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Three arterial grafts improve late survival:

a meta-analysis of propensity matched studies

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Abstract

Background: There is little evidence whether a third arterial graft provides superior outcomes in comparison to the use of two arterial grafts in patients undergoing coronary artery bypass grafting (CABG). A meta-analysis of all the propensity score matched (PSM) observational studies comparing the long-term outcomes of CABG with the use of two (2-ART) vs. three arterial (3-ART) grafts was performed.

Methods: A literature search was conducted using MEDLINE, EMBASE, and Web of Science to identify relevant articles. Long-term mortality in the PSM populations was the primary endpoint. Secondary endpoints were in-hospital/30-day mortality for the PSM populations and long-term mortality for the unmatched populations. In the matched population, time-to-event outcome for long-term mortality was extracted as hazard ratios (HRs) along with their variance. Statistical pooling of survival (time-to-event) was performed according to a random effect model, computing risk estimates with 95% confidence intervals (CI).

Results: A total of 8 PSM studies reporting on 10,287 matched patients (2-ART: 5346; 3-ART: 4941) were selected for final comparison. The mean follow-up time ranged from 37.2 to 196.8 months. The use of three arterial grafts was not statistically associated with early mortality (HR, 0.93; 95% CI, 0.71-1.22; $p = .62$). The use of three arterial grafts was associated with statistically significantly lower hazard for late death (HR, 0.8; 95% CI, 0.75-0.87; $p < .001$), irrespective of sex and diabetic status. This result was qualitatively similar in the unmatched population (HR, 0.57; 95% CI, 0.33-0.98; $p = .04$).

Conclusions: The use of a third arterial conduit in CABG patients is not associated with higher operative risk and is associated with superior long-term survival, irrespective of sex and diabetic status.

Clinical Perspective

What is new?

- The best available evidence suggests that the use of a second arterial graft at the time of coronary artery bypass operations leads to better postoperative survival.
- However, less is known about the potential benefit of a third arterial conduit.
- In the present analysis, we show that adding a third arterial conduit is not associated with an increased operative risk and is associated with improved long-term survival.

What are the clinical implications?

- Arterial grafts are largely underused for coronary artery bypass surgery.
- By showing an association between improved survival and the use of a third arterial graft, these results support such a strategy and provide support for consideration of evaluation and confirmation in prospective randomized trials.

1 **Introduction**

2 Current observational evidence strongly suggests that the use of two arterial grafts at the time
3 of coronary artery bypass surgery (CABG) is associated with long-term survival benefits¹⁻³.
4 However, less is known about the potential benefit of a third arterial conduit.

5 To date, the studies that have compared the long-term survival of CABG patients receiving two
6 vs. three arterial conduits have reported conflicting results⁴⁻¹¹. However, all of these studies
7 come from single centers and have limited sample size. It is highly likely that the potential
8 additional survival benefit of a third arterial conduit is less when compared to that of a second,
9 making it plausible that single institutional studies are underpowered to detect moderate
10 differences in survival.

11 In order to overcome this limitation and to provide the best available evidence on this topic, we
12 present a meta-analysis of propensity score matched (PSM) observational studies that
13 compared the long-term outcomes of CABG in patients who received two vs. three arterial
14 grafts.

15

1 **Methods**

2 Search Strategy and Selection of Studies

3 This systematic review was conducted according to the Preferred Reporting Items for
4 Systematic Reviews and Meta-Analyses (PRISMA) guidelines¹².

5 In August 2016, a literature search using MEDLINE, EMBASE, and Web of Science to identify
6 relevant articles was performed. Observational studies included in the present meta-analysis
7 met the following criteria: (1) patients undergoing first time isolated CABG; (2) comparison of
8 long-term survival of patients receiving two arterial conduits (2-ART) vs. patients receiving
9 three arterial conduits (3-ART); and (3) PSM was used to account for non-random allocation to
10 treatment (2-ART vs. 3-ART). Non-English language, review articles, case reports, and editorials
11 were excluded. Search terms used the controlled vocabularies of MEDLINE and EMBASE alone
12 or in combination with text words including “third arterial conduit CABG”, “third arterial graft
13 CABG”, “total arterial revascularization CABG”, “propensity score”, and “propensity score
14 matching”. Two reviewers (M.G. and A.D.F.) independently reviewed the titles and abstracts to
15 determine whether the study met the inclusion criteria. In the case of disagreement, an
16 agreement was negotiated. In the case of several publications with overlapping study
17 populations, the largest sample size study with longest follow-up available was selected.

