Original Article

Effects of Volatile Anesthetics on Myocardial Ischemia/Reperfusion: a Meta-Analysis

Neda Aram[1], Ali Reza Abadi[2], Zahra Nouri[1], Ali Dabbagh[1*]

Abstract

Background: Ischemia-reperfusion injury is one of the most important cellular mechanisms involved in myocardial injury; there is a possible protective role for volatile agents in myocardial cells against ischemia-reperfusion injury through inhibition of Ca2+ overload; in this review, the effects of volatile agents in myocardial ischemia-reperfusion were assessed using a meta- analysis methodology.

Materials and Methods: From 2007 to 2012, using the following keywords, ischemia reperfusion, volatile agent, volatile anesthetic, preconditioning, myocardial, protection, Sevoflurane, Isoflurane, and Desflurane. To select more related studies, the search was made narrower using "ischemia reperfusion" and "volatile agent" to yield in 38 articles which could be entered into study calculations, directly or indirectly, with one of the following indicators: odds ratio, standardized mean reference, relative risk and effect size.

Results: After final screening, 20 articles remaining as related to "the effects of volatile agents on myocardial ischemia/reperfusion". The study demonstrated significant decrease in myocardial ischemic region related to "exposure to volatile agents" ($p<0.01$); also, there was not statistically significant difference between the coverage areas of confidence intervals of 3 different drug doses: 1 MAC; 1.5 MAC and 2 MAC ($p>0.05$); at the same time, there was no statistically significant difference regarding the protective effects of volatile anesthetic gases on ischemic outcome ($p>0.05$).

Conclusion: This study demonstrated that all volatile anesthetics could lead to attenuation of myocardial infarct size; though there is no difference between different doses of volatile agents regarding their protective effects and the protective effects of volatile anesthetics are not different regarding their the main genes involved in cardio protection.

Keywords: volatile, ischemia reperfusion, ischemia reperfusion

Please cite this article as: Aram N, Abadi A R, Nouri Z, Dabbagh A. Effects of volatile anesthetics on myocardial ischemia/reperfusion: a meta-analysis. J Cell Mol Anesth. 2016;1(4):180-8.

1. Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Community Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding Author:
Ali Dabbagh, MD; Professor, Anesthesiology Research Center, Shahid Modarres Hospital, Sa'adat Abad, Tehran, Iran. Tel: (+98) 912-197 2368; Fax: (+98) 21-2243 2572.
Email: alidabbagh@yahoo.com; alidabbagh@sbmu.ac.ir
Received: August 26. 2016
Accepted: September 15, 2016

Introduction

Anesthetic drugs have multiple effects at the molecular and sub cellular levels; volatile agents being one of the most commonly used anesthetics for more than 150 years; having their important roles in the creation of 3 different aspects of anesthesia: i.e. hypnosis, amnesia and also, some degrees of muscle relaxation (1-3).

Ischemia-reperfusion injury is one of the most important cellular mechanisms involved in myocardial injury; characterized by cellular calcium overload leading to increased contracture of the myocardium (2, 4-7). There are many studies which demonstrate the protective role of volatile agents on myocardial cells against ischemia-reperfusion injury through inhibition of Ca2+ overload (5, 6, 8-10). However, these results are not always in concordance, especially when considering clinical reports, when reviewing the results of other organs or different volatile agents (3, 7, 11-15). This study was conducted to review the effects of volatile agents on myocardial ischemia-reperfusion using meta- analysis methods.

Methods

This study was conducted using meta-analysis method, using the "Strengthening the Reporting of Observational Studies in Epidemiology" (16-18). Those clinical trials investigating the effects of volatile agent on myocardial ischemia reperfusion were included in the study. The search methods: the following data banks and search engines were used: MEDLINE (mainly though pubmed.com), Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Library. The following keywords were used: ischemia reperfusion, volatile agent, volatile anesthetic, preconditioning, myocardial, protection, sevoflurane, Isoflurane, and Desflurane.

Based on the selection criteria and the keywords, 43021 manuscripts were found in this time period with "ischemia reperfusion" keywords; then, adding "volatile agent" to the previous keywords resulted in 85 manuscripts during the study period from 2007 to 2012; their texts were in English. These 85 articles were regarded as the sample size.

Among the above 85 articles, those which had the capability to calculate, directly or indirectly, one of the following indicators remained in the study: Odds ratio, Standardized mean reference, Relative risk, Effect size.

So, after considering the above indicators, only 38 articles matched the study criteria and so, remained for further analysis.

Data collection and analysis

To extract data, we used data collection forms based on table of variables; so, throughout the reviewing process, articles were collected and their data were imported to an Excel sheet. Data pooling and analysis was done using Forest analysis method (19-23).

