

Supplementary Table S1. Search strategy in detail.

| Category | Search terms |
|-------------------------|---|
| Terms | Pubmed: MeSH term Embase: Entrée term with synonyms on major focus Cochrane: Suggested keywords |
| Intervention/Comparison | Pubmed: cilostazol Embase: cilostazol Cochrane: cilostazol |
| Outcomes | Pubmed: 'major adverse cardiovascular events' OR 'myocardial infarction' OR 'stroke' OR 'cardiovascular diseases' Embase: 'cardiovascular disease' OR 'heart infarction' OR 'cerebrovascular accident' Cochrane: 'cardiovascular event rate' OR 'cardiovascular disease' OR 'myocardial infarction' OR stroke |
| Study design | Randomized controlled trial |
| Intervention time | At least 3 months Studies with intervention periods of less than 3 months are excluded, as these cases often transitioned to other conventional therapies or targeted secondary prevention that could be attributed to factors unrelated to atherosclerosis. |
| Restrictions | Filter: humans, English, randomized controlled trial Search field: title or abstract Publication type: article Not animals |
| Search date | From 2000/1/1 to 2023/7/13 |
| Search results | Pubmed: 83 results Embase: 188 results Cochrane: 225 results |

Supplementary Table S2. Definition of cardiovascular events.

| Trial | Major adverse cardiovascular events |
|-----------------------------|---|
| Gotoh F et al. 2000 [95] | Cerebral infarction, intracranial hemorrhage, MI, or vascular death |
| Douglas JS et al. 2005 [96] | Major adverse cardiovascular events not specified |
| Chen YD et al. 2006 [97] | Death, nonfatal MI, stent thrombosis, TLR, or stroke |
| Lee SW et al. 2007 [98] | Death, MI, or target vessel revascularization |
| Hiatt WR et al. 2008 [99] | Total number of cerebrovascular accidents, carotid artery stenosis, femoral artery occlusion, and cardiac arrest |
| Huang Y et al. 2008 [100] | Recurrent stroke, new MI, transient ischemic attack, vascular event—including pulmonary embolism, deep venous thrombosis, or peripheral arterial occlusion disorder—death from vascular causes, or death from any other cause |
| Lee SW et al. 2008 [101] | Death, MI, or target lesion revascularization |
| Guo JJ et al. 2009 [102] | Total number of deaths, acute coronary event, intracerebral hemorrhage, and ischemic stroke |
| Han Y et al. 2009 [103] | Cardiac death, nonfatal MI, stroke, or TVR |

