The patency of graft and anastomoses in sequential and individual coronary artery bypass grafting: A meta-analysis

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Abstract

Objective: To compare the patency of graft and anastomoses in sequential and individual coronary artery bypass grafting (CABG).
Methods: Our study used the Cochrane Library database, Excerpta Medica database, Web of Science, and PubMed. Studies comparing the outcomes of graft or anastomosis patency were assessed independently by two reviewers to identify the literature of satisfaction. We used Review Manager and STATA software for statistical analysis.
Results: Fifteen cohort studies were analyzed, including 10681 patients, 12957 grafts, and 4341 anastomoses, under sequential and individual CABG. Compared with the sequential group, the individual one is statistically significant in the graft patency [risk ratio (RR)=1.07, 95% confidence interval (CI) 1.01–1.13; p=0.02] and anastomosis patency (RR=1.06, 95% CI 1.01–1.12; p=0.005).
Conclusion: Our study suggested that the patency of the individual group, in terms of graft and anastomosis patency, is better than that of the sequential one. *(Anatol J Cardiol 2020; 24: 235-43)*
Keywords: coronary artery bypass grafting, sequential graft, meta-analysis

Introduction

Coronary heart disease (CHD) is currently the primary cause of death worldwide, with the percentage getting higher and higher. Coronary artery bypass grafting (CABG) is one of the common treatments for CHD patients. Flemma et al. (1) introduced the sequential grafting technique in 1971 for the first time. Despite different operations as sequential and individual veins have been applied, controversy still exists about the graft and anastomosis patency of these methods.

We aimed to conduct a meta-analysis of cohort studies for the comparison of the patency of graft and anastomoses in sequential and individual CABG.

Methods

Data sources and search strategy

Relevant trials that were included in this meta-analysis were searched in PubMed, Cochrane Library database, Excerpta Medica database, and Web of Science, using the keywords "coronary artery bypass graft," "sequential," and "individual." The search was limited to trials with humans and without publication date, language, and imposed publication status restrictions. The information on each study was chosen for the abstract. Two investigators reviewed the titles, abstracts, and studies independently to determine whether or not the inclusion criteria were met. The conflict between investigators was solved by consensus. The protocol of the meta-analysis was not registered.

Inclusion selection

The following criteria must be met by literature for it to be included: (1) patients must have undergone CABG; (2) the study must compare the patency of sequential and individual coronary artery bypass; and (3) graft and anastomosis patency denouements of the study were evaluated by ultrafast computed tomography (CT) or angiography. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (2) was followed in our meta-analysis.

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Outcome measures

Our study focused on the occurrence rate of graft and anastomosis patency and graft conduit with the artery or vein, on-pump or off-pump CABG performance, and assessment by ultrafast CT or angiography in patients during follow-up. Each segment was assessed as a separate graft in sequential grafts.

Data extraction

Relevant data were extracted independently and evaluated by two reviewers according to the pre-stipulated search strategy. The baseline demographic and quality characteristics from each study, author names, year of publication, number of patients, patient characteristics (age, percentages of women, comorbidities), follow-up time and rates, assessment method, operation, and conduit style, were extracted. The number of unobstructed graft and anastomoses in sequential and individual groups was recorded. Any disagreements were discussed between the two reviewers.

Quality assessment

The Newcastle-Ottawa Scale (NOS), a cohort study evaluation criteria suggested by the Cochrane Non-Randomized Studies Methods Group (3), was used to assess the methodological quality of this meta-analysis, which was evaluated using the following aspects: study selection, comparability between groups, and outcome determination.

Statistical analysis

The study effect of the destinations was measured using risk ratio (RR) as the pooled estimate, and the results were analyzed based on 95% confidence intervals (CIs). Two-sided p-values <0.05 were considered statistically significant. The chi-square test was conducted to examine the heterogeneity among the studies, and I^2 was also estimated. I^2 <40% might not be important, 30%–60% represent moderate heterogeneity, 50%–90% represent substantial heterogeneity, and <70% represent considerable heterogeneity (4). The fixed effects model was employed when I^2 was < 40%, while the random-effects model was employed when I^2 was ≥40%. The source of heterogeneity was explained using subgroup analyses. When the number of studies was >10, we conducted Egger's test to evaluate the potential of publication bias. Review Manager (Nordic Cochrane Centre, Collaboration) and STATA (Stata Corp, College Station, Texas, USA) software were used for statistical analysis.

Results

Study selection

The search strategy brought out 701 literature, of which 15 (5-19) conformed to our inclusion criteria, and the selection process is shown in Figure 1. The study characteristics and NOS-dependent quality assessment are outlined in Table 1. All manuscripts were middle- to high-quality cohort studies. A total of 10681 patients were included, and 8407 grafts and 2648 anastomoses in the sequential group and 4550 grafts and 1693 anastomoses in the individual group, respectively, were included.

