Supplementary content

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Appendix 2 Search Strategy

Pubmed

(auricular fibrillation OR atrial fibrillation OR AF OR AFib) AND ("meta-analysis as topic"[MeSH:noexp] OR Meta-Analysis[ptyp] OR metaanaly*[tiab] OR meta-analy*[tiab])

Web of science

(TS=(atrial fibrillation AND TS= (meta-analysis OR metaanaly* OR meta-analy*) *AND* **LANGUAGE:** (English) *AND* **DOCUMENT TYPES:** (Article)

Cochrane review

Keyword:

Atrial fibrillation

Embase (Cochrane central database of triasls (373)

(auricular fibrillation OR atrial fibrillation) AND (meta-analysis OR metaanaly* OR meta-analy*)

Appendix 3 List of studies excluded after full-text evaluation with reasoning

eTable 1List of studies excluded after full-text evaluation with reasoning

Author, Year	Reason for exclusion
Zhang, 2016[1]	Different estimate measures
Disertori, 2012[2]	Another outcome
Schneider, 2010[3]	Another outcome
Bhuriya, 2011[4]	Another outcome
White, 2007[5]	Systematic review (no meta-analysis)
Samokhvalov, 2010[6]	Another outcome
Kodama, 2011[7]	Another outcome
Shiga, 2004[8]	Another meta-analysis with larger number of studies with same risk or protective factor
Alghamdi, 2005[9]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Mak, 2009[10]	Another outcome
Leong, 2016[11]	Another outcome
Tanboga,2016[12]	Another outcome
Liu, 2016[13]	Another outcome
Shepherd, 2008[14]	Systematic review (no meta-analysis)
Nomani, 2020[15]	Systematic review (no meta-analysis)
Kontogiorgis, 2016[16]	Systematic review (no meta-analysis)
Madrid, 2004[17]	Another outcome
Yang, 2014[18]	Another outcome
Patel, 2007[19]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Zhou, 2013[20]	Another outcome
Kulik, 2009[21]	Systematic review (no meta-analysis)
Winchester, 2010[22]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Dong, 2011[23]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Liakopoulos, 2012[24]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Chen, 2010[25]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Liakopoulos, 2008[26]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Elgendy, 2015[27]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Goh, 2015[28]	Systematic review (no meta-analysis)
Rezaei, 2016[29]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
An, 2017[30]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF

Yuan, 2017[31]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Zhen-Han, 2017[32]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Ma, 2018[33]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Zhang, 2019[34]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Zhang, 2011[35]	Different estimate measures
Baker, 2007[36]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Whitlock, 2020[37]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Baker, 2016[38]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Hill, 2019[39]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Polymeropoulos, 2016[40]	Systematic review (no meta-analysis)
Shi, 2018[41]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Bagshaw, 2006[42]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Buckley, 2007[43]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Sakamoto, 2014[44]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Ji, 2016[45]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Kim 2021[46]	Overlapping meta-analysis of risk or protective factors of AF
Thein, 2018[47]	Overlapping meta-analysis of risk or protective factors of AF
Weymann, 2017[48]	Different estimate measures
Kuhn, 2015[49]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Cheng, 2005[50]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Wijeysundera, 2005[51]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Zimmer, 2003[52]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Sedrakyan, 2005[53]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Trivedi, 2017[54]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Khan, 2013[55]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Harling, 2011[56]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Ali-Hassan-Sayegh, 2014[57]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF

Lee, 2016[58]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Salih, 2017[59]	Different estimate measures
Harrison, 2013[60]	Another outcome
De Oliveira, 2012[61]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Fairley, 2017[62]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Athanasiou, 2004[63]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Armaganijan, 2011[64]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Benedetto, 2013[65]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Costanzo, 2013[66]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Mozaffarian, 2013[67]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Xin, 2013[68]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Zhang, 2014[69]	Different estimate measures
Wu, 2018[70]	Other design
De Frutos, 2014[71]	Different estimate measures
Cappabianca, 2011[72]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Viviano, 2014[73]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Hu, 2017[74]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Burgess, 2006[75]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Lowres, 2018[76]	Another outcome
Öztürk, 2020[77]	Different estimate measures
Walter, 2020[78]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF
Bjerrum, 2020[79]	Systematic review (no meta-analysis)
Chokesuwattanaskul, 2020[80]	Systematic review (no meta-analysis)
Norhayati, 2020[81]	Another meta-analysis with larger number of studies for the same risk or protective factor of AF