18 We assessed the quality of included studies with the Newcastle-Ottawa Scale for observational
19 studies¹³. The highest possible score is 9 stars, and the quality is graded as low level (<6 stars)
20 or high level (≥6 stars).

21

1 Data Extraction

2 Microsoft Office Excel 2010 (Microsoft, Redmond, Wash) was used for data extraction that was
3 performed independently by 2 researchers (A.D.F. and L.B.O.). In the case of initial
4 disagreement, an agreement was negotiated. Where additional information was deemed
5 necessary, the corresponding author of the relevant study was contacted directly. Study design,
6 study period, country, and center where the study was conducted, unmatched and matched
7 sample size, type of arterial conduits, PSM methods, completeness of follow-up, and follow-up
8 duration were documented. The following patient characteristics in the unmatched and
9 matched groups were also registered: age, female sex, diabetes mellitus, reduced left
10 ventricular ejection fraction (as defined by the authors), chronic obstructive pulmonary disease,
11 renal impairment (as defined by the authors), target vessels, and predicted operative risk
12 according to the EuroSCORE or the Society of Thoracic Surgeons score¹⁴.

13 The primary endpoint was long-term mortality in the matched populations. Secondary
14 endpoints were in-hospital/30-day mortality for the matched populations and long-term
15 mortality in the unmatched populations. In the matched population, time-to-event outcome for
16 long-term mortality was extracted as hazard ratios (HRs) along with their variance.

17 Statistical Analysis

18 Continuous variables are reported as median (25th, 75th percentile) or as mean±standard
19 deviation. Categorical variables are expressed as (%). Statistical pooling of survival, time-to-
20 event, was performed according to a random-effect model, computing risk estimates with 95%
21 confidence intervals (CI), using RevMan 5 (The Cochrane Collaboration, The Nordic Cochrane

1 Centre and Copenhagen, Denmark). From one study we derived the incidence of all-cause
2 mortality from a Kaplan-Meier survival curve using a described method¹⁵. Study bias was
3 appraised by graphical inspection of funnel plots, and Egger’s linear regression method was
4 used to quantify the bias. Hypothesis testing for equivalence was set at the two-tailed 0.05
5 level. Hypothesis testing for statistical homogeneity was set at the two-tailed 0.10 level and was
6 based on the Cochran Q test, with I^2 values of 25%, 50%, and 75% representing mild, moderate,
7 and severe heterogeneity, respectively. Meta-regression analysis and the “one study removed
8 analysis” were performed with Comprehensive Meta-Analysis, reporting results as regression
9 coefficient (i.e. Beta).

10

1 **Results**

2 Selected Studies

3 From 201 abstracts, 21 full-text articles fitting the relevant selection criteria were selected.
4 After evaluating the full-text articles, 13 observational studies that did not perform PSM
5 adjusted comparison between patients receiving two vs three arterial conduits¹⁶⁻²⁸ were
6 excluded. A total of 8 PSM studies were finally selected for the systematic review and meta-
7 analysis⁴⁻¹¹. An outline of the systematic review process is depicted in Figure 1. An overview of
8 the PSM studies is summarized in Tables 1 and 2 (variables included for PSM are summarized in
9 Supplementary Table 1). Overall, selected studies reported on 10,287 matched patients (2-ART,
10 5346; 3-ART, 4941) for final comparisons. PSM populations presented a similar preoperative
11 risk factor distribution in the 2-ART and 3-ART groups (Table 3).

12 Early Mortality

13 All studies except for three^{5,6,8} reported on comparisons of in-hospital/30-day mortality for the
14 PSM series (different definitions were adopted, see Table 1). Glineur et al. did not report any
15 data on in-hospital/30-day mortality and two other studies, Locker et al. and Di Mauro et al.,
16 reported overall mortality without distinguishing between the 2-ART and 3-ART groups. In-
17 hospital/30-day mortality ranged from 0.4% to 2.7% and 0.3% to 2.9% in the 2-ART and 3-ART
18 groups, respectively. Pooled estimates showed no significant difference between the two
19 groups (HR: 0.93; 95% CI, 0.71-1.22; p= .62; Figure 2). Meta-regression analysis showed neither
20 female sex (Beta -0.13 [CI -0.02; +1.75], p= .89) nor diabetes affected early outcome (Beta -0.14
21 [CI -1.47; +1.19], p= .83).