Graft patency

Ten of the 15 studies reported information about graft patency, showing that the individual group had better patency than the sequential group (RR=1.07; 95% CI, 1.01–1.13) (Fig. 2). A considerable statistical heterogeneity (I^2=93%, p<0.00001) was noted among the studies, so a random-effects model was used. However, there was no potential for significant publication bias after Egger's test (p=0.27).

Significant inconsistencies were noted in the follow-up rate, patency evaluation, graft selection (divided into arterial and venous), and operations. To exclude these possible confounding factors, four subgroup analyses were performed (i.e., the studies with a follow-up rate of >70%, the studies of angiography to evaluate graft patency, the studies of grafts by the saphenous vein, and the studies of surgery method by off-pump).

Four studies had follow-up rates of >70%, the results of which showed that the individual group was better than the sequential group (RR=1.09; 95% CI, 1.01–1.18; p=0.02) (Fig. 3a) and that statistical heterogeneity (I^2=96%, p<0.00001) was noted among the studies, but the limited number of subgroups did not allow the assessment of the publication bias.

Seven studies reported on angiography to evaluate graft patency. No statistically significant difference between the two groups (RR=1.07; 95% CI, 0.98–1.18; p=0.15) was noted (Fig. 3b), and the results showed statistical heterogeneity (I^2=92%, p<0.00001) among the studies, but the limited number of subgroups did not allow the assessment of publication bias.