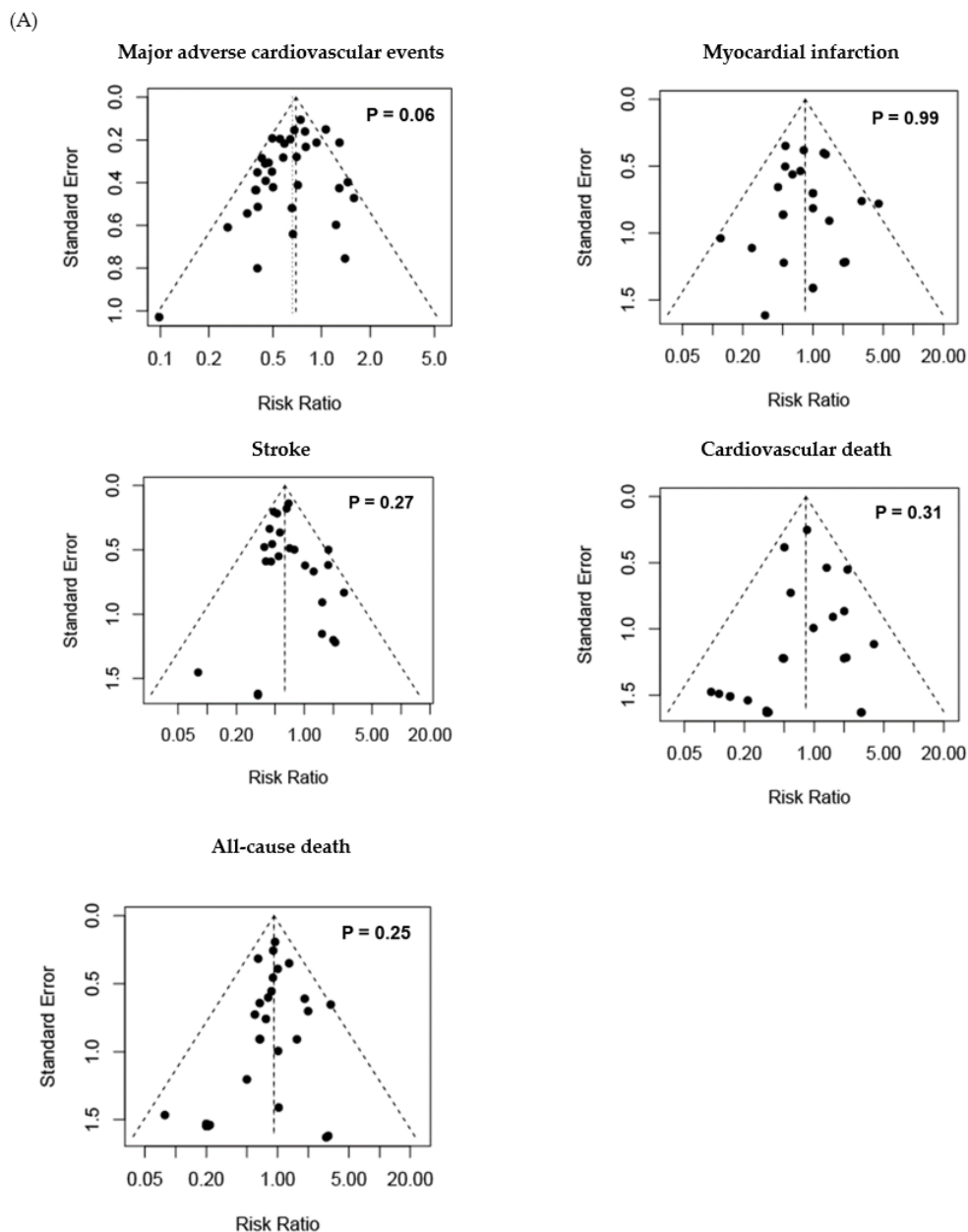
| | |
|------------------------------|--|
| Soga Y et al. 2009 [104] | Total number of deaths, nonfatal MI, stroke, and repeat revascularization |
| Katakami N et al. 2010 [18] | Sudden cardiovascular death, new onset or recurrence of cerebral infarction or transient cerebral ischemia, development of angina or acute myocardial ischemia, or exacerbation of peripheral artery disease |
| Shinohara Y et al. 2010 [20] | Any stroke, transient ischemic attack, angina pectoris, MI, heart failure, or any hemorrhage requiring hospital admission |
| Kwon SU et al. 2011 [105] | Vascular death, nonfatal stroke, or nonfatal MI |
| Lee SW et al. 2011 [106] | Death, MI, or ischemic-driven TLR |
| Lee YS et al. 2011 [107] | Vascular death, nonfatal stroke, nonfatal MI, hospitalization for cardiovascular events |
| Suh JW et al. 2011 [108] | Cardiac death, MI, ischemic stroke, or TLR |
| Iida O et al. 2013 [109] | All-cause death, MI, or stroke |
| Gao W et al. 2013 [110] | Death, MI, or TLR |
| Youn YJ et al. 2014 [111] | All-cause mortality, any MI, or repeat revascularization |
| Uchiyama S et al. 2015 [112] | Death, ischemic stroke, myocardial infarct, or other vascular events |
| Ueda H et al. 2016 [113] | All-cause death, nonfatal MI, nonfatal stroke, or coronary or cerebrovascular revascularization |
| Zheng X-T et al. 2016 [114] | Cardiac death, MI, or TLR |
| Tang Y-D et al. 2018 [115] | All-cause death, MI, target vessel revascularization, or stroke |
| Lee CH et al. 2018 [116] | All-cause death, MI, ischemic stroke, or ischemic-driven TVR |
| Kim BJ et al. 2018 [117] | Stroke (including hemorrhagic stroke), MI, or vascular death |
| Hong S et al. 2019 [118] | Acute MI, coronary-artery bypass graft, PCI, ischemic stroke, hemorrhagic stroke, or death due to any cardiovascular event |
| Toyoda K et al. 2019 [119] | Vascular death, stroke, or MI |
| Chen Y-C et al. 2019 [120] | Death, MI, or revascularization of the original lesion |
| Uchiyama S et al. 2021 [121] | Stroke, MI, or vascular death |
| Kalantzi K et al. 2021 [122] | Acute ischemic stroke, transient ischemic attack, acute MI, or death from vascular causes |
| Sohn M et al. 2022 [123] | Cardiovascular death, nonfatal MI, nonfatal stroke, angina, or hospitalization for heart failure |
| Lin J-L et al. 2022 [124] | Cardiovascular death, nonfatal MI, nonfatal stroke, hospitalization for heart failure, or unplanned coronary revascularization |
| Wardlaw JM et al. 2023 [125] | Total number of stroke, transient ischemic attack, MI, or all-cause death |
| Park S et al. 2023 [129] | All-cause death, recurrent MI, stroke, and repeat revascularization |