1 Long-Term Mortality

2 All studies reported the comparison of long-term mortality for the PSM series. However, Nasso
3 et al.¹⁰ reported survival in a Kaplan Meier survival curve. In this study the HR for long-term
4 mortality was then derived from the Kaplan Meier as described in the Methods section. In the
5 study by Di Mauro et al.⁵ the HR for the 2-ART and 3-ART groups could not be calculated and
6 this study was omitted from the final analysis.

7 The mean follow-up time ranged from 37.2 to 196.8 months (Table 2). The use of three arterial
8 grafts was associated with a statistically significant reduction of late death when compared with
9 the use of two arterial conduits (HR: 0.8; 95%CI, 0.75-0.87; p< .001; Figure 3). This result was
10 confirmed in the studies^{4,6,8,11} that reported the late mortality in the unmatched population
11 (HR: 0.57; 95% CI, 0.33-0.98; p= .04; Figure 4). The leave-one-out analysis confirmed these
12 results (Figure 5).

13 Meta-regression analysis showed neither female sex (Beta 0.13 [-0.23; +0.5), p= .47) nor
14 diabetes affected long-term survival (Beta 0.19 [CI -0.23; +0.64], p= .4).

15 Publication Bias and internal validity appraisal

16 The Newcastle-Ottawa Scale confirmed a high-quality level for all PSM studies included in the
17 main analysis (Supplementary Table 2). Heterogeneity for PSM analysis was high for long-term
18 ($I^2= 58.8\%$) and for 30-day mortality ($I^2= 85.6\%$), and extensive in the overall population analysis
19 ($I^2= 91.3\%$). No significant publication bias was found, as confirmed by Egger's test
20 (Supplementary Figures 1 and 2).

1 **Discussion**

2 Even in the absence of randomized controlled trials (RCTs), the clinical benefits related to the
3 use of two arterial grafts at the time of CABG are strongly supported by abundant
4 circumstantial evidence. In 1999 the Cleveland Clinic investigators were among the first to
5 report a clear survival advantage for patients receiving bilateral internal thoracic artery (BITA)
6 instead of single internal thoracic artery (SITA) grafts²⁹. Since that seminal paper, a substantial
7 amount of observational evidence has reported better clinical outcomes with the use of two vs.
8 one arterial grafts for CABG patients.

9 Most recently, the 5-year interim analysis of the ART trial that randomized 3,102 patients to
10 receive SITA or BITA showed similar mortality, myocardial infraction and stroke³⁰. There are
11 several possible explanations for the similar outcomes. First, the failure rate of saphenous vein
12 is known to be relatively low for the first 5 years after CABG but then increases. Second, very
13 high use of guideline based medical therapy with almost 90% of the patients receiving aspirin
14 and statins and almost three quarters on beta-blockers and ACE inhibitors, may have reduced
15 the risk of development of disease and failure of vein grafts. Third, the simultaneous use of a
16 radial artery (with its proven superior angiographic patency in comparison to vein grafts at 5
17 years³¹) in 20% of the SITA group may also have resulted in a narrowing of differences in mid-
18 term outcome. A further possibility is that while the addition of a second ITA graft makes no
19 difference to 5-year survival, this may change over the longer-term as there is a marked
20 difference in angiographic patency between ITA and vein grafts after 10 years³².

1 While awaiting the 10-year outcomes of ART, current available evidence suggests that the use
2 of two arterial grafts for CABG is associated with significantly better outcome. Indeed, in a
3 meta-analysis of over 15,000 patients receiving SITA or BITA followed for a mean of over 9
4 years, the Oxford group reported a 22% survival benefit for those receiving two arterial
5 conduits (HR: 0.78; CI, 0.72–0.84; $p < .0001$)³³. Similarly, in the only meta-analysis that
6 compared clinical outcomes of patients receiving either a radial artery or a saphenous vein as
7 the second graft, Zhang and coauthors found a significantly lower incidence of cardiac death,
8 myocardial infarction, and repeat coronary procedures in the arterial group (OR: 0.72, 0.68, and
9 0.27 respectively)³⁴.