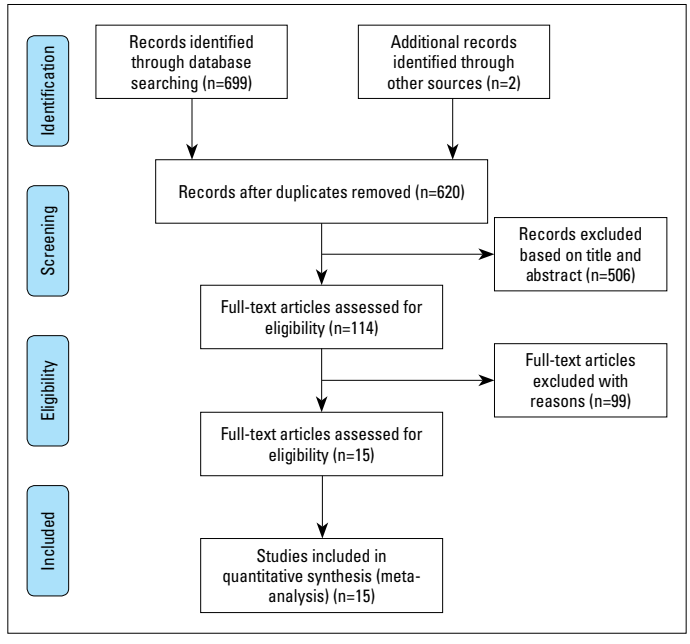

Figure 1. PRISMA flow chart of date selection

Table 1. Study characteristics and quality assessment

Study	Country	Comparability			Follow-up							Quality assessment (NOS)			
		Age	Female	Other factors	Duration	Rate method	Assessment	Patency measured on	Definition of occlusion	Conduit style	Surgical method	Selection	Comparability	Outcome	Total
Wendt et al. (5) 2010	USA	64±2/61±1	7/13	Hypertension, diabetes mellitus	1842±32/ 2070±33 days	>70	CT	Anastomoses	Unclear	LITA	Unclear	4	1	2	7
Vural et al. (6) 2001	Turkey	49±8	11	Atherosclerotic risk factor	5.8±3 year	_	Angiography	Graft, anastomoses	Stenoses ≥50%	SVG	Unclear	4	2	2	8
Schwann et al. (7) 2009	USA	63 (30-90)	17.7	Dyslipidemia diabetes mellitus	970±911 days	<70	Angiography	Graft	Stenoses ≥75%	RA	On-pump	3	2	2	7
Park et al. (8) 2020	South Korea	64.6±8.7/ 63.6±9.2	25/23	Body mass index, diabetes mellitus	88.0 (46.3-119.2) months	>70	CT	Graft	Stenoses≥70%	SVG	Off-pump, on-pump	4	2	2	8
Oz et al. (9) 2006	Turkey	51.1±15.5/ 54.14±12.2	37	Diabetes, smoking	49.4±13.2 months	>70	Angiography	Graft	Stenoses ≥50%	RA, SVG	Unclear	4	2	2	8
Meurala et al. (10) 1982	Finland	48±6.2	10	Acute myocardial infarction	26 (10-62) months	>70	Angiography	Anastomoses	Unclear	SVG	Unclear	4	2	2	8
Kim et al. (11) 2011	South Korea	63.5±8.3	30.5	Hypertension, diabetes mellitus	14.8 (1-70.2) months	>70	CT	Anastomoses	Stenoses ≥50%	SVG	Off-pump, on-pump	4	2	3	9
Gao et al. (12) 2010	China	63.6±10.3	11	_	26.4±23.6 month	_	CT	Graft, anastomoses	Stenoses ≥50%	SVG	Off-pump	4	2	1	7
Fukui et al. (13) 2012	Japan	67.2±10.4	19.5	Previous myocardial infarction	12.1 (2-21) months	<70	Angiography	Graft, anastomoses	Stenoses ≥90%	RA	Off-pump	4	2	2	8
Farsak et al. (14) 2003	Turkey	55.2±9.3	13	Atherosclerotic risk factor	55.4±17.6 months	_	Angiography	Graft, anastomoses	Stenoses ≥50%	SVG	Unclear	4	2	2	8
Ji et al. (15) 2017	China	62.9±9.4 / 63.6±8.5	10/12.5	Diabetes melitus, smoking	27.0±7.3 months, 27.2±7.2 months,	>70	CT	Graft	Stenoses ≥50%	LITA	Off-pump	4	2	3	9
Takazawa et al. (16) 2015	Japan	71±8	28.7	Diabetes, hypertension	Unclear	<70	Angiography	Graft	Unclear	SVG	Off-pump	4	2	1	7
Ohira et al. (17) 2016	Japan	65.7±9.3/ 65.8±8.4	16.6	Body mass index, ejection fraction	Unclear	>70	Angiography, CT	Anastomoses	Unclear	LITA	Off-pump	4	2	2	8
Brower et al. (18) 1981	Netherland	52 (37-65)	5	_	1 year	<70	Unclear	Anastomoses	Unclear	_	Unclear	3	1	2	6
Christenson et al. (19) 1998	Switzerland	58.2±9.2	19	Hypertension, smoking	76 months	>70	Angiography	Graft	Unclear	SVG	On-pump	3	2	3	8

CT - computed tomography; LITA - left internal thoracic artery; RA - radial artery; SVG - saphenous vein graft; NOS - Newcastle-Ottawa scale

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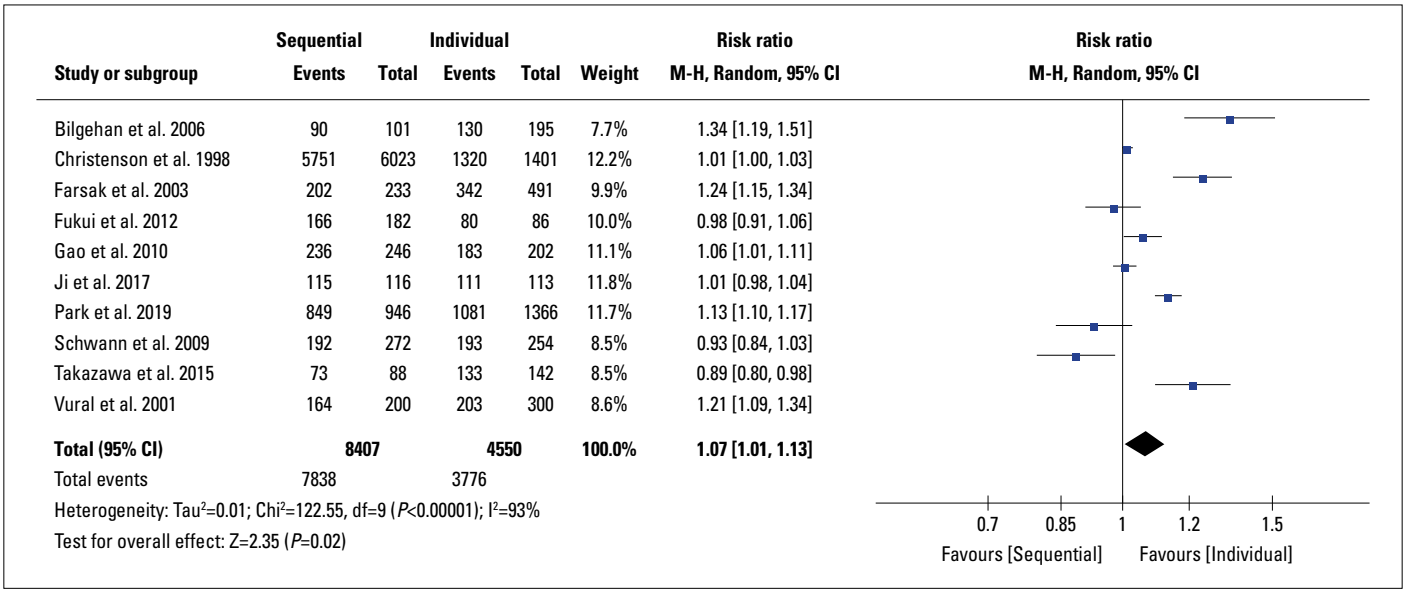


Figure 2. Forest plot of graft patency
M-H - Mantel-Haenszel; CI - confidence interval

Seven studies reported on grafts by a saphenous vein, the results of which showed that the individual group was better than the sequential group (RR=1.11; 95% CI, 1.03–1.21; p=0.01) (Fig. 3c) and that considerable statistical heterogeneity (I^2=95%, p<0.00001) was noted among the studies, but the limited number of subgroups did not allow the assessment of the publication bias.