Appendix 4 Criteria for evaluation of the credibility of evidence

eTable 1. Criteria for evaluation of the credibility of the evidence of observational studies

Classification	**Criteria**
Convincing evidence (Class I)	1. More than 1000 cases 2. Significant summary associations ($p<1x10^{-6}$) per random-effects calculations 3. No evidence of small-study effects 4. No evidence of excess of significance bias 5. Prediction intervals not including the null value 6. Largest study nominally significant ($p<0.05$) 7. No large heterogeneity (i.e., $I^2< 50\%$)
Highly Suggestive evidence (Class II)	1. More than 1000 cases 2. Significant summary associations ($p<1x10^{-6}$) per random-effects calculation 3. Largest study nominally significant ($p<0.05$)
Suggestive Evidence (Class III)	1. More than 1000 cases 2. Significant summary associations ($p<1x10^{-3}$) per random-effects calculations
Weak evidence (Class IV)	1. All other associations with $p\leq0.05$
Non-significant associations (NS)	1. All associations with $p >0.05$

eTable 2. Criteria for evaluation of the credibility of the evidence of RCTs

Grade level of evidence	**Number of downgrades**
High	0 downgrades
Moderate	1 -2 downgrades
Low	3-4 downgrades
Very Low	5-6 downgrades

Note: GRADE: Grading of Recommendations Assessment,Development and Evaluation.

Appendix 5 List of studies included in the umbrella meta-analysis with baseline characteristics

eTable 1 List of studies included in the umbrella meta-analysis with baseline characteristics

Study	**Type of studies included**	**Risk or protective factors of recurrence post cardiac surgery or intervention**	**Exposures**	**Non-exposures (comparator)**	**No of included studies estimates**	**Population (s)**	**AMSTAR 2**
Liu, 2019[82]	RCTs	Dexmedetomidine	Dexmedetomidine use	No use	13	Patients undergoing cardiac surgery	High quality
Miller, 2005[83]	RCTs	Magnesium	Low/high Magnesium dose administration	No administration	20	Patients undergoing cardiac surgery	Critially low quality
Henyan, 2005[84]	RCTs	Magnesium	Pre/intra/postoperative magnesium administration	No administration	5	Patients undergoing cardiothoracic surgery	Critially low quality
Guerra, 2017[85]	RCTs	Ranolazine	Ranolazine use	No use	5	Patients undergoing cardiac surgery	High quality
Patti, 2015[86]	RCTs	Statin pre-treatment	Statin use	No use	11	Patients undergoing	High quality

						cardiac surgery	
Putzu, 2016[87]	RCTs	Perioperative statin treatment	Statin use	No use	19	Patients undergoing cardiac surgery	High quality
Mariani, 2013[88]	RCTs	n-3 PUFAs	n-3 PUFA use	No use	8	Patients undergoing cardiac surgery	High quality
Liu, 2011[89]	RCTs	Omega-3 fatty acids	Omega-3 fatty acids use	No use	10	Patients undergoing cardiac surgery	Critially low quality
Guo, 2014[90]	RCTs	Omega-3 fatty acids combined with vitamin C and vitamin D	Use of omega-3 fatty acids combined with vitamin C and vitamin D	No use	11	Patients undergoing cardiac surgery	Moderate quality
Gu, 2012[91]	RCTs	Thoracic epidural anaesthesia post coronary artery bypass grafting	Use of thoracic epidural anaesthesia post coronary artery bypass grafting	No use	5	Patients undergoing coronary artery bypass grafting	Critially low quality
Li, 2020[92]	RCTs	Perioperative Glucose-Insulin-Potassium	Perioperative Glucose-Insulin-Potassium use	No use	13	Patients undergoing cardiac surgery	Moderate quality