10 The benefits related to the addition of a third arterial conduit are much more controversial. The
11 few studies that have directly compared the outcomes of patients receiving two vs. three
12 arterial grafts have reported conflicting results. Di Mauro et al., analyzing a cohort of 885
13 patients with BITA to the left coronary artery system, described increased mortality and
14 cardiac-death rates when the gastroepiploic artery instead of the saphenous vein was used to
15 graft the right coronary artery⁵. Similarly, Nasso and associates found no additional clinical
16 benefits with the addition of a third arterial graft in a large cohort of 10,752 CABG patients¹⁰. In
17 addition, Benedetto et al. and Mohammadi et al. found that using the radial artery or the
18 saphenous vein in addition to BITA did not improve long-term outcomes^{4,9}.

19 On the other hand, the Mayo Clinic group reported improved late survival with the use of three
20 arterial conduits⁸ and Glineur et al. had superior outcomes using the gastroepiploic artery,
21 instead of a saphenous vein, to complement the two ITAs⁶. Both Grau and Shi and coauthors, in

1 two large propensity matched series, reported a significant survival benefit for patients who
2 received three vs. two arterial conduits^{7,11}.

3 One possible reason for these contradictory findings is that the survival benefit provided by the
4 use of a third arterial graft is lower when compared to the use of the first or second arterial
5 conduit. Consequently, in view of their relatively small individual populations, most of the single
6 institutional studies were underpowered to detect moderate differences in survival. The
7 present study was meant to overcome this potential limitation by using a meta-analytic
8 approach.

9 Even though meta-analyses of PSM studies are not as methodologically robust as meta-analyses
10 of RCTs, they are emerging as an attractive alternative. In view of the paucity of evidence from
11 RCTs in the surgical literature, the meta-analytic approach based on PSM studies can be relied
12 on as evidence when RCTs are not possible or not available³⁵.

13 Our analysis pooled data from 10,287 matched patients receiving two vs. three arterial
14 conduits. Our main finding is that the use of a third arterial graft is not associated with an
15 increase in the operative risk but rather with a 24% survival benefit at a mean follow-up of 77.9
16 months. This survival advantage is independent of the patient's sex and diabetic status.

17 The most likely explanation for these findings is the demonstrated lower attrition rate of
18 arterial grafts. All the studies that have compared the angiographic patency of arterial vs.
19 venous bypass grafts have consistently shown a better patency rate for the former, with the
20 difference in patency increasing with the length of the follow-up^{31,36}.

1 Indeed, we have recently described how 20 years after CABG the risk of graft failure for the
2 venous grafts is almost three times higher than that of arterial conduits³². An additional
3 potential contributor to the improved outcomes of patients who received three arteries is
4 probably the protective effect of arterial grafts against the development of atherosclerotic
5 disease in the native coronary circulation³⁷.

6 Unfortunately, the available data do not allow a further analysis of eventual survival differences
7 related to the location of the third arterial conduit on the left or right coronary system or the
8 type of graft configuration used. These are important points that require further investigation.

9 It is important to note that in the US only 6% of the patients undergoing primary isolated CABG
10 receive more than one arterial graft³⁸. A similar situation exists in Europe and in Asia^{38,39}. Even
11 in the absence of global data, the current literature suggests that the proportion of patients
12 receiving a second arterial conduit at the time of CABG worldwide is in the 15-20% range.

13 The reasons for this underuse of arterial grafts are complex and multifactorial. The increasing
14 complexity of the population of patients referred for CABG, but also the increasing pressure
15 toward higher surgical “productivity” and the importance of short-term “quality metrics”, such
16 as the avoidance of sternal complications, are possible explanations.

17 Limitations

18 The present analysis has intrinsic limitations. First, any matching system can only adjust for
19 measurable and included variables. It is likely that while selecting which patients should receive
20 three arterial grafts the operating surgeons relied on an immeasurable, but reliable, “eye-

1 balling” that comes from experience and cannot be neutralized by any statistical method. This
2 means that healthier patients are more likely to have received three arterial conduits.

3 Secondly, propensity matching by definition increases internal validity at the expense of
4 generalizability. The fact that only about two thirds of the overall population was included in
5 the matched comparison clearly limits the ability to extend our findings to the majority of CABG
6 patients.

7 Also, looking at Table 3, it is evident that the population of patients included in most of the
8 examined studies is younger and in general healthier than that seen by most cardiac surgery
9 centers in their everyday clinical practice. It is highly likely that this patients’ population
10 represents a selected group of the totality of cases referred for CABG and it is possible that the
11 described benefits associated with the use of a third arterial grafts does not apply to the
12 generality of the CABG population.