Four studies with surgery methods by off-pump were noted, the results of which demonstrated no statistically significant difference among the two groups (RR=1.00; 95% CI, 0.94–1.05; p=0.87) (Fig. 3d) and substantial statistical heterogeneity (I^2=72%, p<0.00001) among the studies, but the limited number of subgroups did not allow the assessment of publication bias.

Anastomosis patency

Nine studies described the information about anastomosis patency, the results of which showed that the individual group also had better patency than the sequential group (RR=1.06; 95% CI, 1.02–1.11) (Fig. 4) and that considerable statistical heterogeneity (I^2=93%, p<0.00001) was noted among the studies, but the limited number of studies did not allow the assessment of the publication bias. Four subgroup analyses were also performed (i.e., the studies with a follow-up rate of >70%, the studies of angiography to evaluate graft patency, the studies of grafts by saphenous vein, the studies of surgery method by off-pump) to exclude these possible confounding factors.

Four studies had follow-up rates of >70%, the results of which demonstrated no statistically significant difference among the two groups (RR=1.06; 95% CI, 1.00–1.13; p=0.04) (Fig. 5a) and substantial statistical heterogeneity (I^2=78%, p=0.003) among the studies, but the limited number of subgroups did not allow the assessment of the publication bias.

Four studies with angiography evaluated graft patency, the results of which showed that the individual group was better than the sequential group (RR=1.11; 95% CI, 1.03–1.19; p=0.004) (Fig. 5b) and that substantial statistical heterogeneity (I^2=60%, p=0.06) was noted among the studies, but the limited number of subgroups did not allow the assessment of the publication bias.

Seven studies with grafts by a saphenous vein were noted, the results of which showed that the individual group was better than the sequential group (RR=1.10; 95% CI, 1.06–1.15; p<0.00001) (Fig. 5c) and that moderate heterogeneity (I^2=47%, p=0.11) was noted among the studies, but the limited number of subgroups did not allow the assessment of the publication bias.

Three studies with surgery methods by off-pump were noted, the results of which demonstrated no statistically significant difference among the two groups (RR=1.03; 95% CI, 1.00–1.07; p=0.05) (Fig. 5d) and no statistical heterogeneity (I^2=38%, p=0.20) among the studies.

Sensitivity analyses

By excluding individual studies one by one, we performed two sensitivity analyses on graft and anastomosis patency, respectively (Fig. 6a and 6b). No statistical significance was noted, suggesting that our results were stable and the comprehensive results were not influenced by this heterogeneity.

Discussion

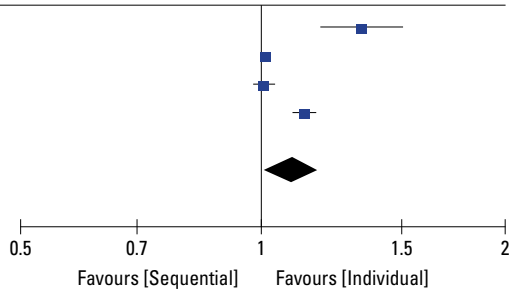
Main finding

To our knowledge, this meta-analysis is the most comprehensive one, including 15 studies and 10681 patients in total, comparing the patency of graft and anastomoses in patients who underwent sequential and individual CABG, which indi-

a

Study or subgroup	Sequential Events	Total	Individual Events	Total	Weight	Risk ratio M-H, Random, 95% CI
Bilgehan et al. 2006	90	101	130	195	17.1%	1.34 [1.19, 1.51]
Christenson et al. 1998	5751	6023	1320	1401	28.3%	1.01 [1.00, 1.03]
Ji et al. 2017	115	116	111	113	27.5%	1.01 [0.98, 1.04]
Park et al. 2019	849	946	1081	1366	27.1%	1.13 [1.10, 1.17]
Total (95% CI)	**7186**		**3075**		**100.0%**	**1.09 [1.01, 1.18]**
Total events	6805		2642			