Heterogeneity of studies was calculated using Tau-square calculation and if it was statistically significant, random effect (DerSimonian and Laird) model was used for data pooling; data were considered homogenous if I square result was less than 50%; otherwise, it was considered as heterogeneity; per needed, subgroup analysis was done using new recording. The results were demonstrated using Forest plot (21, 24-29). Egger's regression asymmetry test with funnel plot was used for detection and prevention of publication bias (30-32). Data analysis was done using Stata software, version 11.

Results

Using the study keywords, a total of 192 studies were enrolled; among them, 85 were related to the period of 2007 to 2012. From the above 85 studies, 38 ones were homogenous studies regarding volatile agents; which entered further analysis. Classifying them to “myocardial related” and “non myocardial related” studies, ended in 20 articles remaining as related to "the effects of volatile agents on myocardial ischemia/reperfusion".

After random effect analysis of the drug effects, the study demonstrated significant decrease in myocardial ischemic region related to "exposure to volatile agents" ($p<0.01$); the results of the "exposure" and "control" groups are demonstrated in Figures 1 and 2, respectively. Also, their related Forest plots are demonstrated in Figures 3 and 4, respectively.

On the other hand, the drug doses had no significant effect; in other words, there was not a

Study	ES	[95% Conf.	Interval]	% Weight
32	43.000	12.315	73.685	4.74
33	84.000	51.866	116.134	4.50
30	25.000	-12.955	62.955	3.68
31	28.000	-11.356	67.356	3.51
25	15.000	-7.131	37.131	6.42
26	21.600	-3.905	47.105	5.70
27	23.000	-8.175	54.175	4.66
28	26.000	-9.097	61.097	4.06
17	15.000	-7.131	37.131	6.42
18	64.000	21.927	106.073	3.20
19	55.000	33.197	76.803	6.50
20	65.000	35.438	94.562	4.93
22	49.000	18.016	79.984	4.69
34	17.000	-13.056	47.056	4.85
3	12.900	-8.999	34.799	6.48
15	19.700	-15.162	54.562	4.09
1	14.300	-16.385	44.985	4.74
5	14.900	-7.170	36.970	6.44
7	18.300	-5.665	42.265	6.02
10	17.163	-15.887	50.213	4.36
D+L pooled ES	30.090	21.051	39.129	100.00

Heterogeneity chi-squared = 37.75 (d.f. = 19) p = 0.006
I-squared (variation in ES attributable to heterogeneity) = 49.7%
Estimate of between-study variance Tau-squared = 203.5532

Test of ES=0 : z= 6.52 p = 0.000

Fig. 1. Summary of studies demonstrating ischemia results in "exposure group".

Study	ES	[95% Conf.	Interval]	% Weight
32	48.000	17.035	78.965	5.45
33	76.000	38.565	113.435	4.82
30	69.000	28.461	109.539	4.53
31	51.000	7.183	94.817	4.24
25	41.000	10.516	71.484	5.50
26	42.500	11.861	73.139	5.48
27	45.000	8.146	81.854	4.87
28	44.000	4.282	83.718	4.60
17	41.000	10.516	71.484	5.50
18	113.000	79.405	146.595	5.19
19	26.000	6.776	45.224	6.61
20	126.000	90.525	161.475	5.01
22	148.000	95.760	200.240	3.57
34	48.000	8.024	87.976	4.58
3	68.000	37.524	98.476	5.50
15	39.800	-3.105	82.704	4.32
1	25.000	-12.955	62.955	4.77
5	43.000	12.315	73.685	5.48
7	29.400	1.163	57.637	5.73
10	48.361	4.558	92.164	4.24
D+L pooled ES	56.747	43.204	70.290	100.00

Fig. 2. Summary of studies demonstrating ischemia results in "control group".

statistically significant difference between the coverage areas of confidence intervals of 3 different drug doses: 1 MAC; 1.5 MAC and 2 MAC (p value>0.05); the related results and its Forest plot are demonstrated in Figures 5 and 6, respectively.

Meanwhile, based on the gene group used for assessment of the effects, there was no statistically significant difference regarding the protective effects of volatile anesthetic gases on ischemic outcome (p value>0.05); the genes included group 1 (PI3 kinase, Akt, and PKC); group 2 (anti-apoptosis genes), and group 3 (caveolin 3, ICAM 1 and NF). The related results and its Forest plot are demonstrated in Figures 7 and 8, respectively.