13 Moreover, not all the studies evaluated all the outcomes of interest, so we specified the
14 number of the studies and of patients for each outcome; most of the results are based on very
15 small numbers of deaths. Group level analysis also introduced the problem of ecological bias
16 for regression of ecologic variables such as sex or diabetes, potentially failing to detect these
17 interactions⁴⁰.

18 Finally, the different authors used different grafting strategies and matching models so that the
19 homogeneity of the included populations cannot be regarded as optimal.

20 In conclusion, in a meta-analysis of the PSM studies comparing the use of two vs. three arterial
21 grafts for CABG, we found that the use of three arterial conduits is not associated with an

- 1 increase in the operative risk but is associated with a statistically significant survival benefit at
- 2 long-term follow-up. These finding support the concepts that complete revascularization and
- 3 extensive use of arterial grafts should be the cornerstone of modern coronary artery surgery.

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Figure Legends

Figure 1. Flow chart for study selection.

Figure 2. Forest plot comparing the effect of the use of three arterial conduits (3-ART) vs. two arterial conduits (2-ART) on in-hospital/30-day mortality across individual propensity score-matched studies. CI, confidence interval (5 studies including 9106 patients).

Figure 3. Forest plot comparing the effect of the use of three arterial conduits (3-ART) vs. two arterial conduits (2-ART) on late mortality across individual propensity score-matched studies. CI, confidence interval. (7 studies including 9402 patients).

Figure 4. Forest plot comparing the effect of the use of three arterial conduits (3-ART) vs. two arterial conduits (2-ART) on late mortality across individual unmatched studies. CI, confidence interval. (4 studies including 3742 patients).

Figure 5. Forest plot of the leave-one-out analysis comparing the effect of the use of three arterial conduits (3-ART) vs. two arterial conduits (2-ART) on late mortality. CI, confidence interval.

Supplementary Figure 1. Funnel plot comparing the effect of the use of three arterial conduits (3-ART) vs. two arterial conduits (2-ART) on late mortality across individual propensity score-matched studies.

Supplementary Figure 2. Funnel plot comparing the effect of the use of three arterial conduits (3-ART) vs. two arterial conduits (2-ART) on in-hospital/30-day mortality across individual propensity score-matched studies.

Table 1. Overview of propensity score-matching studies included in the primary analysis

Study	Year	Country	Centers	Study	Conduits	Conduits	PSM Methodology	SV target	Outcomes of interest
				period	2-ART	3-ART		(2-ART UNM)	reported (PSM populations)
Benedetto ⁴	2016	United Kingdom	Bristol Heart Institute	1996- 2015	BITA-GSV	BITA-RA	Greedy 1:1 matching with caliber width of 0.2 SD	CX, DIA, RCA	In-hospital mortality. All-cause late mortality.
Di Mauro ⁵	2008	Italy	University of Chieti	1991- 2002	BITA-GSV	BITA-RA BITA-RGEA	2:1 matching method not reported	RCA	Long-term death from any cause.
Glineur ⁶	2013	Belgium	Cliniques Universitaire St Luc, Brussels	1985- 1995	BITA-GSV	BITA-RGEA	Matching method not reported	RCA	Overall survival.
Grau ⁷	2015	United States	The Valley Columbia Heart Center, Ridgewood, NJ. University of Pennsylvania, Philadelphia, PA	2000-2013	BITA-GSV	BITA-RA	Greedy 1:1, 5-1 digit matching	CX, LAD, RCA	30-day mortality. Long-term survival.
Locker ⁸	2012	United States	Mayo Clinic, Rochester, MN	1993- 2009	BITA-GSV	BITA-RA	1:1 matching method not reported	CX, DIA, RCA	Late death: after 30 days.

Mohammadi ⁹	2016	Canada	Quebec Heart and Lung University Institute, Quebec City, Quebec	1991- 2013	BITA-GSV	BITA-RA	5-digit 1:1 matching without replacement	CX, RCA	Short-term (in-hospital) mortality. Long-term all-cause mortality.
Nasso ¹⁰	2012	Italy	Anthea Hospital, GVM Care & Research, Bari	2003-2008	BITA-GSV	BITA-RA	1:1 matching nearest-neighbor matching caliber width of ± 0.1	CX, RCA	Operative death: within 30 days of the operation or before hospital discharge). Long-term mortality.
Shi ¹¹	2016	Australia	St. Vincent's Hospital, University of Melbourne, Melbourn	1995- 2010	BITA-GSV	BITA-RA	Greedy 1:1 matching with fixed caliber width of 0.05 without replacement	CX, RCA	Short-term (30-day) mortality. Long-term survival.

