response could not be calculated from the available data. This dose difference remains one of the primary determinants of heterogeneity in this analysis.

The phenomenon of BB withdrawal is also a very important question that we were concerned about before our analysis. However, due to the limited data availability, most of the studies did not provide detailed information for us to analyze the significance of any BB withdrawal phenomenon in the occurrence of POAF. From the available data, approximately half of the control patients had been using BB before study inclusion. Thus, when these studies began, BB treatments were discontinued in these patients before surgery. Burt et al. [15] found that the incidence of POAF in patients withdrawn from BB was 39 %, an incidence substantially greater than the incidence of POAF in patients receiving BB preoperatively and postoperatively (20 %, $p < 0.001$) and greater than all combined patients not at risk of BB withdrawal (22 %, $p < 0.0001$). These results provide further information regarding the effects of BBs.

This study also had several limitations. First, the number of studies included in this meta-analysis was so small that it prevented the accurate assessment of the situation in the real world. Second, most of the trials were short term and did not provide long-term data for us to analyze. However, the network meta-analysis appears to be a reasonable tool and provides a cost-saving approach for evaluating comparative effectiveness in the absence of head-to-head clinical trials [18, 25]. Third, the network meta-analysis, which was conducted based on mixed treatment comparisons, might have led to a higher probability of heterogeneity among studies. We chose a consistency model in the analysis for each endpoint because all P values were greater than 0.05. Fourth, patients with CHF, COPD, a history of AF and an operation that combined CABG and valve procedures were excluded from many of the RCTs because these patients were at a higher risk for AF occurrence. Thus, the general conclusion of our study may not apply to these higher risk patients. Fifth, we did not assess the possible connection between gastroesophageal reflux disease (GERD) and AF induction in this meta-analysis because of a lack of information in the original studies. It is known that both diseases share some common risk factors, such as obesity, diabetes and sleep apnea, which may play a pivotal role in their pathogenesis [26]. The usage of BBs can relax visceral smooth muscle (β2 effect), which can reduce GERD to avoid new-onset AF. However, it is unfortunate that no studies have investigated this relationship thus far. Sixth, most of the studies did not provide discontinued timing of BBs in the control group patients who had already been taking BBs. Therefore, we cannot determine whether new-onset AF was induced by discontinuation of BB. Finally, head-to-head trials provide the strongest evidence when comparing interventions. However, the comparison in most head-to-head trials is often against placebo as opposed to another active treatment. Thus, evidence from our network comparison provides weaker evidence than head-to-head trials. Accordingly, the conclusions should be interpreted with caution, particularly the probabilities of which treatment is best, as these data can be tenuous if the network is sparse.

Conclusions

In summary, our meta-analysis has several limitations, but our findings are sufficiently provocative to suggest the continued use of BBs to prevent post-CABG AF. By setting our starting point at 1995, we attempted to minimize the confounding factors related to the evolution of CABG protocols and the medical management of CHD. According to our network meta-analysis, although no significant differences were found among the 8 BB treatments, bisoprolol and landiolol+bisoprolol might be better alternatives compared with the other treatments. Further research is required to investigate the best drug regimen for the prevention of POAF in patients who have undergone CABG.

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Compliance with ethical standards

Conflict of interest None declared.

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