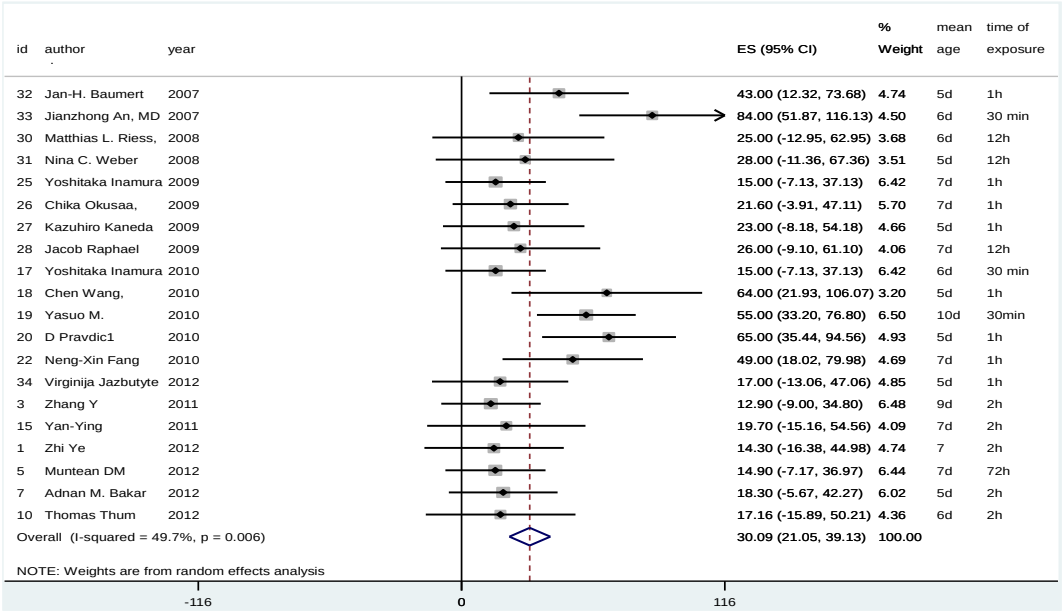


Fig. 3. Forest plot of the exposure group.

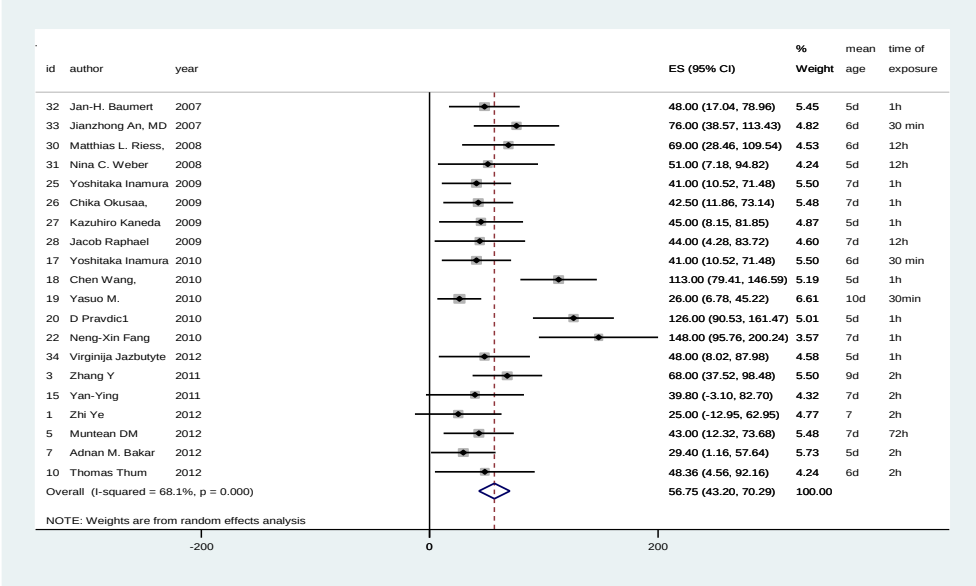


Fig. 4. Forest plot of the control group.