Gillespie, 2005[93]	RCTs	Postoperative amiodarone	Postoperative Amiodarone use	No use	15	Patients undergoing cardiac surgery	Moderate quality
Chatterjee, 2013[94]	RCTs	Amiodarone	Oral, iv, pre- and peri-operative amiodarone use	No use	15	Patients undergoing cardiac surgery	Low quality
Ali-Hassan-Sayegh, 2015[95]	RCTs	Glucose–insulin–potassium treatment	Glucose–insulin–potassium treatment	No treatment	14	Patients undergoing cardiac surgery	High quality
Espinosa, 2016[96]	RCTs	Clevidipine	Clevidipine use	No use	4	Patients undergoing cardiac surgery	High quality
Violi, 2014[97]	RCTs	Antioxidants use	Antioxidants use	No use	15	Patients undergoing cardiac surgery	Critially low quality
Ling, 2018[98]	RCTs	Dexmedetomidine	Dexmedetomidine use	No use	9	Patients undergoing cardiac surgery	High quality
DiNicolantonio, 2014[99]	RCTs	Carvedilol use	Carvedilol use	Metoprolol use	4	Patients undergoing cardiac surgery	High quality
Li, 2015[100]	RCTs	Landiolol	Landiolol use	No use	9	Patients undergoing	High quality

						cardiac surgery	
Ho, 2009[101]	RCTs	Corticosteroids	Corticosteroids use	No use	18	Patients undergoing cardiac surgery	High quality
Athanasiou, 2004[102]	Retrospective cohorts	Off-pump technic	Off-pump technic	No Off-pump technic	8	Elderly patients undergoing cardiac surgery	Critially low quality
Wiesbauer, 2007[103]	RCTs	B-blockers	B-blocker use	No use	26	Patients undergoing cardiac surgery	Critially low quality
Litton, 2012[104]	Prospective cohorts, Retrospective cohorts	BNP or NT-proBNP	High BNP/NT-proBNP	Low BNP/ NT-proBNP	4	Patients undergoing cardiac surgery	Critially low quality
Phan, 2016[105]	Prospective cohorts, Retrospective cohort s	Obesity	Obese	Non-obese	32	Patients undergoing cardiac surgery	High quality
Liu, 2018[106]	Prospective cohort	blood transfusion	blood transfusion	No blood transfusion	8	Patients undergoing cardiac surgery	High quality
Rabi, 2010[107]	RCTs	Peri-operative GI/GIK infusion	Peri-operative GI/GIK infusion use	No use	12	Patients undergoing	Critially low quality

						cardiac surgery	
Liu, 2015[108]	RCTs	Anterior fat pad removal	Anterior fat pad removal	Anterior fat pad left intact	7	Patients undergoing CABG	Moderate quality
Geng, 2017[109]	RCTs	Perioperative antioxidant vitamin administration	Perioperative antioxidant vitamin administration	No administration	11	Patients undergoing cardiac surgery	High quality
Lennerz, 2017[110]	RCTs	Colchicine	Colchicine use	No use	5	Patients undergoing cardiac surgery	Moderate quality
Zhu, 2018[111]	RCTs	Dexmetodimine	Dexmetodimine use	No use	5	Patients undergoing cardiac surgery	High quality
Kaw, 2016[112]	RCTs	Diastolic dysfunction	Diastolic dysfunction	Normal diastolic function	3	Patients undergoing cardiac surgery	Moderate quality
Liu, 2014[113]	RCTs	N-acetylcysteine	N-acetylcysteine use	No use	10	Patients undergoing cardiac surgery	Critially low quality
Qaddoura, 2014[114]	Prospective cohorts	OSAS	OSAS	No OSAS	7	Patients undergoing CABG	Moderate quality