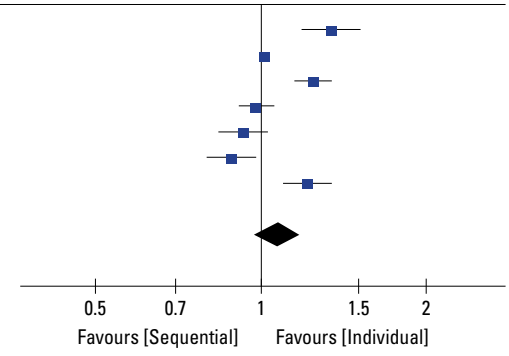
Heterogeneity: Tau²=0.01; Chi²=71.46, df=3 (*P*<0.00001); I²=96%
Test for overall effect: Z=2.25 (*P*=0.02)



b

Study or subgroup	Sequential Events	Total	Individual Events	Total	Weight	Risk ratio M-H, Random, 95% CI
Bilgehan et al. 2006	90	101	130	195	12.9%	1.34 [1.19, 1.51]
Christenson et al. 1998	5751	6023	1320	1401	16.4%	1.01 [1.00, 1.03]
Farsak et al. 2003	202	233	342	491	14.8%	1.24 [1.15, 1.34]
Fukui et al. 2012	166	182	80	86	14.9%	0.98 [0.91, 1.06]
Schwann et al. 2009	192	272	193	254	13.7%	0.93 [0.84, 1.03]
Takazawa et al. 2015	73	88	133	142	13.6%	0.89 [0.80, 0.98]
Vural et al. 2001	164	200	203	300	13.7%	1.21 [1.09, 1.34]
Total (95% CI)	**7099**		**2869**		**100.0%**	**1.07 [0.98, 1.18]**
Total events	6638		2401			

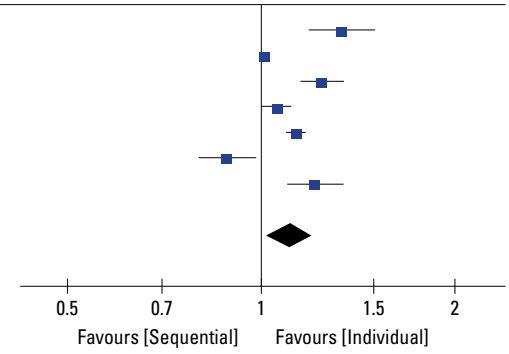
Heterogeneity: Tau²=0.01; Chi²=74.96, df=6 (*P*<0.00001); I²=92%
Test for overall effect: Z=1.45 (*P*=0.15)



c

Study or subgroup	Sequential Events	Total	Individual Events	Total	Weight	Risk ratio M-H, Random, 95% CI
Bilgehan et al. 2006	90	101	130	195	12.0%	1.34 [1.19, 1.51]
Christenson et al. 1998	5751	6023	1320	1401	16.4%	1.01 [1.00, 1.03]
Farsak et al. 2003	202	233	342	491	14.3%	1.24 [1.15, 1.34]
Gao et al. 2010	236	246	183	202	15.4%	1.06 [1.01, 1.11]
Park et al. 2019	849	946	1081	1366	16.0%	1.13 [1.10, 1.17]
Takazawa et al. 2015	73	88	133	142	12.9%	0.89 [0.80, 0.98]
Vural et al. 2001	164	200	203	300	13.0%	1.21 [1.09, 1.34]
Total (95% CI)	**7837**		**4097**		**100.0%**	**1.11 [1.03, 1.21]**
Total events	7365		3392			

Heterogeneity: Tau²=0.01; Chi²=114.31, df=6 (*P*<0.00001); I²=95%
Test for overall effect: Z=2.59 (*P*=0.010)



d

Study or subgroup	Sequential Events	Total	Individual Events	Total	Weight	Risk ratio M-H, Random, 95% CI
Fukui et al. 2012	166	182	80	86	22.4%	0.98 [0.91, 1.06]
Gao et al. 2010	236	246	183	202	28.1%	1.06 [1.01, 1.11]
Ji et al. 2017	115	116	111	113	33.5%	1.01 [0.98, 1.04]
Takazawa et al. 2015	73	88	133	142	16.0%	0.89 [0.80, 0.98]
Total (95% CI)	**632**		**543**		**100.0%**	**1.00 [0.94, 1.05]**
Total events	590		507			

Heterogeneity: Tau²=0.00; Chi²=10.90, df=3 (*P*=0.00001); I²=72%
Test for overall effect: Z=0.17 (*P*=0.87)

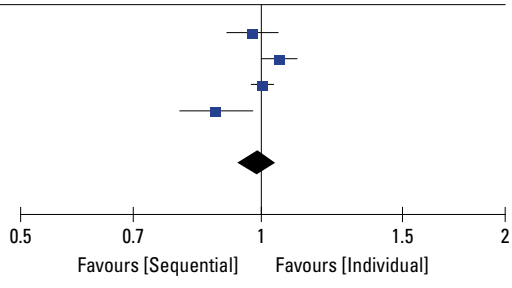


Figure 3. Forest plot for subgroup analysis of (a) follow-up rates >70%; (b) angiography to evaluate graft patency; (c) grafts by saphenous vein; and (d) surgery method by off-pump