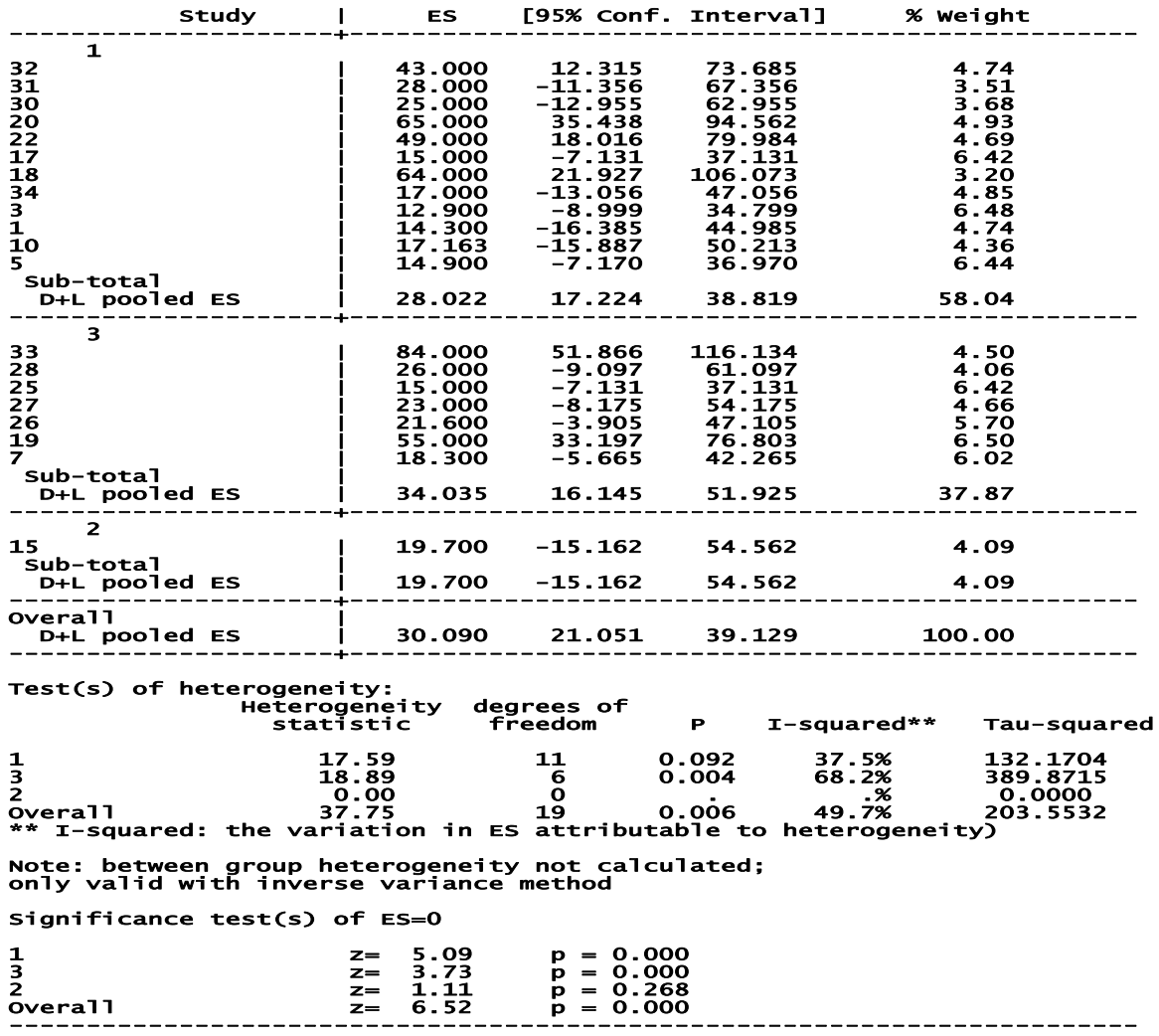
Also, the results of Egger's regression asymmetry test with funnel plot were not statistically significant to detection and prevention of publication bias (Table 1 and Figure 9).

Discussion

The results of this study demonstrated that volatile agents could decrease the size of myocardial infarct; while the drug dose and the related genes are not as much important in the final outcome.

Myocardial ischemia and infarction are not only among the leading causes of perioperative mortality, but are also among the main causes of prolonged hospitalization and patient readmission to the hospital. A number of these patients undergo anesthesia; while their exposure to volatile agents is a major point of concern.

This study demonstrated that myocardial



Study	ES	[95% Conf.	Interval]	% Weight
1				
32	43.000	12.315	73.685	4.74
31	28.000	-11.356	67.356	3.51
30	25.000	-12.955	62.955	3.68
20	65.000	35.438	94.562	4.93
22	49.000	18.016	79.984	4.69
17	15.000	-7.131	37.131	6.42
18	64.000	21.927	106.073	3.20
34	17.000	-13.056	47.056	4.85
3	12.900	-8.999	34.799	6.48
1	14.300	-16.385	44.985	4.74
10	17.163	-15.887	50.213	4.36
5	14.900	-7.170	36.970	6.44
Sub-total				
D+L pooled ES	28.022	17.224	38.819	58.04
3				
33	84.000	51.866	116.134	4.50
28	26.000	-9.097	61.097	4.06
25	15.000	-7.131	37.131	6.42
27	23.000	-8.175	54.175	4.66
26	21.600	-3.905	47.105	5.70
19	55.000	33.197	76.803	6.50
7	18.300	-5.665	42.265	6.02
Sub-total				
D+L pooled ES	34.035	16.145	51.925	37.87
2				
15	19.700	-15.162	54.562	4.09
Sub-total				
D+L pooled ES	19.700	-15.162	54.562	4.09
Overall				
D+L pooled ES	30.090	21.051	39.129	100.00

Test(s) of heterogeneity:

	Heterogeneity statistic	degrees of freedom	P	I-squared**	Tau-squared
1	17.59	11	0.092	37.5%	132.1704
3	18.89	6	0.004	68.2%	389.8715
2	0.00	0	.	.%	0.0000
Overall	37.75	19	0.006	49.7%	203.5532

** I-squared: the variation in ES attributable to heterogeneity)

Note: between group heterogeneity not calculated;
only valid with inverse variance method

Significance test(s) of ES=0

1	z= 5.09	p = 0.000
3	z= 3.73	p = 0.000
2	z= 1.11	p = 0.268
Overall	z= 6.52	p = 0.000

Fig. 5. Summary of studies regarding the effect of drug dose on ischemia results.

infarct size is decreased due to exposure to any of the volatile anesthetics. Reiss et al. demonstrated the effect of Sevoflurane at clinical effects (33). However, the results of this study demonstrated that exposure to volatile agents during anesthesia, regardless of agent or dose, could lead to attenuation of myocardial ischemia-reperfusion and decreasing the myocardial infarct size.