Hu, 2016[115]	RCTs	posterior pericardiotomy	posterior pericardiotomy	No posterior pericardiotomy	10	Patients undergoing CABG	High quality
Zhou, 2017[116]	Prospective cohort, Case-control	preoperative hypertension treatment	preoperative hypertension treatment	No preoperative hypertension treatment	25	Patients undergoing cardiac surgery	Moderate quality
Langlois, 2017[117]	RCTs	PUFA	PUFA use	No use	17	Patients undergoing cardiac surgery	High quality
Chen, 2019[118]	RCTs, Prospective cohorts	RAASi	RAASi use	No use	11	Patients undergoing cardiac surgery	High quality
Liu, 2014[119]	RCTs	Glucocorticoids	Use of different dose-schemes of glucocorticoids	No glucocorticoids	19	Patients undergoing cardiac surgery	High quality
Chen, 2020[120]	Prospective cohorts, Retrospective cohorts and Case controls	CHA2DS2-VASc	CHA2DS2-VASc ≥2	CHA2DS2-VASc <2	8	Patients undergoing cardiac surgery	Moderate quality
Guan, 2020[121]	Prospective cohorts, Retrospective cohorts	off-pump CABG	off-pump CABG	on-pump CABG	13	Patients with HF undergoing cardiac surgery	High quality

Liu, 2020[122]	Prospective cohorts, Retrospective cohorts	Postoperative	High Neutrophil/Lymphocyte Ratio	Low Neutrophil/Lymphocyte Ratio	12	Patients undergoing cardiac surgery	High quality
Ruan, 2020[123]	RCTs	Atrial pacing	Atrial pacing	No atrial pacing	21	Patients undergoing cardiac surgery	High quality
Yousuf Salmasi, 2020[124]	Retrospective cohort	Mini-sternotomy	Mini-sternotomy	Right anterior thoracotomy	5	Patients undergoing aortic valve replacement	Moderate quality
Khan, 2020[125]	RCTs	TAVR	TAVR	SAVR	5	Patients undergoing aortic valve replacement	High quality
Sun, 2020[126]	Retrospective cohort	RAASi	RAASi use	No use	2	Patients undergoing TAVR	Moderate quality
Angsubhakorn, 2020[127]	Retrospective cohorts	Transfemoral	Transfemoral	No transfemoral	7	Patients undergoing TAVR	Critially low quality
Reynolds, 2021[128]	RCTs	HTK	HTK	multidose cardioplegia	4	Patients undergoing cardiac surgery	Moderate quality

AF: Atrial Fibrillation; BMI: Body mass index; CABG: coronary artery bypass graft; CHADS VASc: Congestive heart failure, Hypertension, Age>75 years, DHA: docosahexaenoic acid; Diabetes, Stroke, Vascular disease, Age>65, female Sex; BNP: B-natriuretic peptide; CPAP: continuous positive airway pressure; DC: direct current; EPA: eicosapentaenoic acid; GIK: glucose insulin potassium infusion; HF: heart failure; HTK: Histidine-Tryptophan-Ketoglutarate; NAC: N-acetylcysteine; NT-proBNP: N-terminal pro B-natriuretic peptide; PUFAs: Polyunsaturated fatty acids; RAASi: renin angiotensin aldosterone system

inhibitors OSAS: obstructive sleep apnea syndrome; RCT: randomized controlled trial; SAVR: surgical aorta valve replacement; TAVR: transcatheter aorta valve replacement

Appendix 6 Non-significant risk/protective factors for postoperative AF, in meta-analyses of RCTs

eTable 1. Non-significant risk/protective factors for postoperative AF, in meta-analyses of RCTs