M-H - Mantel-Haenszel; CI - confidence interval

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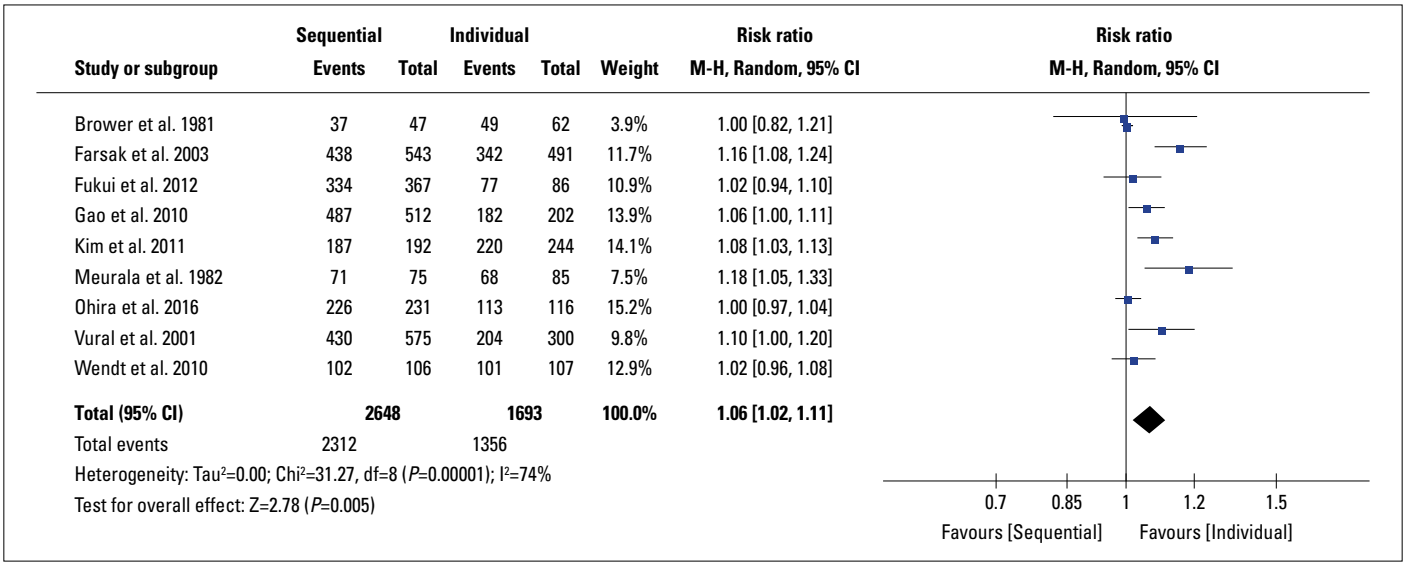

Figure 4. Forest plot of anastomosis patency
M-H - Mantel-Haenszel; CI - confidence interval

cated that the individual group in graft and anastomoses has a higher patency than that of the sequential one.

Compared with prior studies

Our studies suggested that the individual group has better patency than the sequential group in graft and anastomoses, the result of which is not consistent with previous studies by Li et al. (20) in 2011 and Li and Liu (21) in 2019. The earliest article indicated that the patency in sequential grafts was greater than in the individual group (RR=0.67; 95% CI, 0.60–0.74) and the rate of patency in side-to-side anastomoses was significantly greater than that of end-to-side anastomoses. This difference is first due to the surgical level not being mature enough at that time and people preferring sequential anastomoses and, second, due to the high proportion of SVG in their articles, up to 75%. The article published in 2019 suggested no significant statistical differences between these groups on the patency of grafts (RR=0.96; 95% CI, 0.91–1.02) and anastomoses (RR=0.95; 95% CI, 0.91–1.00), which is different from our research results because we have included more subjects and a larger sample size. Secondly, it may be related to Park et al.'s (8) study, which reported that the patency rate of a single branch is higher than that of the sequential.

The type of graft may be associated with the long-term patency rate. As the gold standard for CABG grafts (22), the internal thoracic artery has reached international consensus with clinical benefits of improving survival and reducing cardiovascular events. Raza et al. (23) found the sequential bridges to have the same long-term patency rate as single bridges and to be higher than Y-type grafts in a study comparing the long-term patency rates of individual segments of different internal thoracic artery grafts. The radial artery, as an alternative to the recommended internal thoracic artery graft (22), has a better long-term patency rate than the great saphenous vein (24) but is not routinely used. If a radial artery graft is used, it should be anastomosed to a highly stenotic (>90%) target vessel for maximum clinical benefit (25). Mehta et al.'s trial (26), a phase 3, randomized, double-blind, placebo-controlled, and multicenter trial, indicated that the vein graft occlusion rate was higher for the sequential group than for the individual one (adjusted odds ratio 1.24; 95% CI, 1.03–1.48). Park et al. (8), in a 10-year long-term follow-up, found that sequential bridges have a higher rate of venous graft patency than single branch bridges (HR 0.61; 95% CI, 0.45–0.82; p<0.001), which are very safe and effective. The difference in the proportion of cardiopulmonary bypass used between the two groups may be associated with the difference in outcomes.