Ischemia reperfusion injury is prevented by volatile agents due to the anesthetic preconditioning effects of these agents involving the Ca2+ homeostasis mechanisms inside myocardial mitochondria and myocardial sarcoplasmic reticulum (34). This cardioprotective effect is mediated through a number of different cellular enzymatic processes including mitogen-activated protein kinases which could be blocked by hyperglycemia (35, 36). At the same time, the protective effects of volatile agents are mediated through increase level of "nitric oxide", nuclear factor-kappa B (NF-kappaB), "protein kinase B phosphorylation" and "glycogen synthase kinase 3 beta phosphorylation", regulation of the "expression of aromatase", activation of "protein kinase C: PKC" –which leads to a number of protective mechanisms including prevention of apoptotic pathways- and also, decrease in the level of "glycogen synthase kinase 3 beta" (36-43). Some of the studies have stressed on PKC-alpha and PKC-epsilon (and not PKC-delta) in creating the protective effects of Sevoflurane (40, 42, 44) and Isoflurane (36, 39).

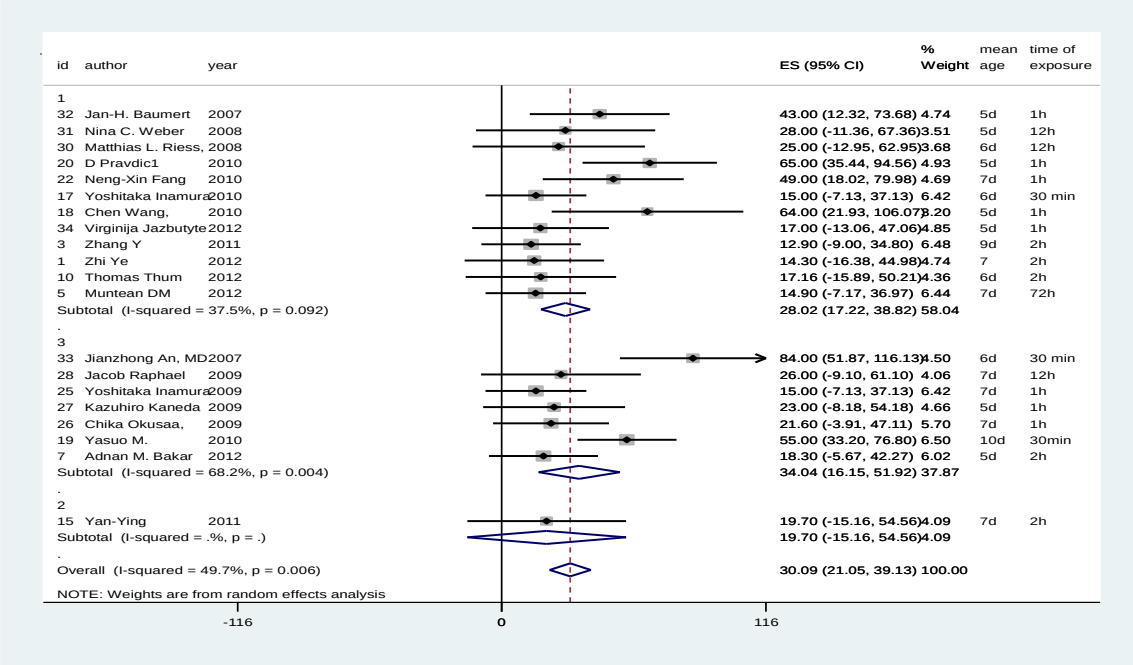


Fig. 6. Forest plot for the effect of drug dose on ischemia results.

Study	ES	[95% Conf.	Interval]	% Weight
1				
1	14.300	-16.385	44.985	4.74
3	12.900	-8.999	34.799	6.48
5	14.900	-7.170	36.970	6.44
20	65.000	35.438	94.562	4.93
27	23.000	-8.175	54.175	4.66
28	26.000	-9.097	61.097	4.06
31	28.000	-11.356	67.356	3.51
Sub-total				
D+L pooled ES	24.923	11.210	38.636	34.81
2				
7	18.300	-5.665	42.265	6.02
Sub-total				
D+L pooled ES	18.300	-5.665	42.265	6.02
.				
10	17.163	-15.887	50.213	4.36
15	19.700	-15.162	54.562	4.09
17	15.000	-7.131	37.131	6.42
18	64.000	21.927	106.073	3.20
22	49.000	18.016	79.984	4.69
25	15.000	-7.131	37.131	6.42
26	21.600	-3.905	47.105	5.70
33	84.000	51.866	116.134	4.50
34	17.000	-13.056	47.056	4.85
Sub-total				
D+L pooled ES	31.493	15.953	47.033	44.25
3				
19	55.000	33.197	76.803	6.50
30	25.000	-12.955	62.955	3.68
32	43.000	12.315	73.685	4.74
Sub-total				
D+L pooled ES	46.303	30.207	62.399	14.92
Overall				
D+L pooled ES	30.090	21.051	39.129	100.00

Fig. 7. Summary of studies regarding the effect of drug dose on ischemia results.