Author, Year	Predictor	Exposed/Unexposed as included in MA	k	n/N	Metric	ES (95% CI)	p	PI include null value	I2 %	SSE	ESB	LS sign	High RoB	GLE	AMSTAR 2 Quality
Reynolds 2021	HTK	HTK or multidose cardioplegia	4	76/363	OR	1.18(0.39, 3.57)	0.768	Yes	74.23	Yes	NP	No	>25%	NS	Moderate
Ruan 2020	left atrial pacing	left atrial pacing or not	3	85/224	OR	0.59(0.34, 1.02)	0.06	Yes	3.30	No	NP	No	≤25%	NS	High
Ruan 2020	right atrial pacing	right atrial pacing or not	8	191/764	OR	0.76(0.49, 1.18)	0.225	Yes	24.70	No	No	No	≤25%	NS	High
Liu 2015	High dose glucocorticoids	High dose glucocorticoids or not	3	55/208	RR	0.90(0.57, 1.42)	0.653	Yes	0.01	No	NP	No	>25%	NS	High
Zhu 2018	Dexmetodimine	Dexmetodimine or not	5	56/698	RR	0.70(0.26, 1.87)	0.481	Yes	55.14	No	No	No	>25%	NS	High
Kaw 2016	Diastolic dysfunction	Diastolic dysfunction or not	3	195/733	OR	2.67(0.45, 15.80)	0.276	Yes	91.66	No	No	No	>25%	NS	Moderate
Rabi 2010	GI/GIK infusion	GI/GIK infusion or not	12	688/1952	OR	1.04(0.36, 2.98)	0.940	Yes	95.06	No	Yes	No	>25%	NS	Critially low
Liu 2015	Anterior fat pad removal	Anterior fat pad removal or not	7	216/991	RR	1.41(0.85, 2.32)	0.180	Yes	70.38	Yes	Yes	No	>25%	NS	Moderate
Ling 2018	Sedation by Dexmetodimine	Sedation by Dexmetodimine compared to propofol, morphin and placebo	9	251/1295	OR	0.73(0.4, 1.33)	0.303	Yes	60.55	No	No	No	>25%	NS	High
Ali-Hassan-Sayegh 2015	GIK therapy	GIK therapy or not	14	277/1799	OR	0.72(0.48, 1.07)	0.108	Yes	56.20	No	Yes	No	≤25%	NS	High
Espinosa 2016	clevidipine	clevidipine or not	4	74/1820	RR	1(0.45, 2.25)	0.989	Yes	60.72	No	NP	No	≤25%	NS	High
Li 2020	Glucose-Insulin-Potassium Therapy	Glucose-Insulin-Potassium Therapy or not	13	203/1700	RR	0.8(0.63, 1.02)	0.074	Yes	1.43	Yes	No	Yes	>25%	NS	Moderate
Gu 2012	Epidural anaesthesia	Epidural anaesthesia or not	5	155/540	RR	0.57(0.27, 1.22)	0.149	Yes	83.03	Yes	Yes	No	>25%	NS	Critially low
Hemila 2017	Vitamin C use	Vitamin C use or not	5	268/889	RR	0.93(0.64, 1.35)	0.690	Yes	63.17	Yes	No	Yes	≤25%	NS	High
Henyan 2005	Intra-operative and postoperative initiation of magnesium administration	Intra-operative and postoperative initiation of magnesium administration or not	4	133/528	OR	1.02(0.68, 1.52)	0.942	Yes	1.38	No	NP	No	>25%	NS	Critially low

Henyan 2005	Preoperative initiation of magnesium administration	Preoperative initiation of magnesium administration or not	4	154/706	OR	0.38(0.14, 1.03)	0.06	Yes	81.56	Yes	No	No	>25%	NS	Critially low
Mariani 2013	n-3 PUFAs	n-3 PUFAs use or not	8	859/2687	RR	0.83(0.64, 1.06)	0.136	Yes	73.80	Yes	Yes	No	>25%	NS	High
Liu 2011	Omega-3 fatty acids	Omega-3 fatty acids use or not	10	903/1955	OR	0.81(0.57, 1.15)	0.240	Yes	64.68	No	No	No	>25%	NS	Critially low

Abbreviations: AF, Atrial Fibrillation; CE, class of evidence; CI, confidence interval; ES, effect size; ESB, excess significance bias; GIK, glucose insulin potassium infusion; GLE, GRADE level of evidence; GRADE: GRADE, Grading of Recommendations Assessment, Development and Evaluation; HTK, Histidine-Tryptophan-Ketoglutarate; I2, heterogeneity; K, number of studies for each factor; LS, largest study with significant effect; n, number of cases; N, total number of cohort per factor; NA, not assessable; NP, not pertinent, because the number of observed studies is less than the expected; NR, not reported; OR, odds ratio; PI, prediction interval; PUFAs: Polyunsaturated fatty acids; RoB, risk of bias; RR, risk ratio; SSE, small study effects; RCT, randomized controlled trial; vit, vitamin.

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