BITA, bilateral internal thoracic arteries; CX, circumflex coronary system; DIA, diagonal coronary artery; GSV, greater saphenous vein; LAD, left anterior descending artery; PSM, propensity score-matched; RA, radial artery; RCA, right coronary artery; RGEA, Right gastroepiploic artery; UNM, unmatched.

Table 2. Overview of propensity score-matching studies included in the primary analysis.

Study	Overall	UNM	UNM	PSM	PSM	Mean/median follow-up	Completeness	PSM-HR for
	population, n	2-ART, n	3-ART, n	2-ART, n	3-ART, n	(months)	of follow-up (%)	long-term mortality provided
Benedetto ⁴	764	489	275	275	275	2-ART= 126 ± 58.8 3-ART= 126 ± 54	100	Yes
Di Mauro ⁵	1015	643	372	590	295	2-ART= 88 3-ART= 128	100	No
Glineur ⁶	297	204	93	203	93	2-ART= 196.8 ± 74.4 3-ART= 192 ± 64.8	NR	Yes
Grau ⁷	751	568	183	183	183	NR (max 14 years)	100	Yes
Locker ⁸	1184	1029	155	NR	NR	Mean: 91.2 ± 55.2 Median: 87.6	94	No
Mohammadi ⁹	1750	1495	255	249	249	2-ART= 97.8 (IQR, 0.03- 22.6) 3-ART=97.2 (IQR, 0.02-17)	100	Yes
Nasso ¹⁰	7767	NR	NR	3584	3584	Mean: 37.2	98	No
Shi ¹¹	1497	460	1037	262	262	2-ART= 144 ± 60 3-ART= 144 ± 60	100	No

ART, arteries; HR, hazard ratio; IQR, inter-quartile range; NR, not reported; PSM, propensity score-matched; UNM, unmatched.

Table 3. Risk factor distribution in the matched populations in studies included in the primary analysis.

Study	Matched							
	Age (y) Mean±SD	Female (%)	DM (%)	EF (%)	COPD (%)	CRF (%)	STS score (%)	EuroSCORE (%)
Benedetto⁴								
2-ART	NR	5.8	5.5	NR	2.5	0.7	NR	NR
3-ART	NR	6.5	6.5	NR	2.9	0.4	NR	NR
Di Mauro⁵								
2-ART	62.6 ± 8.7	12.5	21.4	60.6 ± 12.8	5.1	0	NR	3.5 ± 2.9
3-ART	62.1 ± 8.0	11.9	20.7	59.5 ± 12.0	4.4	0.3	NR	3.1 ± 2.8
Glineur⁶								
2-ART	NR (quintiles)	NR (quintiles)	NR (quintiles)	NR (quintiles)	NR (quintiles)	NR (quintiles)	NR (quintiles)	NR (quintiles)
3-ART	NR (quintiles)	NR (quintiles)	NR (quintiles)	NR (quintiles)	NR (quintiles)	NR (quintiles)	NR (quintiles)	NR (quintiles)
Grau⁷								
2-ART	58 ± 9	6.6	5.5	53 ± 11	2.2	0	0.8	NR
3-ART	57 ± 10	7.7	6.0	52 ± 10	2.7	0	0.8	NR
Locker⁸								
2-ART	NR	NR	NR	NR	NR	NR	NR	NR
3-ART	NR	NR	NR	NR	NR	NR	NR	NR
Mohammadi⁹								
2-ART	55.8±8.9	11.2	13.7	57.9±12.8	6.8	1.6	11.2	11.2

3-ART	56.1±8.9	9.6	12.1	59.9±12.5	4.4	2.4	9.6	9.6
Nasso ¹⁰								
2-ART	67.3 ± 9.3	20.4	48.2	NR (ranges)	9.9	NR	NR	NR (ranges)
3-ART	67.1 ± 9	20.1	48.0	NR (ranges)	10.0	NR	NR	NR (ranges)
Shi ¹¹								
2-ART	NR (ranges)	9	13	NR (ranges)	NR	0	NR	NR
3-ART	NR (ranges)	10	13	NR (ranges)	NR	1	NR	NR

COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure (different definitions adopted); DM, diabetes mellitus; EF, ejection fraction; NR, not reported; SD, standard deviation; STS,

Society of Thoracic Surgeons score.