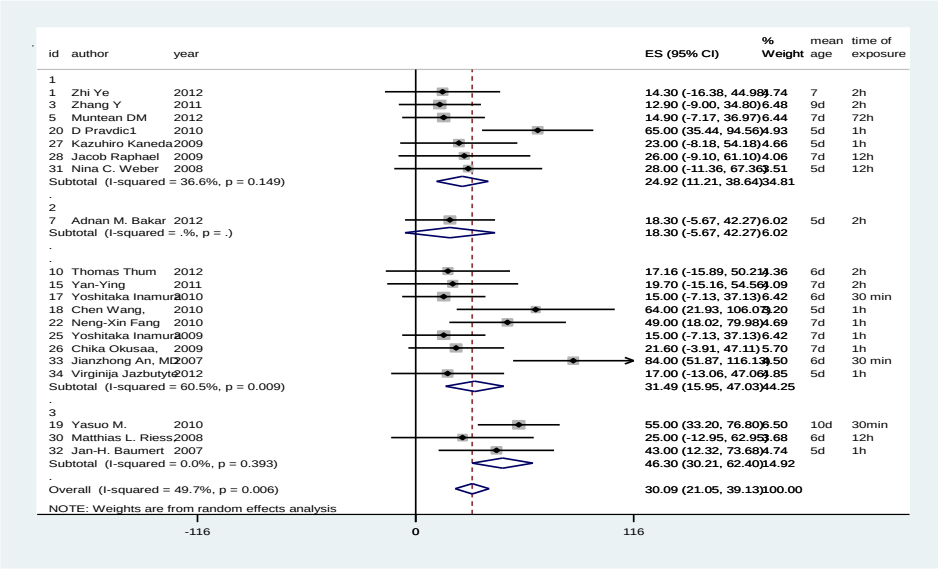


Fig. 8. Forest plot for the effect of drug dose on ischemia results.

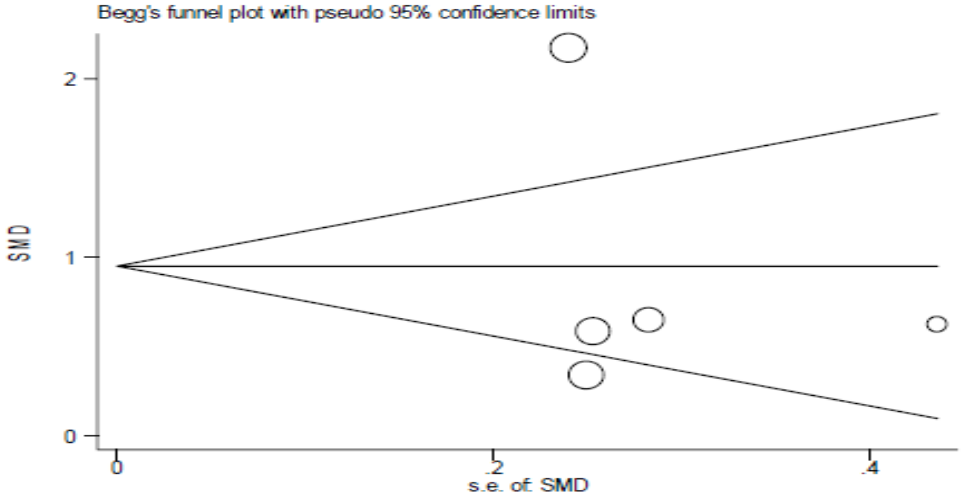


Fig. 9. Funnel plot for publication bias of selected studies.

Conclusion

Finally, the results of this meta-analysis demonstrated that the results are as the below:

1. All volatile anesthetics could lead to attenuation of myocardial infarct size.
2. There is no difference between different doses of volatile agents regarding their protective effects.
3. The protective effects of volatile anesthetics are not different regarding their the main genes involved in cardioprotection: group 1 (PI3 kinase, Akt, and PKC); group 2 (anti-apoptosis genes) and group 3 (caveolin 3, ICAM 1 and NF); all of them make ATP-

Table 1: Results of Egger's test for assessment of publication bias.

	Coefficient	Standard Error of Measurement	P value
Slope	1.99	2.99	0.43
Bias	-3.87	7.98	0.66

dependent potassium channels open.

