Supplementary

Table S1 Search strategy

Databases	Search strategy	Total (articles)
Cochrane Library	 #1 ranolazine #2 late sodium channel blocker #3 #1 or #2 #4 (microvascular angina) or (microcirculatory function) #5 (cardiac syndrome X) or (nonobstructive coronary artery disease) or (coronary microvascular dysfunction) or (ischemic heart disease without obstructed coronary arteries) or (nonobstructive coronary artery disease) or (INOCA) or (angina with nonobstructive coronary arteries) or (ANOCA) #6 #4 or #5 #7 #3 and #6 	42
PubMed	(ranolazine) OR (late sodium channel blocker) AND (cardiac syndrome X OR nonobstructive coronary artery disease OR coronary microvascular dysfunction OR ischemic heart disease without obstructed coronary arteries OR nonobstructive coronary artery disease OR INOCA OR angina with nonobstructive coronary arteries OR ANOCA)	57
Embase	('ranolazine'/exp OR ranolazine OR 'late sodium channel blocker' OR (late AND ('sodium'/exp OR sodium) AND channel AND blocker)) AND ('cardiac syndrome x'/exp OR 'cardiac syndrome x' OR (cardiac AND ('syndrome'/exp OR syndrome) AND x) OR 'coronary microvascular dysfunction'/exp OR 'coronary microvascular dysfunction' OR (coronary AND microvascular AND dysfunction) OR 'microcirculatory function'/exp OR 'microcirculatory function' OR (microcirculatory AND function) OR 'ischemic heart disease without obstructed coronary arteries' OR (ischemic AND ('heart'/exp OR heart) AND ('disease'/exp OR disease) AND without AND obstructed AND coronary AND ('arteries'/exp OR arteries)) OR 'nonobstructive coronary artery disease'/exp OR 'nonobstructive coronary artery disease' OR (nonobstructive AND coronary AND ('artery'/exp OR artery) AND ('disease'/exp OR disease)) OR INOCA) OR 'angina with nonobstructive coronary arteries' OR (('angina'/exp OR angina) AND with AND nonobstructive AND coronary AND ('arteries') oR (ANOCA)	
CNKI	(主题:雷诺嗪)AND(主题:心绞痛 + 缺血性心肌病 + 非阻塞性冠状动脉疾病 + 冠状动脉微循环)NOT (篇名:进展 + Meta分析 + 综述)	58
CBM	(((缺血) OR (心绞痛)) OR (((cardiac syndrome X) or (nonobstructive coronary artery disease) or (coronary microvascular dysfunction) or (ischemic heart disease without obstructed coronary arteries) or (nonobstructive coronary artery disease) or (INOCA) or (angina with nonobstructive coronary arteries) or (ANOCA)) OR (心脏X综合征) OR (冠脉微循环))) AND (雷诺嗪)	78

INOCA, ischemia with nonobstructive coronary arteries; ANOCA, angina with nonobstructive coronary arteries; CNKI, China National Knowledge Infrastructure; CBM, Chinese BioMedical Literature Database.



Figure S1 Results of the Cochrane risk of bias summary.



Figure S2 The sensitivity analysis of CFR among patients followed up for 2 to 12 weeks. CFR, coronary flow reserve.

	Ran	olazin	e	pl	acebo			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Villano 2013	1.76	0.4	15	1.74	0.5	15	16.9%	0.04 [-0.67, 0.76]	
Tagliamonte 2015	2.54	0.44	29	1.99	0.32	29	0.0%	0.55 [0.35, 0.75]	
Shah 2017	1.82	0.83	35	1.8	0.9	35	39.5%	0.02 [-0.45, 0.49]	
Safdar 2017	1.9	0.4	21	1.6	0.4	10	14.3%	0.73 [-0.05, 1.51]	+ · · · ·
Koh 2020	2.12	0.98	11	2.04	1.09	11	12.4%	0.07 [-0.76, 0.91]	
Golino 2018	1.18	0.15	15	1.17	0.13	15	16.9%	0.07 [-0.65, 0.79]	
Total (95% CI)			97			86	100.0%	0.14 [-0.15, 0.44]	-
Heterogeneity: Chi ² = 2.59, df = 4 (P = 0.63); I ² = 0%									-1 -0.5 0 0.5 1
Test for overall effect: Z = 0.94 (P = 0.34)								Favours (control) Favours (Ranolazine)	