MI, myocardial infarction; PCI, percutaneous coronary intervention; TLR, target lesion revascularization; and TVR, target vessel revascularization

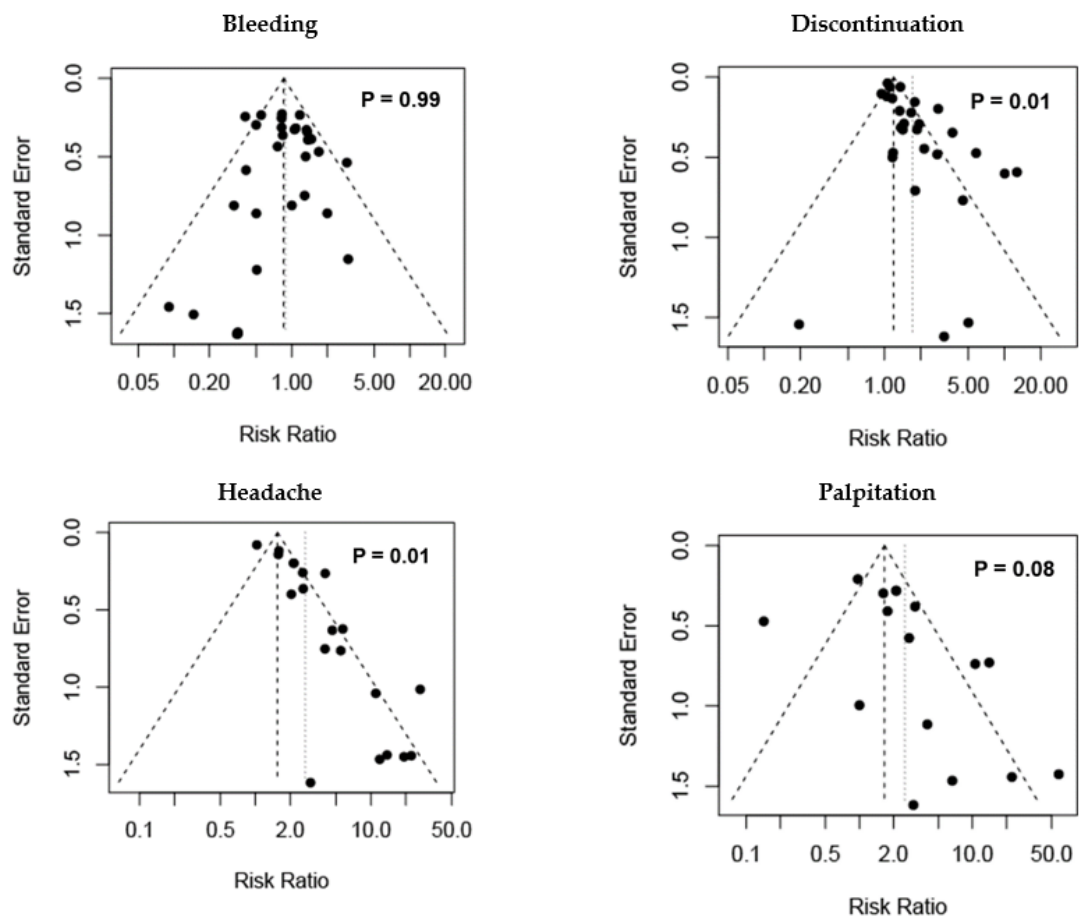
| | Gotoh F et al. 2000 | Douglas JS et al. 2005 | Chen YD et al. 2006 | Lee SW et al. 2007 | Huatt WR et al. 2008 | Huang Y et al. 2008 | Lee SW et al. 2008 | GUO T et al. 2009 | Han Y et al. 2009 | Sora Y et al. 2009 | Kakihara N et al. 2010 | Shimohara Y et al. 2010 | Kwon SU et al. 2011 | Lee SW et al. 2011 | Lee YS et al. 2011 | Shih IW et al. 2011 | Iida O et al. 2013 | Gao W et al. 2013 | Youn YI et al. 2014 | Uchiyama S et al. 2015 | Ueda H et al. 2016 | Zheng X-T et al. 2016 | Tang Y-D et al. 2017 | Lee CH et al. 2018 | Kim BI et al. 2018 | Hong S et al. 2019 | Tovoda K et al. 2019 | Chen Y-C et al. 2019 | Uchiyama S et al. 2021 | Kalantzi K et al. 2021 | Sohn M et al. 2022 | Lin T-L et al. 2022 | Wardlaw IM et al. 2023 | Paul S et al. 2023 |
|--|---------------------|------------------------|---------------------|--------------------|----------------------|---------------------|--------------------|-------------------|-------------------|--------------------|------------------------|-------------------------|---------------------|--------------------|--------------------|---------------------|--------------------|-------------------|---------------------|------------------------|--------------------|-----------------------|----------------------|--------------------|--------------------|--------------------|----------------------|----------------------|------------------------|------------------------|--------------------|---------------------|------------------------|--------------------|
| D1: Bias arising from the randomization process. | + | + | + | + | ? | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| D2: Bias due to deviations from intended intervention. | ? | + | + | + | + | + | + | + | + | + | + | + | + | + | ? | + | + | + | + | + | ? | ? | + | + | + | + | + | + | ? | ? | + | + | + | + |
| D3: Bias due to missing outcome data. | + | ? | + | + | + | + | ? | + | + | + | + | + | + | + | ? | + | + | + | + | + | + | + | + | ? | ? | + | + | + | + | + | + | + | + | + |
| D4: Bias in measurement of the outcome. | + | + | + | + | ? | + | ? | + | + | + | + | ? | + | + | + | + | + | + | + | + | ? | + | + | + | + | + | + | + | + | + | + | + | + | + |
| D5: Bias in selection of the reported result. | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