Acknowledgment

The authors would like to acknowledge the personnel of Anesthesiology Research Center, SBMU, Tehran, Iran for their kind help.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

References

1. Solt K, Forman SA. Correlating the clinical actions and molecular mechanisms of general anesthetics. Curr Opin Anaesthesiol. 2007 Aug;20(4):300-6.
2. Kojima A, Kitagawa H, Omatsu-Kanbe M, Matsuura H, Nosaka S. Sevoflurane protects ventricular myocytes against oxidative stress-induced cellular Ca(2+) overload and hypercontracture. Anesthesiology. 2013 Sep;119(3):606-20.
3. Blum FE, Zuo Z. Volatile anesthetics-induced neuroinflammatory and anti-inflammatory responses. Med Gas Res. 2013;3(1):16.
4. Kojima A, Kitagawa H, Omatsu-Kanbe M, Matsuura H, Nosaka S. Sevoflurane protects ventricular myocytes from Ca2+ paradox-mediated Ca2+ overload by blocking the activation of transient receptor potential canonical channels. Anesthesiology. 2011;115(3):509-22.
5. Ma LL, Zhang FJ, Kong FJ, Qian LB, Ma H, Wang JA, et al. Hypertrophied myocardium is refractory to sevoflurane-induced protection with alteration of reperfusion injury salvage kinase/glycogen synthase kinase 3beta signals. Shock. 2013;40(3):217-21.
6. Ma LL, Zhang FJ, Qian LB, Kong FJ, Sun JF, Zhou C, et al. Hypercholesterolemia blocked sevoflurane-induced cardioprotection against ischemia-reperfusion injury by alteration of the MG53/RISK/GSK3beta signaling. Int J Cardiol. 2013 Oct 9;168(4):3671-8.
7. Muntean DM, Ordodi V, Ferrera R, Angoulvant D. Volatile anaesthetics and cardioprotection: lessons from animal studies. Fundam Clin Pharmacol. 2013 Feb;27(1):21-34.
8. Xu Y, Ma LL, Zhou C, Zhang FJ, Kong FJ, Wang WN, et al. Hypercholesterolemic myocardium is vulnerable to ischemia-reperfusion injury and refractory to sevoflurane-induced protection. PLoS One. 2013;8(10):e76652.
9. Swyers T, Redford D, Larson D. Volatile anesthetic-induced preconditioning. Perfusion. 2013 Sep 3.
10. Kojima A, Kitagawa H, Omatsu-Kanbe M, Matsuura H, Nosaka S. Presence of store-operated Ca2+ entry in C57BL/6J mouse ventricular myocytes and its suppression by sevoflurane. Br J Anaesth. 2012;109(3):352-60.
11. Singh P, Chauhan S, Jain G, Talwar S, Makhija N, Kiran U. Comparison of cardioprotective effects of volatile anesthetics in children undergoing ventricular septal defect closure. World J Pediatr Congenit Heart Surg. 2013;4(1):24-9.
12. Kiani A, Mirmohammad Sadeghi M, Gharipour M, Farahmand N, Hoveida L. Preconditioning by isoflurane as a volatile anesthetic in elective coronary artery bypass surgery. ARYA Atheroscler. 2013;9(3):192-7.
13. Turer AT, Hill JA. Pathogenesis of myocardial ischemia-reperfusion injury and rationale for therapy. Am J Cardiol. 2010;106(3):360-8.
14. Lang XE, Wang X, Zhang KR, Lv JY, Jin JH, Li QS. Isoflurane preconditioning confers cardioprotection by activation of ALDH2. PLoS One. 2013;8(2):e52469.
15. Van Allen NR, Krafft PR, Leitzke AS, Applegate RL, 2nd, Tang J, Zhang JH. The role of Volatile Anesthetics in Cardioprotection: a systematic review. Med Gas Res. 2012;2(1):22.
16. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453-7.
17. Ebrahim S, Clarke M. STROBE: new standards for reporting observational epidemiology, a chance to improve. Int J Epidemiol. 2007;36(5):946-8.
18. Brand RA. Standards of reporting: the CONSORT, QUORUM, and STROBE guidelines. Clin Orthop Relat Res. 2009;467(6):1393-4.
19. Lewis S, Clarke M. Forest plots: trying to see the wood and the trees. BMJ. 2001 Jun 16;322(7300):1479-80.
20. Yeh J, D'Amico F. Forest plots: data summaries at a glance. J Fam Pract. 2004;53(12):1007.
21. Ioannidis JP. Interpretation of tests of heterogeneity and bias in meta-analysis. J Eval Clin Pract. 2008;14(5):951-7.
22. Jansen JP, Crawford B, Bergman G, Stam W. Bayesian meta-analysis of multiple treatment comparisons: an introduction to mixed treatment comparisons. Value Health. 2008 Sep-Oct;11(5):956-64.
23. Thorlund K, Imberger G, Johnston BC, Walsh M, Awad T, Thabane L, et al. Evolution of heterogeneity (I2) estimates and their 95% confidence intervals in large meta-analyses. PLoS One. 2012;7(7):e39471.
24. Higgins JP. Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified. Int J Epidemiol. 2008;37(5):1158-60.
25. Patsopoulos NA, Evangelou E, Ioannidis JP. Sensitivity of between-study heterogeneity in meta-analysis: proposed metrics and empirical evaluation. Int J Epidemiol. 2008;37(5):1148-57.
26. Patsopoulos NA, Evangelou E, Ioannidis JP. Heterogeneous views on heterogeneity. Int J Epidemiol. 2009;38(6):1740-2.
27. Coory MD. Comment on: Heterogeneity in meta-analysis should be expected and appropriately quantified. Int J Epidemiol. 2010 Jun;39(3):932; author reply 3.
28. Jackson D, White IR, Thompson SG. Extending DerSimonian and Laird's methodology to perform multivariate random effects meta-analyses. Stat Med. 2010 May 30;29(12):1282-97.
29. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177-88.
30. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997 Sep 13;315(7109):629-34.
31. Song F, Khan KS, Dinnes J, Sutton AJ. Asymmetric funnel plots