Figure 1.

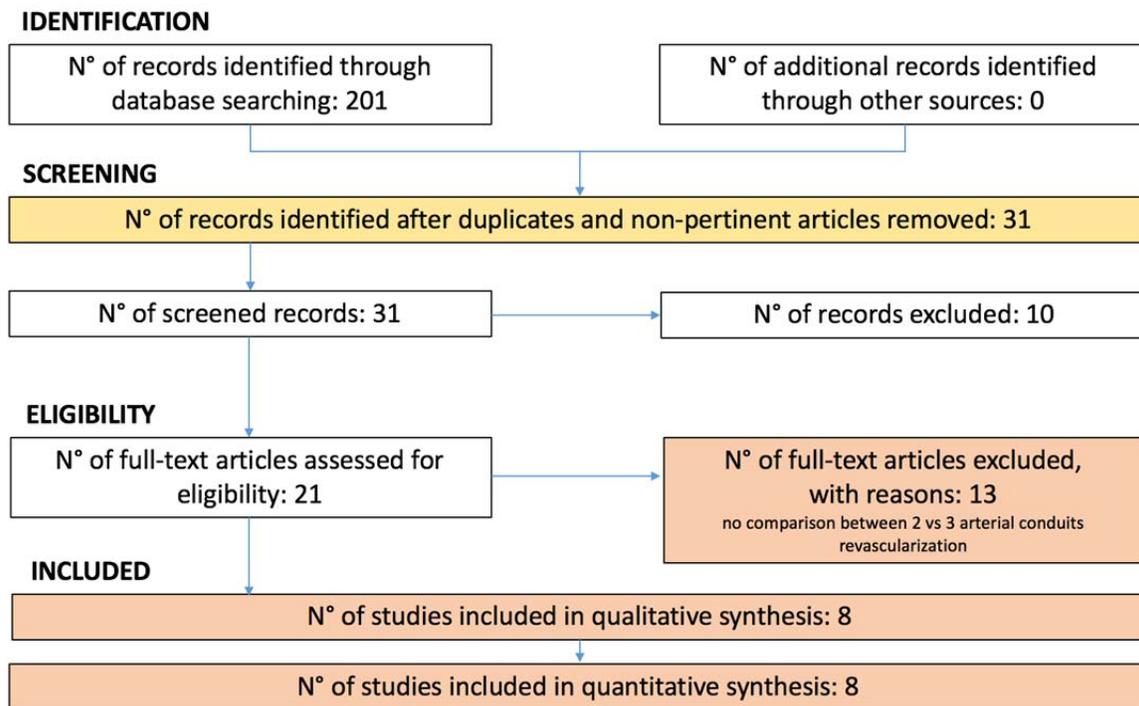


Figure 2.