Judgement: + low risk; ? some concerns; - high risk

Supplementary Figure S1. Risk-of-bias among trials included in the meta-analysis.

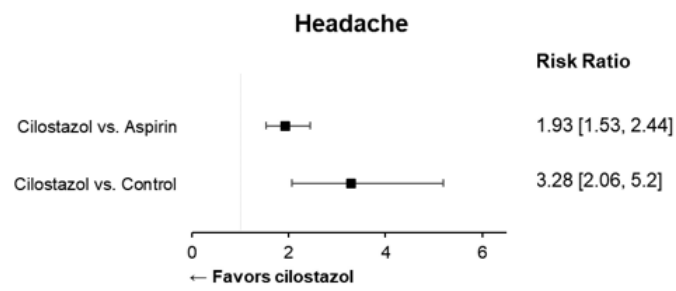


(B)

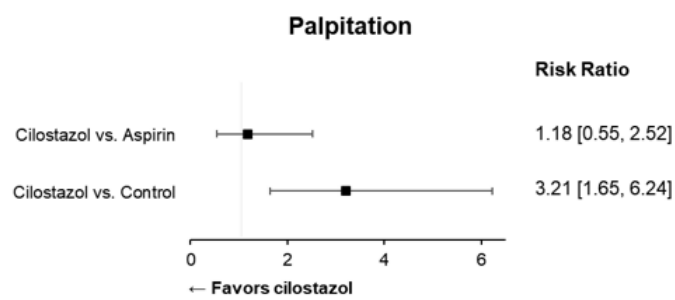


Supplementary Figure S2. Funnel plot of meta-analysis of clinical trials with (A) cardiovascular events and (B) other safety events.

(A)



(B)



Supplementary Figure S3. Forest plots of cilostazol in adverse events: (A) headache and (B) palpitation.