Different surgical methods may affect graft patency. ROOBY trial (27), a large prospective randomized controlled clinical, was followed up by angiography 1 year later, which showed a significantly lower rate of the graft patency in the off-pump coronary artery bypass graft group than that in the on-pump coronary artery bypass graft group (82.6% vs. 87.8%). However, both the CORONARY (28) and the GOPCABE (29) trials were followed up for 5 years, the results of which showed no significant difference in the rate of revascularization between both bypass graft groups. Zhang et al. (30) showed that the operation of on-pump CABG significantly reduced the risk of saphenous vein graft occlusion than off-pump CABG (RR=1.41; 95% CI, 1.24–1.60), which is not identical with the result of our subgroup analysis.

Heterogeneity

In our study, the heterogeneities of graft and anastomosis patency were considerably high, which may be due to the provision of occlusion or patency of some studies. Errors, causing heterogeneity between studies, are due to the conversion of this information on occlusion into patency data and differences in age, sex, ethnicity, disease severity, and primary disease. The

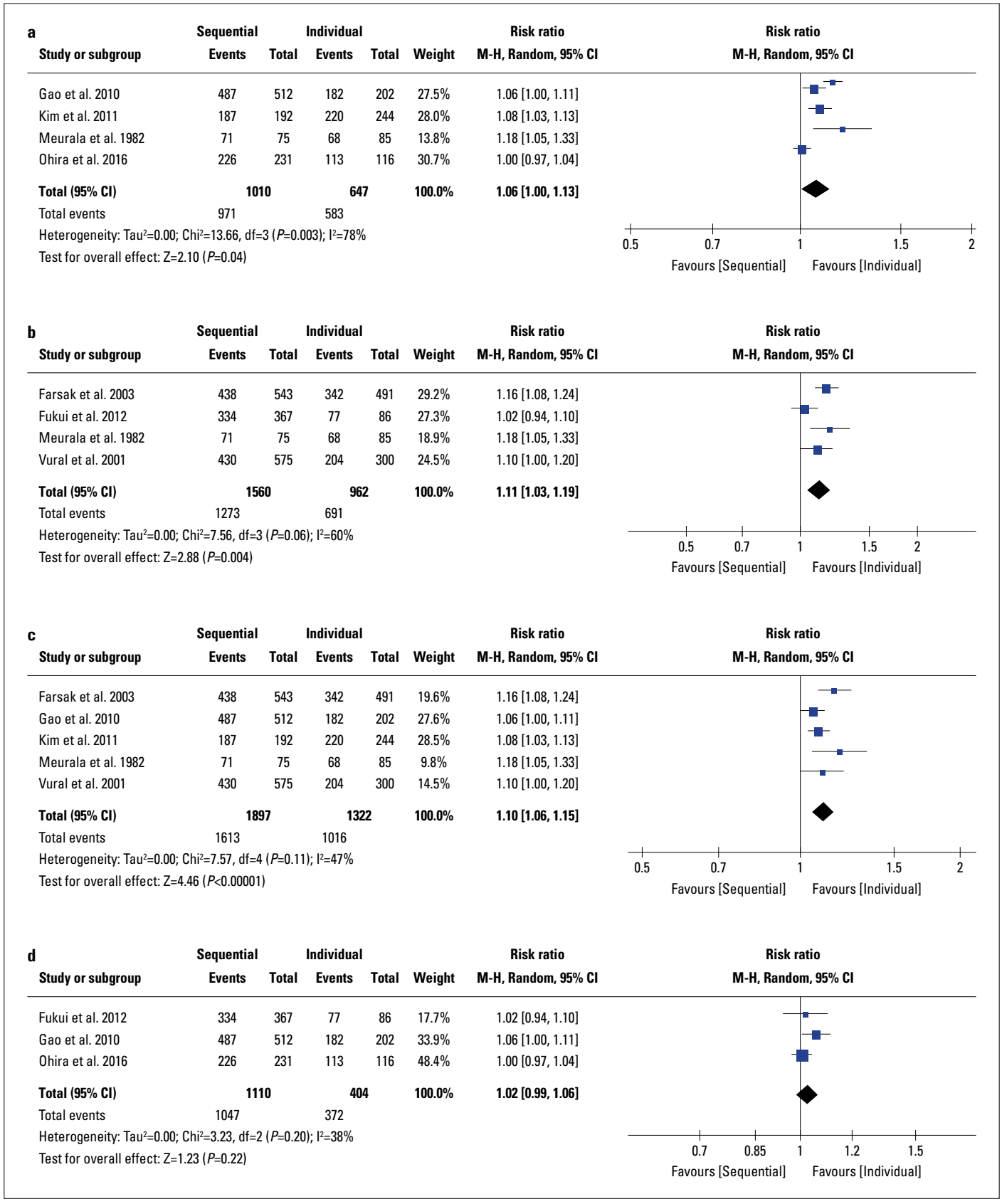

Figure 5. Forest plot for subgroup analysis of (a) follow-up rates >70%; (b) angiography to evaluate anastomosis patency; (c) grafts by saphenous vein; and (d) surgery method by off-pump

M-H - Mantel-Haenszel; CI - confidence interval

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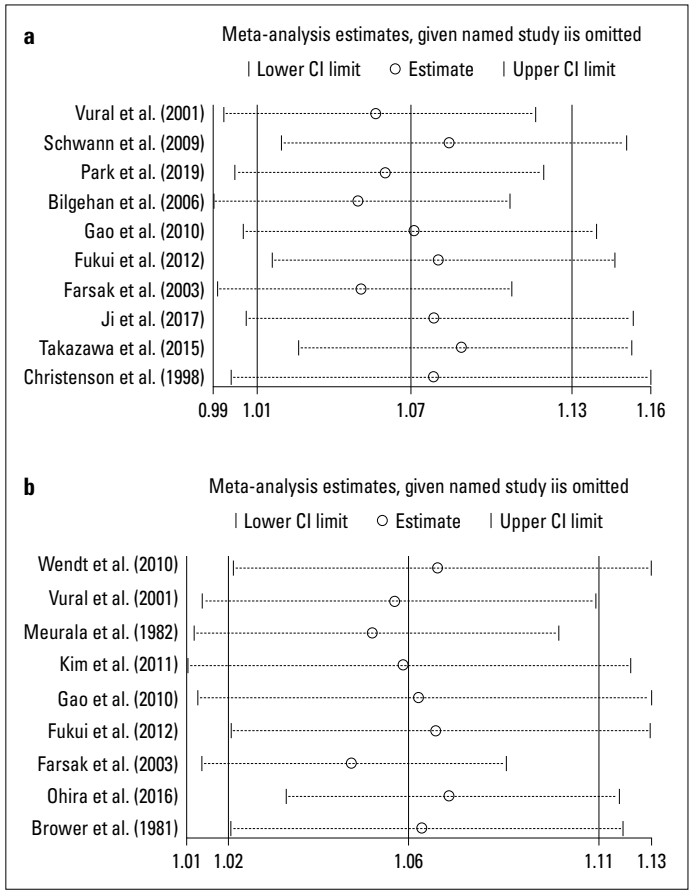

Figure 6. Sensitivity analysis of (a) graft patency and (b) anastomosis patency

high heterogeneities may also be ascribed to differences in time background, the level of surgeons' expertise, economy levels, and regional and cultural differences. However, these were not analyzed in our study because the data was not enough. Our meta-analysis used a random-effects model to explain these heterogeneities. In research evaluating graft patency, four