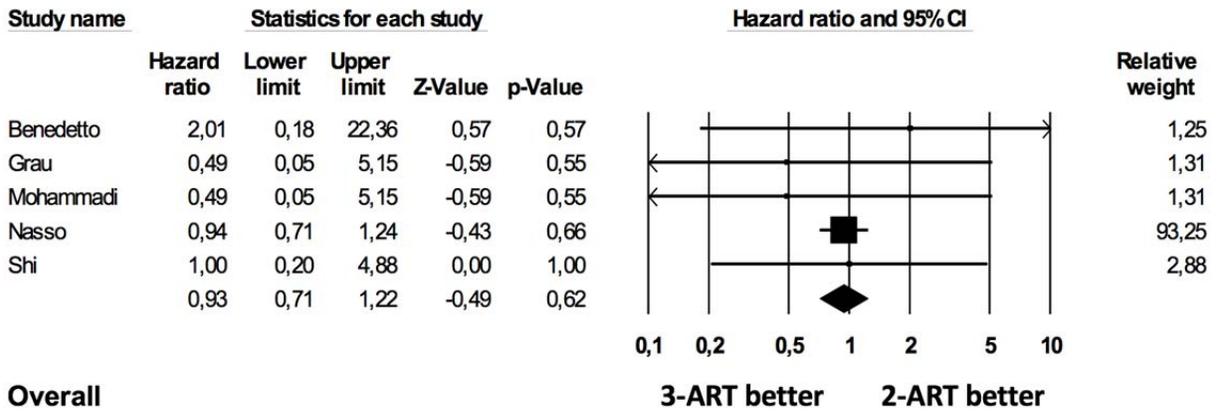


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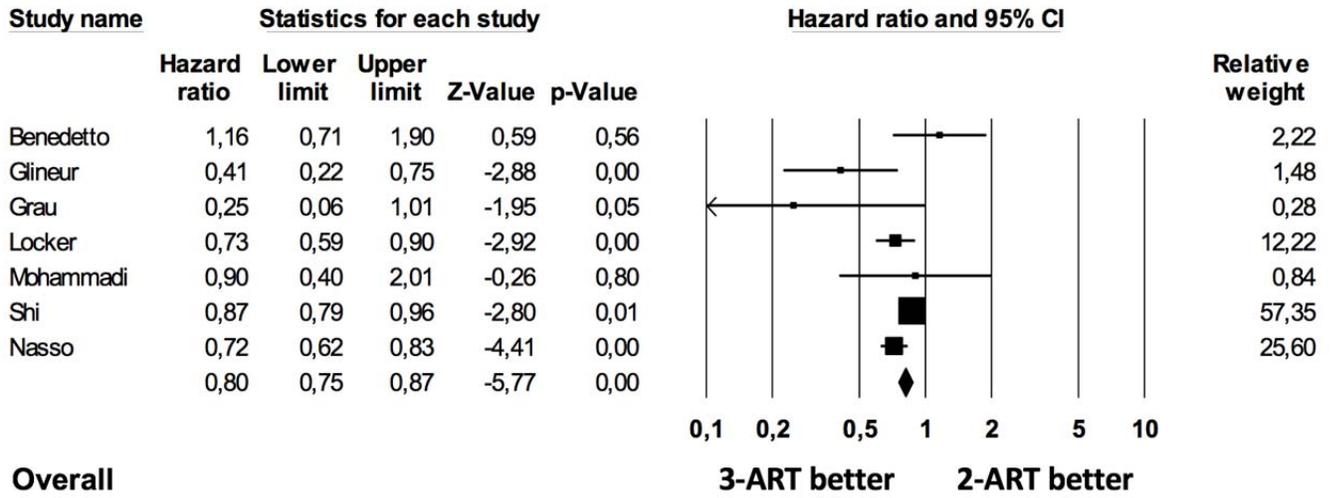


Figure 4.

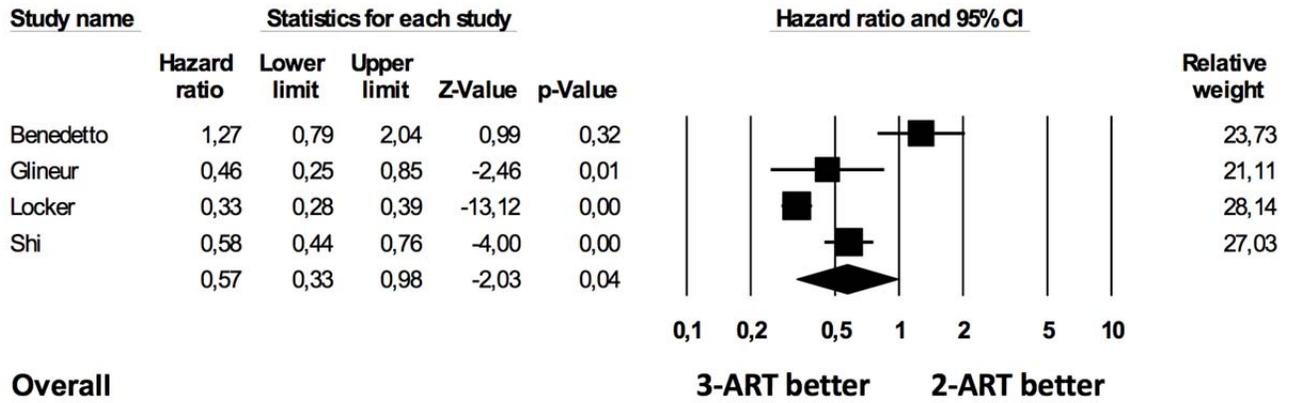


Figure 5.