and publication bias in meta-analyses of diagnostic accuracy. Int J Epidemiol. 2002;31(1):88-95.
32. Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Comparison of two methods to detect publication bias in meta-analysis. JAMA. 2006;295(6):676-80.
33. Riess ML, Costa AD, Carlson R, Jr., Garlid KD, Heinen A, Stowe DF. Differential increase of mitochondrial matrix volume by sevoflurane in isolated cardiac mitochondria. Anesth Analg. 2008;106(4):1049-55, table of contents.
34. An J, Bosnjak ZJ, Jiang MT. Myocardial protection by isoflurane preconditioning preserves Ca2+ cycling proteins independent of sarcolemmal and mitochondrial KATP channels. Anesth Analg. 2007;105(5):1207-13.
35. Weber NC, Goletz C, Huhn R, Grueber Y, Preckel B, Schlack W, et al. Blockade of anaesthetic-induced preconditioning in the hyperglycaemic myocardium: the regulation of different mitogen-activated protein kinases. Eur J Pharmacol. 2008;592(1-3):48-54.
36. Raphael J, Gozal Y, Navot N, Zuo Z. Hyperglycemia inhibits anesthetic-induced postconditioning in the rabbit heart via modulation of phosphatidylinositol-3-kinase/Akt and endothelial nitric oxide synthase signaling. J Cardiovasc Pharmacol. 2010;55(4):348-57.
37. Inamura Y, Miyamae M, Sugioka S, Kaneda K, Okusa C, Onishi A, et al. Aprotinin abolishes sevoflurane postconditioning by inhibiting nitric oxide production and phosphorylation of protein kinase C-delta and glycogen synthase kinase 3beta. Anesthesiology. 2009;111(5):1036-43.
38. Kaneda K, Miyamae M, Sugioka S, Okusa C, Inamura Y, Domae N, et al. Sevoflurane enhances ethanol-induced cardiac preconditioning through modulation of protein kinase C, mitochondrial KATP channels, and nitric oxide synthase, in guinea pig hearts. Anesth Analg. 2008;106(1):9-16.
39. Raphael J, Zuo Z, Abedat S, Beeri R, Gozal Y. Isoflurane preconditioning decreases myocardial infarction in rabbits via up-regulation of hypoxia inducible factor 1 that is mediated by mammalian target of rapamycin. Anesthesiology. 2008;108(3):415-25.
40. Inamura Y, Miyamae M, Sugioka S, Domae N, Kotani J. Sevoflurane postconditioning prevents activation of caspase 3 and 9 through antiapoptotic signaling after myocardial ischemia-reperfusion. J Anesth. 2010;24(2):215-24.
41. Wang C, Xie H, Liu X, Qin Q, Wu X, Liu H, et al. Role of nuclear factor-kappaB in volatile anaesthetic preconditioning with sevoflurane during myocardial ischaemia/reperfusion. Eur J Anaesthesiol. 2010;27(8):747-56.
42. Fang NX, Yao YT, Shi CX, Li LH. Attenuation of ischemia-reperfusion injury by sevoflurane postconditioning involves protein kinase B and glycogen synthase kinase 3 beta activation in isolated rat hearts. Mol Biol Rep. 2010 Dec;37(8):3763-9.
43. Jazbutyte V, Stumpner J, Redel A, Lorenzen JM, Roewer N, Thum T, et al. Aromatase inhibition attenuates desflurane-induced preconditioning against acute myocardial infarction in male mouse heart in vivo. PLoS One. 2012;7(8):e42032.
44. Okusa C, Miyamae M, Sugioka S, Kaneda K, Inamura Y, Onishi A, et al. Acute memory phase of sevoflurane preconditioning is associated with sustained translocation of protein kinase C-alpha and epsilon, but not delta, in isolated guinea pig hearts. Eur J Anaesthesiol. 2009;26(7):582-8.