subgroup analyses were conducted to explain the high heterogeneity, but the results did not obtain the source of heterogeneity. So, Egger's test was performed, the results of which indicated no significant publication bias. We also implemented sensitivity analysis, which proved that our result is stable and this heterogeneity is not influenced by the merged result. In research evaluating anastomosis patency, four subgroup analyses were also conducted to explain the heterogeneity, which was reduced into two subgroups (i.e., the studies of grafts by saphenous vein, the studies of surgery method by off-pump). We also implemented sensitivity analysis, which testified that our result is stable and this heterogeneity is not influenced by the merged result.

Study limitations

However, our meta-analysis also has some inherent limitations. First, some studies only provided the rate of occlusion. Data differences may be noted after conversion to the patency rate, which may have influenced the dependability of the final results. Second, the coronary artery bypass anastomoses are not uniform, since both side-to-side and end-to-side anastomoses are found in our meta-analysis, which may influence the stability of the final results. Third, in our study, national research in Asia accounts for the majority, which may have some bias and is not representative of the whole world. In addition, our study included standard cohort studies rather than randomized trials, lowering the level of evidence. Therefore, it is necessary to conduct a larger, multicenter, prospective, and randomized international trials to further confirm these results.

Conclusion

Despite the inherent limitations of this meta-analysis, our findings show that the patency of the individual graft was better than that of the sequential group and that the patency of individual anastomoses was better than that of the sequential one.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

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