Figure S3 The forest plot of the fixed-effects model showing the effects of ranolazine on the change in CFR among patients followed up for 2 to 12 weeks. After this outlier study was removed, the forest plot showed no significant differences in the improvement of CFR among patients followed up for 2 to 12 weeks. Std, standardized; SD, standard deviation; CI, confidence interval; IV, inverse variance; CFR, coronary flow reserve.



Figure S4 The sensitivity analysis of CFR in the subgroup with a dose variability of 500 to 1,000 mg. CFR, coronary flow reserve.

	Ran	olazin	е	placebo				Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl	
1.3.1 within 500 mg										
Villano 2013	1.76	0.4	15	1.74	0.5	15	21.1%	0.04 [-0.67, 0.76]		
Golino 2018	1.18	0.15	15	1.17	0.13	15	21.0%	0.07 [-0.65, 0.79]		
Subtotal (95% CI)			30			30	42.1%	0.06 [-0.45, 0.56]	-	
Heterogeneity: Tau ² =	0.00; C	hi² = 0.	00, df=	= 1 (P =	0.96);	l ² = 0%				
Test for overall effect:	Z = 0.22	2 (P = 0	1.83)							
1.3.2 500mg to 1000	mg									
Fagliamonte 2015	2.54	0.44	29	1.99	0.32	29	23.6%	1.41 [0.83, 1.99]		
3hah 2017	1.82	0.83	35	1.8	0.9	35	0.0%	0.02 [-0.45, 0.49]		
Safdar 2017	1.9	0.4	21	1.6	0.4	10	19.9%	0.73 [-0.05, 1.51]		
<oh 2020<="" td=""><td>2.67</td><td>0.74</td><td>6</td><td>2.08</td><td>1.03</td><td>7</td><td>14.4%</td><td>0.60 [-0.52, 1.73]</td><td></td></oh>	2.67	0.74	6	2.08	1.03	7	14.4%	0.60 [-0.52, 1.73]		
Subtotal (95% CI)			56			46	57.9%	1.04 [0.52, 1.56]		
Heterogeneity: Tau ² =	0.06; C	hi ² = 2.	71, df=	= 2 (P =	0.26);	1 ² = 269	%			
Fest for overall effect:	Z = 3.89	9 (P < 0	.0001)							
fotal (95% CI)			86			76	100.0%	0.59 [0.01, 1.17]	-	
Heterogeneity: Tau ² =	0.29; C	hi ^z = 1	1.96, di	'= 4 (P =	= 0.02)	; I² = 67	7%		-2 -1 0 1 2	
Fest for overall effect:	Z=1.98	B(P = 0)	.05)							
Test for subaroup diff	erences	: Chi ²	= 7.00.	df = 1 (F	P = 0.0	08), I ² =	= 85.7%		Favours [control] Favours [Ranolazine]	

Figure S5 The forest plot of the random-effects model showing the effects of ranolazine on the change in CFR in the dose variability subgroup. After this outlier study was removed, the forest plot showed the improvement of ranolazine on CFR in the subgroup with a dose variability from 500 to 1,000 mg. Std, standardized; SD, standard deviation; CI, confidence interval; IV, inverse variance; CFR, coronary flow reserve.



Figure S6 The sensitivity analysis of the physical functioning score.



Figure S7 The sensitivity analysis of the angina stability score.



Figure S8 The forest plot of the random-effects model showing the effects of ranolazine on the angina stability score. After this outlier study was removed, the forest plot showed the effects of ranolazine on the change of the angina stability score. SD, standard deviation; CI, confidence interval; IV, inverse variance.



Figure S9 The sensitivity analysis of the quality of life score.



Figure S10 The forest plot of the random-effects model showing the effects of ranolazine on the change of the quality of life score in the subgroup of the follow-up period. SD, standard deviation; CI, confidence interval; IV, inverse variance.